A. OVERALL COVER PAGE

Project Title: mHealth Center for Discovery, Optimization, and Translation of Temporally-Precise Interventions (mDOT)	
Grant Number: 5P41EB028242-04	**Project/Grant Period:** 07/15/2020 - 11/30/2025
Reporting Period: 12/01/2022 - 11/30/2023	**Requested Budget Period:** 12/01/2023 - 11/30/2024
Report Term Frequency: Annual	**Date Submitted:**
Program Director/Principal Investigator Information: SANTOSH KUMAR , PHD **Phone Number:** 9016782487 **Email:** skumar4@memphis.edu	**Recipient Organization:** UNIVERSITY OF MEMPHIS UNIVERSITY OF MEMPHIS ADMINISTRATION 315 MEMPHIS, TN 381520001 **DUNS:** 055688857 **UEI:** F2VSMAKDH8Z7 **EIN:** 1620648618A1 **RECIPIENT ID:**
Change of Contact PD/PI: NA	
Administrative Official: STEPHANIE THOMPSON 315 Administration Building Memphis, TN 38152 **Phone number:** 901-678-4146 **Email:** sthmps24@memphis.edu	**Signing Official:** STEPHANIE THOMPSON 315 Administration Building Memphis, TN 38152 **Phone number:** 901-678-4146 **Email:** sthmps24@memphis.edu
Human Subjects: Yes **HS Exempt:** NA **Exemption Number:** **Phase III Clinical Trial:** NA	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The mHealth Center for Discovery, Optimization & Translation of Temporally-Precise Interventions (the mDOT Center) will develop technologies and approaches to provide the methods, tools, and infrastructure for researchers to pursue the discovery, optimization and deployment of temporally-precise, mHealth-enabled interventions that tackle antecedent health behaviors linked to chronic diseases.

mHealth has progressed rapidly, resulting in widespread deployment of simple digital biomarkers (e.g., steps per day, sleep) to promote health and wellness. We envision a radically more powerful paradigm for applying mHealth to maintain health and managing the growing burden of chronic diseases, specifically, temporally-precise interventions that are individualized to the moment-to-moment context of each individual to directly manage, treat, and prevent medical conditions. The rapidly growing array of mHealth biomarkers captures the temporal dynamics of an individual's state, behaviors, and surrounding environment that drive cumulative risk for an individual's total disease burden. But, we lack the tools to discover which (combinations) of these continuous biomarkers are the most relevant, at different moments, for selecting the target risk driver(s) and deciding the delivery timing of sensor-guided interventions. Current mHealth interventions derive largely from expert knowledge and are usually not optimized for long-term engagement in self-care. Further, they either lack personalization, or if personalized, learn slowly. Finally, personally optimized, temporally-precise mHealth interventions will improve health outcomes only if they can be deployed at scale. Real-life deployment of increasingly complex mHealth interventions that can leverage a growing number of biomarkers to optimize the selection, adaptation, and timing of intervention delivery, is challenged by limited battery and compute capacity, the emergence of high data rate sensors, and the need to ensure privacy and data security. The mDOT Center will realize its vision through the following specific aims:

Aim 1: Enable the discovery, optimization, and translation of temporally-precise mHealth interventions via three technology research and development cores (TR&D).

Aim 2: Collaborate with investigators of a diverse array of collaborative projects (CP) and service projects (SP) to engage the health research community in joint development, iterative evaluation, and broadening impact.

Aim 3: Maximize the scientific and societal impact via technology training and dissemination (TT&D).

Aim 4: Provide the managerial and operational structures for mDOT to achieve its research, development, collaboration, training, and dissemination goals.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Publications, Talks, & Presentations: mDOT Center investigators have published or have submitted and under review a total of 33 papers related to mDOT Center research for project Year 3. In addition, mDOT Center investigators have participated in 168 talks and presentations at 152 global meetings since the Center's inception.

The mDOT Center disseminates information to communities of interest via its website, mdotcenter.org (more than 19,500 page views since launch on July 1, 2020).

Recordings of webinars are posted to the mDOT Center's YouTube channel, where they are accessible by the general public; 40 mDOT Center-hosted webinars in the series have been released to date. More than 260 videos posted on the mDOT Center's YouTube channel have been viewed a total of more than 50,500 times on the channel, which now has 360 subscribers and more than 4,400 hours of watch time.

A second website, mHealthHUB, serves as a portal for the greater mHealth community (more than 52,400 unique users and more than 172,600 page views since its November 2015 launch).

A third website, mhti.md2k.org, exists for the purpose of providing information about the NIH mHealth Summer Training Institute and has received 17,300 users and over 59,200 page views through September 2023.
The mDOT Center runs, maintains, and disseminates information on the following websites:

mDOTCenter.org: https://mdotcenter.org/

mHealthHUB: https://mhealth.md2k.org/

mHealth Training Institute: https://mhti.md2k.org/

Mobile Open Observation of Daily Stressors (MOODS): https://github.com/MD2Korg/moods

Social Media Channels
mDOT Center YouTube Channel: https://www.youtube.com/c/mdotcenter

mDOT Center LinkedIn: https://www.linkedin.com/in/mdotcenter/

mDOT Center Reddit: https://www.reddit.com/user/mDOT_Center/

mDOT Center TikTok: https://www.tiktok.com/@mdotcenter

Repositories
Tools Repository: https://colab.research.google.com/drive/1hjYdqVUFThpZtV7sagQdhFZudTUsuIXU?usp=sharing

mDOT Center GitHub Repository: https://github.com/MD2Korg/

mDOT Center pJITAI Toolbox: https://github.com/mDOT-Center/pJITAI

CardiacGen: https://github.com/ SENSE-Lab-OSU/cardiac_gen_model

TinyNS: https://github.com/nesl/neurosymbolic-tinym

WristPrint: https://github.com/MD2Korg/wrist-print

Auritus: https://github.com/nesl/auritus

TinyOdom: https://github.com/nesl/tinyodom

MotionSenseHRV: https://github.com/SENSE-Lab-OSU/MotionSenseHRV_v3

Cerebral Cortex: https://github.com/MD2Korg/CerebralCortex

mCerebrum: https://github.com/MD2Korg/mCerebrum

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In TR&D1 we're submitting an initial manuscript on advanced imputation methods for All of Us research project data, sharing the code for our benchmark dataset, and exploring scalability and generalizability to new datasets. Simultaneously, we delve into imputation with uncertainty modeling in hierarchical biomarker computation graphs. We're also embarking on developing composite risk scores for sedentary behavior and smoking lapses, harnessing personalized risk factor modeling and advanced uncertainty quantification techniques. Additionally, we're crafting a manuscript on personalized stress detection using labeled data from the MOODS study. We also plan to unveil stressors following stress detection. Additionally, we're committed to delivering two more manuscripts, one on personalized drivers of momentary stress and another on self-supervised learning of mHealth signal representations, with a focus on uncertainty quantification and improved risk prediction accuracy. We're also exploring the potential of using large-scale unlabeled waveform data for enhancing mHealth applications.

TR&D2's work involves advanced imputation methods for the All of Us research project data, including benchmark dataset creation and scalability exploration. They will also focus on developing composite risk scores for sedentary behavior and smoking lapses, emphasizing personalized risk factor modeling and enhanced uncertainty quantification. Lastly, their research will delve into personalized stress detection using MOODS study data, with a keen eye on identifying stressors post-detection. Additionally, they too are committed to publishing two manuscripts, one on personalized momentary stress drivers and another on self-supervised learning for mHealth signal representations, featuring uncertainty quantification techniques. They will also explore leveraging large-scale unlabeled waveform data to augment mHealth applications.

In TR&D3, specifically the RF bio-imaging area, we will focus on enhancing imaging accuracy through invertible neural networks for stochastic posterior sampling and the creation of generative models for RF biosensor data, expanding the capabilities of data-intensive biomarker discovery. In the privacy domain, we plan for an interview-based user study to understand privacy concerns in industry-deployed mHealth applications. Additionally, we aim to provide valuable insights and tools through the mDOT Center website, offering recommended privacy best practices and resources for the broader research community. Furthermore, our report highlights a new collaboration involving UWB RF-based remote respiration waveform sensing in the context of health management and breathing exercises.

Technical Training and Dissemination Core will continue its multifaceted initiatives, including the analysis and publication of the 2023 mHTI findings, with plans for the 2024 mHTI to further drive multidisciplinary healthcare innovation. Our commitment to knowledge-sharing will continue with monthly mDOT webinars, fostering interactive discussions on cutting-edge topics. We will also highlight the Flight Tracker tool, which monitors scholars' career trajectories and underscores our program's impact. Additionally, a major redesign of the mDOT Center website is underway, aimed at showcasing research publications, fostering collaboration, increasing search engine visibility, and enhancing user engagement and will be completed in Year 4. Furthermore, we plan to launch an expanded social media campaign and a newsletter to help broaden our outreach and collaborations.

The Admin Core will continue to provide administrative, managerial, and infrastructure support to enable the mDOT Center to accomplish its Year 4 goals in research, training, and dissemination activities. In addition to continuing its successful strategies for communication and management, the administrative team will shepherd the hosting of the pJITAI project to the University of Michigan. The decision to transfer the project to Michigan is based on the fact that the development will be located with the same teams that are currently co-developing and will be the first adopters using the service, resulting in a more cohesive and impactful product.

All of the Center's plans and activities are laid out in more detail in the respective TR&D and Core sections of this RPPR.

B.2 What was accomplished under these goals?

B.2.1. - TR&D1 - DISCOVERY

In Year 3, the TR&D1 undertook several activities in collaborations with CP1, CP3, CP4, CP5, and CP8 to fulfill its goals. Our work towards fulfilling Aim 1 centered around modeling and addressing uncertainty in mHealth biomarkers to enhance decision-making in delivering precise mHealth interventions. It specifically involved imputing missing step count data from Fitbit devices, analyzing data from two trials with over 10,000 participants and millions of hourly step count observations. Various imputation methods were tested, and a custom self-attention-based model was developed, with the goal of creating a generalizable foundation model for step count imputation and forecasting. We also conducted additional investigations into using deep learning-based transformer models for imputing pulsative biophysical signals like ECG and PPG, which have a quasiperiodic morphology. We examined the incorporation of uncertainty modeling into our Bottleneck Dilated Convolutional (BDC) architecture using the PulseImpute dataset created in Year 2 and explored integrating architectural elements from the Heteroscedastic Temporal Variational Autoencoder (HeTVAE) and investigated self-attention weights within the BDC model. To address the challenge of sparse labels in mHealth signal data, we developed a novel self-supervised representation learning approach. This method utilized reconstruction error in imputation to identify positive and negative examples within a contrastive learning framework, particularly for pulsative waveforms. Training an embedding function using this approach yielded a surprisingly effective feature representation for downstream tasks, with the results documented in a manuscript set to be submitted in October 2023. To further understand dynamic relationships between personalized risk factors and disease progression for precise interventions through our work in Aim 3, we completed the MOODS study with 122 participants who used our MOODS app and wore a Fossil smartwatch for 100 days. They rated their stress levels multiple times daily, identified stressors, and received weekly data visualizations. We analyzed the impact of the study on self-reported stress ratings and the variety of stressors reported by the participants.

B.2.2. - TR&D2 – OPTIMIZATION

In Year 3, the TR&D2 undertook a variety of activities (as described below) to fulfill its goals. In the past year, our research in RL algorithms, particularly those related to dental health and cannabis reduction, was driven by collaborations with CP2 and CP8. We deployed the Oralytics RL algorithm to improve dental health, with the pilot phase underway and plans for the full Oralytics trial. We also developed statistical methods to account for data dependence in adaptive sampling for treatment effect assessments. Additionally, we worked on the MiWaves RL algorithm for cannabis reduction, employing a flexible approach to pooling data across participants based on their responses. The MiWaves trial is scheduled for piloting in October 2023. Furthermore, we began exploring RL algorithms for dyads, focusing on target individuals (e.g., adolescents with bone marrow transplants) and their care partners, with intervention options spanning different time scales, utilizing concepts from hierarchical RL. These developments were driven by our collaboration with CP8. In collaboration with CP3 (physical activity), we continued design of the pJITAI toolbox that allows health scientists to design their RL algorithm for use in conducting mHealth studies. We were able to complete a beta version of the toolbox web interface and obtained IRB approval for user studies involving behavioral health scientists interested in using RL for personalization in clinical trials. We are now in the initial stages of transferring the pJITAI toolbox to a University of Michigan consortium consisting of CP3 & CP8 teams. Additionally, we collaborated with CP3 to draft a paper introducing "pJITAI" (personalizing JITAI) and discussing the first RL algorithm, "Thompson-Sampling," which is widely used in industry for personalization purposes, with plans to submit it to a behavioral science journal. Finally, we worked on designing a capability to determine when to trigger stress-related EMA's and interventions, as part of Aim 2. Using data from the MOODS study in collaboration with CP7, we developed new methods and tools to guide the timing of prompts for stress-related interventions and EMA's in micro-randomized trials. This analysis showed that using an AI algorithm to estimate the likelihood of events being stressful reduced the necessary prompts from 6 to 2 per day. We also initiated a collaboration with stress experts at Penn State to create a method and tool for optimizing prompting schedules in future studies, aiming to minimize the number of prompts needed to catch participants in high and low-stress moments, with a planned submission to npj Digital Medicine.

B.2.3. - TR&D3 - TRANSLATION

In Year 3, the TR&D3 undertook a variety of activities (as described below) to fulfill its goals and collaborated with CP1, CP6, and with some new collaborators to explore potential new CP's. Towards Aim 1, to overcome the challenge of limited publicly available datasets for Machine Learning algorithms using physiological signals like ECG, we developed a Deep Learning framework called CardiacGen. This framework generated synthetic but physiologically accurate cardiac signals, improving the performance of Deep Learning classifiers through data augmentation. CardiacGen comprised two modules, one for Heart-Rate-Variability characteristics and another for signal morphologies, and it proved to be an effective tool for generating realistic synthetic data for training deep learning models. For Aim 1, we also focused on designing a scalable radio frequency (RF) array and developing deep-learning models to address the inversion problem of estimating subcutaneous fluid content in layered tissue from backscattered measurements. The RF array included components like the transceiver front-end, flexible antenna design, and a central processor. We designed and characterized the transceiver front-end, ensuring it met performance metrics such as RF budget analysis, cascaded gain, noise figure, Input 3rd order intercept point (IIP3), and 1dB compression point (P1dB). Currently, we are in the process of manufacturing a prototype array to support a pilot research program for lymphedema detection. In the past, we focused on improving Ultrawideband (UWB) radar sensors for assessing internal tissue properties. To address antenna-related limitations, we developed a data-driven calibration method using an Invertible Neural Network (INN) to recover the Green's function of multilayered tissue profiles. We generated a synthetic dataset and conducted simulation experiments, demonstrating that the trained INN effectively inverted antenna transfer functions to estimate Green's functions from noisy measurements, even for previously unseen multilayer profiles. Previously, our goal was to optimize the antenna design for BioRF sensors, with an emphasis on meander-line antennas. We aimed to direct energy into the body effectively, taking into account how tissues attenuate RF signals at different frequencies. By maximizing RF power at lower frequencies for deeper tissue penetration and minimizing reflections in the low-frequency band, we developed designs suitable for lung-fluid detection and lymphedema detection. Additionally, we optimized the thickness of a matching medium with known electrical characteristics to enhance RF power coupling to tissue layers. Towards Aim 1, we also introduced an unsupervised Siamese adversarial learning approach, calibrating the model to new individuals without requiring their intervention. Our approach proved effective, especially for biomarkers involving subtle motion features, as demonstrated through a user study with 134 volunteers. The Siamese domain adversarial neural network approach continually adapted the model over time, resulting in improved accuracy for specific users, and a paper reporting this work was accepted at the ACM Symposium on User Interface Software and Technology (UIST). Currently, we are applying this approach to various motion and non-motion biomarker computations. We also developed TinyNS, a novel platform-aware neurosymbolic architecture search framework, to jointly optimize symbolic and neural operators. This framework automatically generated microcontroller code for various neurosymbolic models, combining symbolic techniques with machine learning models to balance context awareness and robustness. TinyNS utilized a gradient-free Bayesian optimizer to find the best combination of symbolic code and neural networks within hardware constraints, ensuring deployability by interacting with the target hardware during optimization. Through case studies, we demonstrated TinyNS's superior performance over purely neural or purely symbolic approaches while guaranteeing execution on real hardware. A paper describing TinyNS was recently published in the ACM Transactions on Embedded Computing Systems. Finally, for Aim 3, we proposed PrivacyOracle, an innovative Large Language Model (LLM)-based privacy firewall. PrivacyOracle utilized LLMs trained on law, medicine, and ethics texts to validate new sensor data flows against privacy norms, ensuring compliance with social, ethical, and legal regulations. We designed various strategies and interfaces based on Contextual Integrity (CI) informational flows and evaluated its performance across multiple tasks, including validation of data flows under HIPAA, agreement with social norms, and recommending sensor deployments with varying privacy risk knowledge. Preliminary findings from this work are currently under submission in a paper.

B.2.4. - SOFTWARE

In Year 3, the software team played a critical role in providing technical support for the all-virtual MOODS study. Their efforts focused on troubleshooting technical challenges in real-time, ensuring a seamless user experience. Additionally, they worked on enhancing the app's performance, refining features, and rigorously addressing bug reports from user feedback and error logs. These systematic efforts improved app stability and functionality, aligning it with evolving research requirements. The software team also explored the porting of the existing MOODS watch code to other wearable devices. The group looked at newer hardware (i.e., late-model Samsung smartwatches) as the current units had begun to age. The goal was to make use of the already available inter-beat interval on the newer hardware and to reduce the processing resources and make the app more user-friendly. Additionally, in this project period, an intellectual property agreement was filed with the University of Memphis Office of Technology Transfer regarding the MOODS software that consists of a Wear OS smartwatch app, a cross-platform smartphone app, and cloud services. This application governed the intellectual property resulting from the software development, testing, and deployment used in the MOODS study. We also achieved a significant milestone by launching a dedicated website for the pJITAI project, facilitating dissemination and collaboration in the research community. We made improvements to the pJITAI platform, including bug fixes, user interface enhancements, and the addition of new features like displaying intervention probability based on study parameters. The backend was further developed to collect and analyze data according to user study configurations, with support for data upload, validation, multiple RL algorithms, and an exposed API. The current version of the pJITAI website is ready for an internal user study, and plans are in place to transition to the University of Michigan for a pilot study in Year 4. In the past, we initiated a dedicated GitHub repository for the pJITAI project, which played a crucial role in promoting collaborative development and version control. This repository served as a centralized hub for managing project code and tools, facilitating seamless collaboration, integration, debugging, and enhancement. The repository's branching and versioning capabilities allowed the team to work concurrently on different project aspects while ensuring code integrity and transparency in research development practices. This establishment emphasized our commitment to efficient and transparent research practices while providing a structured environment for code sharing and innovation.

B.2.5. - NEW DATASET

We were able to successfully conduct multiple rounds of data collection using the MOODS software platform developed by the mDOT Center. With the necessary IRB oversight, we enrolled and onboarded 136 participants for this all-virtual study, resulting in the collection of approximately 65,000 hours of sensor data. This dataset also includes 26,732 annotated stress/non-stress events and 11,222 recorded stressors by participants. In 2023, we introduced a sub-cohort with a modified MOODS protocol to investigate stress and stressor detection's impact on bias and interventional response within an observational study. After curation, we plan to release relevant data publicly. As a unique dataset collected from the field setting on stress and stressor together with associated sensor data, we expect it to have a significant impact on modeling and across various other scientific domains.

B.2.6. - TRAINING & DISSEMINATION

In Year 3, the main focus of the training (Aim 1) was the development and conduct of the 2023 mHealth Training Institute (mHTI). This entailed the development of a comprehensive, online application management system (Smarter Select). From a pool of 131 applicants, 30 were chosen as scholars for the 2023 mHTI (2023 mHTI Scholars). A corresponding group of faculty, comprising both academics and NIH Program Officers (2023 mHTI Faculty), was also recruited. The hybrid 2023 mHTI, incorporating both virtual and in-person components, was conducted between April 10 and July 20, 2023 (2023 mHTI Program). Short-term evaluation of educational effectiveness was conducted by the evaluation team; long-term evaluation of post-mHTI career trajectories is being tracked by the Flight Tracker software. With a specific objective to train a cadre of transdisciplinary mHealth scientists to develop national capacity, the training core set out to answer a series of process (or implementation) and outcome (or impact) questions relative to the 2023 mHTI. The process evaluation questions investigate aspects of the design and implementation of the mHTI, and outcome evaluation questions focus on the extent to which intended goals were achieved. The mHTI was used as a testbed to apply advanced quantitative methods to study the formation of transdisciplinary teams and the development of team processes central to the effective functioning of highly diverse teams. The results of the advanced quantitative methods studying the formation of transdisciplinary teams and the development of team processes are being readied for publication in two peer-reviewed open-access scientific journals with high impact factor (a) Journal of Clinical and Translational Science, and (b) PLOS One.

For Aim 2 (Dissemination), the mHealthHUB, the mDOT's primary platform for dissemination, was comprehensively reconfigured to develop a more versatile training and dissemination portal. The remodel was aimed at promoting a wider dissemination of information and facilitating the conduct of webinars. A dedicated webinar platform was integrated into the interface to streamline online training sessions, allowing for seamless communication, live discussions, and the sharing of multimedia content. Additionally, improved navigation features and advanced search options were implemented to aid in the broad dissemination of information. These enhancements aimed to provide a more user-friendly and efficient resource for all mHTI users, enabling them to access relevant training resources and stay up to date with the latest mHealth trends and discussions. The redesign also incorporated analytics and tracking features to monitor and analyze engagement metrics, allowing continuous improvement in delivering training content. To date 43 mDOT webinars have been recorded and curated for asynchronous access. In addition, the mHealthHUB now hosts 120 mHTI-recorded lectures and talks so that all training content can be accessed in one central location. To date, the mHealthHUB has 172,621 page views from 52,437 users from 174 countries with the top 10 being: U.S., China, Germany, U.K., India, Canada, France, Switzerland, Japan, and Australia.

B.2.7. - ADMINISTRATION CORE

The mDOT Center Operations Office, housed in Memphis, Tenn., is the main hub for mDOT Center administration. The Center is structured to include full-time operations management, business management, administration, and communications staff, who are collectively responsible for the day-to-day management of the Center, including providing support for the activities of the investigators. In Year 3, the mDOT Center is hosting a 1-day visioning workshop to delve into the impact of generative mHealth interventions on emerging wearables. To be held in conjunction with the mDOT Center Annual Meeting on the campus of Harvard University in Boston, MA, the mDOT Center leadership is bringing together researchers and stakeholders from industry, academia, and medicine to discuss both the significant opportunity that the conjunction of generative AI and novel wearables represent in the mobile health space and the significant scientific and socio-technical challenges that need to be overcome to ensure that resulting approaches are safe, efficacious, ethical, contextually appropriate, engaging and adaptive. With about 40 attendees consisting of health researchers and AI/wearable tech experts, the workshop's core objective is to chart out a research agenda for the next 5-10 years to explore how generative AI and emerging wearables can lead to innovative mHealth interventions.

The Admin team is also coordinating and hosting the Year 3 mDOT Center Annual Meeting at Harvard University (home site of TR&D2 Lead Susan Murphy) in Boston, MA. This is the only chance where all mDOT Center investigators, students, EAC members, and other stakeholders can gather once a year to discuss research, strategies, brainstorm, and network in person and requires the skills and expertise of the entire administrative staff to plan and execute. This will be the first annual meeting held outside of Memphis (where the Admin team is located) and planning from afar is providing a new wrinkle to this year's preparation.

Last fall, the mDOT Center investigators and Executive Advisory Committee (EAC) decided to revamp their review process. Instead of individual presentations tailored to EAC members' expertise, the EAC would now review the entire Center as a group during a 3-hour block. This change involved the Admin team presenting relevant portions of the RPPR to EAC members a week in advance, allowing for a more comprehensive discussion and enabling investigators to address questions and topics in advance of the review. This new approach aimed to foster collaborative, future-thinking discussions with the EAC and streamline the reporting process for the RPPR submission. We were able to execute this new approach successfully and it produced a more thoughtful review and provided several new ideas for the center.

We expanded the service projects for the mDOT Center by two in Year 3 and will enhance their research being done through the work being done in TR&2. Our process for vetting and admitting a new CP/SP was rigorous to ensure "fit" within the mDOT Center research mission and need within the temporally-precise mHealth intervention community. Our TR&D2 Lead, Dr. Susan Murphy, recognized a synergy with a recently awarded R01 and a clinical trial using digital health interventions that were headed by former research colleagues at Northwestern University and Harvard University respectively. A one-page proposal for each potential SP was introduced by Dr. Murphy to the mDOT Center Executive Committee. The Executive Committee, consisting of Center Leadership, reviewed the merits of the potential collaborations. After vetting from the mDOT Center Executive Committee it was determined that both would be good candidates for an SP spot. From there, the SP proposals were brought by the Center Director to the Executive Advisory Committee (EAC) for their review and final recommendation and upon their approval, submitted to the NIH program officer for her review and final approval. SP7 - Toward Optimizing Digital Mental Health Interventions: A Clinical Trial Aimed at Understanding What Drives Patient Engagement is led by Dr. Jessica M. Lipschitz at Harvard University and funded by NIMH through 2025 and SP8 - A Micro-Randomized Trial to Optimize Just-in-Time Adaptive Intervention for Binge Eating & Weight-related Behaviors is led by Dr. Andrea K. Graham at Northwestern University and funded by an NIDDK R01 through 2027. Finally, due to lessons learned during the COVID pandemic, the training program continued its hybrid approach blending, delivery methods centered around in-person scholarship and virtual consumption.

B.3. Center Highlights

B.3.1. Imputing missing mHealth biomarkers: Step count data is now widely used due to its growing accessibility from activity trackers. But, a large amount of missingness due to non-wear and data losses poses a challenge when using in health research. To impute step count data at the hourly level as produced by ubiquitous off-the-shelf wearables including Fitbit devices, we began with the analysis of missing step count data for the participants in CP3's HeartSteps II trial. We then expanded this work to include data from the All of Us Research Project (SP1). This work has included setting up a project within the All of Us data enclave, processing the minute-level Fitbit data for over 10,000 All of Us participants, extracting an initial experimental cohort of 100 individuals and over 3,000,000 hourly step count observations. To date we have produced step count imputation results for multiple baseline methods including mean imputation, median imputation, forward filling, backward filling, linear regression imputation, K-nearest neighbor imputation, and multiple imputation by chained equations. Once this is applied to all data in All of Us, it can be directly used by all researchers working with this large dataset.

- Vadera, Meet P; Samplawski, Colin; Marlin, Benjamin M: Uncertainty Quantification Using Query-Based Object Detectors. In: Computer Vision–ECCV 2022 Workshops, Part VIII, pp. 78–93, 2023.

B.3.2. RL Algorithm for Dyads: This year we have made the very first steps toward developing an RL algorithm for dyads. This is a very exciting new research direction. This work is motivated by our collaboration with CP8. In this case, the dyad is composed of a target person (here an adolescent/young adult who had a bone marrow transplant) and their care partner. In this setting, there are different sets of intervention options corresponding to whether the intervention option is for the target person or the care partner or, quite interestingly, for improving the social connection between the target person and care partner. These different sets of intervention options operate at different time scales (some over a week, others daily). To tackle this problem, we are using ideas from hierarchical RL.

- S. Li, L. Salvat Niell, S. Choi, I. Nahum-Shani, G. Shani, S. Murphy (2023). Dyadic Reinforcement Learning. (Submitted)

B.3.3. RF Sensor Arrays for Subcutaneous Fluid Detection: We designed a scalable radio frequency (RF) array and are developing deep-learning models to solve the inversion problem of estimating subcutaneous fluid content of layered tissue from backscattered measurements. The scalable RF array consists of the transceiver front-end, flexible antenna design and a central processor that controls the module, samples the backscattered signal, and implements the learning methods to estimate the tissue edema levels. The transceiver front-end comprises of the phase-locked loops for synthesizing agile waveform for illuminating the area of interest, an RF mixer, and filter to demodulate the reflected signal, and an analog-to-digital converter (ADC) to digitize the signal. The design is validated using Ansys HFSS (high-frequency structure simulator) simulations. We are currently manufacturing a prototype array to support a pilot research program on lymphedema detection.

- Y. Chang, N. Sugavanam, and E. Ertin, “Removing antenna effects using an invertible neural network for improved estimation of multilayered tissue profiles using uwb radar,” in 2023 IEEE International Symposium on Antennas and Propagation and USNC-URSI Radio Science Meeting (AP-S/URSI). IEEE, 2023, pp. 53–54.
- T. Agarwal and E. Ertin, “CardiacGen: A Hierarchical Deep Generative Model for Cardiac Signals,” Extended Abstract at Machine Learning for Health (ML4H) symposium, Nov 2022.

B.4. Other Outcomes

<u>**Progress Towards Proposed Activity Milestones**</u>
Overall in Project Period Year 3, of this reporting, the mDOT Center has met/currently meeting 30 of the current 35 proposed activities laid out in the submission timelines. These activity milestones completed for each project component (TR&Ds, TT&D, etc.) are as follows:

- **TR&D1: Discovery** has met/currently meeting 5 of 6 the proposed activity milestones up until Year 3
  - ‘Major Software Releases’ have been slightly delayed to later project years
- **TR&D2: Optimization** has met/currently meeting 14 of 14 the proposed activity milestones up until Year 3
- **TR&D3: Translation** has met/currently meeting 6 of 10 the proposed activity milestones up until Year 3
  - The Privacy Milestones (x3) are being re-evaluated and Developer workshops are being pushed to later years based on software launches
- **Technical Training & Development Core** has met/currently meeting 5 of 5 the proposed activity milestones up until Year 3

As of now, most of the remaining activity milestones are slated to be completed within their proposed timeline.

B.3.4. CENTER SUMMARY TABLE
Grant Number: P41EB028242-03
Reporting Period: (12/01/2022 - 11/30/23)

	TR&D Projects	Collaborative Projects	Service Projects	Training & Dissemination	TOTAL
Number of Publications*	17	14	5	2	33*
Number of Patents	0	0	0	0	0
Number of Investigators	37	10	10	44	101
% of Center Funds Allocated	78%	8%	3%	11%	100%
% of Center Funds for AIDS	0%	0%	0%	0%	0%
Service Fees Collected ($)					

**Some publications overlap between CPs & SPs, as they were published in collaboration with multiple projects*

B.3.5. CENTER CUMULATIVE TABLE
Grant Number: P41EB028242
Reporting Period: (07/01/2020 - 11/30/23)

	TR&D Projects	Collaborative Projects	Service Projects	Training & Dissemination	TOTAL
Number of Publications*	39 (8 - 14 - 17)	29 (7 - 8 - 14)	13 (4 - 4 - 5)	4 (0 - 2 - 2)	73* (16 - 24 - 33)
Number of Patents	0	0	0	0	0

**Some publications overlap between CPs & SPs, as they were published in collaboration with multiple projects*

The mDOT Center assembled a high-profile External Advisory Committee (EAC) that includes 5 thought leaders, each representing an expertise in different domains of research and operations.

1. **Dr. David Kennedy**, Professor of Psychiatry at UMass Medical School – Dr. Kennedy is an expert in neuro-informatics, known for his contributions to the advent of MRI-based morphometric analysis, functional MRI, and diffusion tensor pathway analysis. He is the PI of P41 Center called the "Center for Reproducible Neuroimaging Computation (CRNC)". He is advising mDOT on its administrative and training activities.
2. **Dr. Jimeng Sun**, Professor of Computer Science at the University of Illinois at Urbana Champaign (UIUC) – Dr. Sun develops AI for Healthcare who is known for contributions in deep learning for drug discovery, computation phenotyping, clinical predictive modeling, treatment recommendation, and clinical trial optimization. He is advising mDOT's TR&D1 team on uncertainty-aware modeling of personalized risk dynamics from sensor-derived biomarkers to enable the discovery of new mHealth interventions.
3. **Dr. David Mohr**, Professor, Preventive Medicine (Behavioral Medicine), Medicinal Social Sciences, & Psychiatry and Behavioral Sciences at Northwestern University Feinberg School of Medicine – Dr. Mohr's work lies at the intersection of behavioral science, technology, and clinical research, focusing on the design and implementation of interventions that harness digital technologies to promote mental health and wellness. He is well versed in the use of data from smartphone and wearable sensors to identify behavioral and psychological targets that can be used for intervention. Dr. Mohr is advising the mDOT Center's TR&D2 team that develops personalized interventions and wants to work closely with behavioral health researchers. Dr. Mohr helps to provide a voice from that community to better assess the value and utility of products coming from TR&D2 for health research.
4. **Dr. Veena Misra**, Distinguished Professor of Electrical and Computer Engineering at North Carolina State University (NCSU) – Dr. Misra is an expert in ultra-low power and self-powered biosensor design, hybrid silicon-molecular electronics, and nano-magnetics. She is the PI of NSF Nanosystems Engineering Research Center (ERC) on Advanced Self-Powered Systems of Integrated Sensors and Technologies (ASSIST). She is advising mDOT's TR&D3 team on sensor and signal processing architectures to support resource-efficient real-time computation of complex biomarkers on resource-constrained high data-rate sensor arrays.
5. **Dr. Jason Hong**, Professor in the HCI Institute in School of Computer Science at Carnegie Mellon University (CMU) – Dr. Hong works at the intersection of human-computer interaction (HCI), privacy, security, and computing systems. His work discovers novel utility of sensors for improving human lives while making security and privacy easier for every human. He is advising the mDOT team on ensuring users' behavioral privacy and anonymity during mHealth biomarker data analytics, optimization of sensor-triggered mHealth interventions, and real-life deployment of mHealth interventions.

Recruitment was deliberate to balance demographics to further ensure a diversity of perspectives and experiences among committee members. The EAC provided high-level guidance, oversight and review of progress towards research and training goals and the efficacy of Center operating structures and policies for Year 3. This group also provided future-oriented feedback on mDOT research and training directions as well as to help establish new connections for the center that can extend the impact and reach of our activities.

The EAC meeting took place virtually using the Zoom teleconferencing system. All Committee Member were given a technical summary a week before being presented a high-level review of the mDOT Center and other aspects of research that were tailored toward discussion and advisement. The EAC's next meeting is expected to be convened in-person as a group with all 5 members at the mDOT Center's Annual Meeting. The EAC has provided the below report to team members regarding the planned implementation of specific guidance received or alternate strategies to be pursued as mDOT Center heads into Year 4.

mDOT Center Y3 EAC Review Report (2023)

Administration Core

Notable Strengths

- Good institutional support is indicated, monetizing this support will be important for the renewal.
- Good metrics to date: 33+ publications, patents, 2 startups
- Good pipeline of new funding from NSF, NIH, and other sources
- Great team, good leadership, good organization, and collaboration across campuses.
- Deep technical work and strong interdisciplinary collaborations across the board
- Initial commercialization of some of the technologies developed through mDOT via startups is promising

mDOT Center Response

We thank the EAC for noting these strengths.

Apparent Weakness

1.a. Eventually, how the Center will Service the SPs should be incorporated in the presentations.

1.b. Make sure that claimed Administrative Core 'activities' are related to the Administration Core Specific Aims, some of the claimed Administration Core activities may be better attributed to other portions of the center.

1.c. Having good Center milestones for the next 5 years and next 10 years would be a good aspirational goal (and help motivate the overall story for the renewal

1.d. A potential threat is not getting funding renewed; however, the team seems well-focused at the preparation for renewal in the next year or so

mDOT Center Response

1.a. Thank you for this important suggestion. It will be incorporated in future presentations.

1.b. This is a good suggestion. As such we have restructured our current RPPR text, moving some items out of the Administrative Core write-up and moving them to other more applicable areas (i.e., Training & Dissemination). Those this was not reflected in the initial EAC technical summaries it will be in the final RPPR submitted to NIH.

1.c. Thank you for this wonderful suggestion. The visioning workshop to be held during the center's annual meeting will help shape our 5–10-year vision. We can then undertake this concrete activity to develop milestones that reflect the path to realizing our long-term vision.

1.d. We also acknowledge this threat. We would love to continue working with our EAC to position our center for a successful renewal so we can continue to advance the science and help the community.

Overall Direction for Year 4

- Getting industry integrated into the efforts of the Center

mDOT Center Response

Thank you for the acknowledgement.

Training & Dissemination

Notable Strengths

- The mHealth (MHTI) training fellowship seems well-liked by the participants.
- The potential to track trainee outcomes (using FlightTracker) may provide valuable data.
- Strong outcomes for students and postdocs, in terms of faculty and industry positions.

mDOT Center Response

Thank you for the acknowledgement.

Apparent Weakness

2.a. Identification of key deliverables is not clear.

2.b. Dissemination of P41-developed resources not well itemized/addressed.

2.c. The current website does not reflect the breadth of activities being undertaken.

2.d. Underrepresentation of the “Dissemination” aspect of the “Training and Dissemination” Core.

2.e. Better identification of the tools being developed that others can use or build on is warranted.

2.f. More information about the sharing of data sets and tools on the website and a more streamlined website to clearly highlight what the Center provides are opportunities that should be taken advantage of.

mDOT Center Response

2.a. Thank you for pointing this out. Although not showcased during the review or in the original technical summary submitted to EAC, we have expanded on this suggestion and revised the Training and Dissemination Core Year 3 report to reflect more detail to the deliverables expected through this Core's activities, including commencement of the annual mHTI, development and curation of content for the mHealth (webinars, instructional webinars, etc.), and evaluation of the training and dissemination activities.

2.b. The dissemination components were scattered in multiple areas of the Center report. Reacting to the feedback, we have consolidated all the dissemination activities and Center-related website & repository holdings within the Technical Training & Dissemination portion of the RPPR (Section B.5.).

2.c. The rehaul of the website is a work in progress. Galvanized by the feedback, we plan to continue with the redesign and optimization of the mDOT Center's website in Year 4 to enhance its online presence and engagement with its target audience. Briefly, our redesign will focus on a few key objectives: a) Showcasing the research publications and outcomes; b) Highlighting the CPs & SPs; c) Curating the Center's websites & tools for easy access; d) Facilitating engagement and collaboration; and e) Increasing search engine visibility. All of these are described in more detail in our Training Report for Year 3 in Section B.6.

2.d. Agreed, and again we have rectified this by going into more detail on how the Center results have been disseminated to communities of interest in the final Technical Training & Dissemination portion of the RPPR (Section B.5.) based on this recommendation.

2.e. The mDOT Center does have many repositories and tools that others in the mHealth community may benefit from and we concur that these need to be better identified in both our RPPR and on our upcoming redesigned website. Tools, such as the tutorial created by the mDOT Center that brings together computational tools for researchers working with wearable sensor data, have been developed and will be prominently showcased. This Tools Repository is designed to help students, researchers, and professionals to introduce rigor in their approach to handling the data diversity and noise that comes from high-frequency sensor data, especially when using them to reliably infer behavioral and momentary contexts. We will submit a comprehensive list of our websites and repositories as part of the RPPR, and as mentioned, it will be a focal point of the newly revamped mDOT Center homepage once launched in Year 4.

2.f. This item is the culmination of many of the suggestions brought forth by the EAC during their review. We will look to make this a priority with the mDOT Center website redesign in Year 4. The mDOT Center website will be the new central home for all other mDOT Center websites, tools, and repositories so that visitors can access all the resources in one centralized location.

Overall Direction for Year 4
● Consider getting MHTI participants and others to use mDOT data sets and tools in the classes they teach
mDOT Center Response
We plan to introduce the mDOT data sets and tools to future mHTI participants by utilizing the didactic components of the institute. Additionally, the explanatory webinars will be curated on the mHealthHUB to allow asynchronous access by a broader audience.

TR&D1: Discovery
Notable Strengths
● Exceptional technical expertise coupled with a robust track record in research output. ● Deep technical work and strong interdisciplinary collaborations across the board. ● Missing data handling for sensor data is very important for diverse m-health applications.
mDOT Center Response
Thank you.
Apparent Weakness
3.a. Provide more software tools and resources that others can use or build on.
mDOT Center Response
3.a. Thank you for this feedback. In Y4 we will be focused on a large-scale dissemination of our imputation models, which has been a significant accomplishment of the first three years of the center. We will release models for four major mHealth datatypes: Stepcount, PPG, EMA, and ECG. These modalities cover a large portion of the existing data modalities used in mHealth research. We are planning to organize these methods into a toolbox for data imputation which will be designed to be usable by researchers in the behavioral and health science, as well as bioengineering.

Overall Direction for Year 4
● The team's next steps are: a. Submit a manuscript and release code on data imputation methods, with a focus on scalability and applicability. b. Develop composite risk scores for sedentary behavior and smoking lapse. c. Submit a manuscript on robust stress detection and identification models based on the MOODS study data. d. Additional work will aim to improve risk prediction and explore uncertainty methods. ● The research direction is comprehensive and aligned with the aims. In addition to research publications, it will be great to consider providing tools and promoting research results to the communities.
mDOT Center Response
Thank you.
Other Thoughts/Comments
● Beyond publications, providing community-accessible tools could amplify impact.
mDOT Center Response
We agree. Please see responses to 2.e and 3.a above.

TR&D2: Optimization
Notable Strengths
● In Year 3, TR&D2 achieved multiple objectives across the teams: a. HARV completed the Oralytics RL algorithm, establishing templates for real-time use of RL in clinical trials and methods for post-trial analysis. b. UMASS's simulation study revealed that accounting for state probability distributions can mitigate the negative effects of noisy state estimates in RL policies.

c. Memphis completed the MOODS study with 122 participants, demonstrating that stress detection prompts could be reduced from 6 to 2 per day using smartwatch data. A submission to npj Digital Medicine journal is in preparation.

- Impressive educational and mentorship results have been achieved, with several team members transitioning into academic roles due to their involvement in this project.
- Novel use of RF technologies in identifying new modalities
- Good connection with CPs and good flow of new CPS entering the program

mDOT Center Response

Thanks!

Apparent Weakness

4.a. Industry involvement is weak at the present time

mDOT Center Response

4.a. We are working on two industry collaborations. The first is with the Oralytics team, CP2 and P&G. CP2 is facilitating this; a Provisional Patent Application has been filed to support this project. This application was filed based on a paper from TR&D2.

The second industry collaboration is in its infancy--this is with Raia Health. Raia Health is a startup--they have developed a chatbot for helping patients obtain information about side effects due to cancer drugs. This is joint with CP8. We aim to collaborate with them to include this chatbot intervention component in a pilot study involving RL. We won't use RL with the chatbot for the pilot study, but the idea is to use this to jumpstart a deeper collaboration.

Overall Direction for Year 4

- In Year 4, the focus is on:
    a. Running clinical trials with RL algorithms for personalized interventions, supported by a new statistical package.
    b. Finalizing an online RL monitoring system as a research template.
    c. Refining an RL toolbox through ongoing collaboration.
    d. Advancing research on intermediate outcomes in RL algorithms.
    e. Studying uncertainty effects in RL and moving toward sample-efficient algorithms.
    f. Improving JITAI simulation tool for modeling individuals.
- These proposed directions are sufficient and well-aligned with the aims.

mDOT Center Response
Thanks!
Other Thoughts/Comments
● To enhance the project's translational impact, consider innovative strategies like adding professional developers and engineers to the team. These roles could be budgeted for in the grant renewal process.
mDOT Center Response
Yes, we would very much appreciate this. We are working on several initiatives with CP8 and CP3 on this to obtain funding for more professional support.

TR&D3: Translation
Notable Strengths
● The TR&D3 activities cover a wide range of innovative approaches to healthcare and biometrics, primarily focusing on deep learning, radio frequency sensor arrays, and privacy regulation. Activity 1.1 introduces CardiacGen, a deep-learning framework for generating synthetic cardiac signals like ECGs, aiming to address data limitations. Activity 1.2 and 1.3 explore scalable RF arrays and calibration techniques for detecting subcutaneous fluids and tissue profiles, with an emphasis on lymphedema detection. Activity 1.4 further optimizes antenna design for these RF sensors. Activity 1.5 presents an unsupervised method to adapt digital biomarkers for individual variations, validated through a large-scale user study. Activity 1.6 outlines TinyNS, a platform-aware neurosymbolic architecture for optimizing both symbolic and neural operations in resource-constrained wearable devices. Finally, Activity 1.7 focuses on privacy issues, proposing an LLM-based solution to regulate sensory information flows in complex environments. These activities collectively address issues ranging from data limitations and hardware constraints to privacy concerns in sensor-based healthcare applications. ● OSU's CardiacGen model showed high physiological accuracy in generating cardiac signals, improving emotion and identity recognition from ECG signals significantly. ● UCLA's Siamese domain adversarial neural network effectively adapted machine learning models to new individuals without requiring new labeled data, achieving increasingly high accuracy rates

mDOT Center Response
We thank the EAC for noting these strengths, and in the coming years hope to build upon them.
Apparent Weakness
5.a. Privacy is addressed at research level through IRB but needs more insights into problems that industry faces for tech adoption. Consider some interview-based user studies to probe this issue.
mDOT Center Response
5.a. Yes, we agree with this suggestion and thank Dr. Jason Hong for bringing it up during the oral session as well. While historically mDOT has focused on mHealth technologies targeting health science researchers, for privacy-enabling technologies that has not been a useful approach as privacy is less of a concern to those researchers as well as the nature of research studies. We will explore the interview-based user study approach.
Overall Direction for Year 4
● Consider identifying existing mHealth companies to understand their privacy concerns and compliance issues, to help pave the way for adoption of methods and technologies in the long term
mDOT Center Response
Thanks for this suggestion, and, as noted above, we will undertake this and reach out to get additional advice from EAC members as we do that.
Other Thoughts/Comments
● There is an opportunity for creating new kinds of LLMs and foundation models for mhealth data, for modeling and generating synthetic data and for speeding up training of new models ● Threat: Insufficient training data or computing resources for their multi-modal foundation model research
mDOT Center Response

We agree that multimodal foundation models targeting sensory data (along with text) hold promise in multiple dimensions - synthetic data and as reusable components that can be used for embedding and as fine-tunable analytics modules. In addition to insufficient data and computing, we also recognize other concerns such as privacy (in case of text and image-based models) and robustness. Despite these hurdles, we believe it is important for a center like mDOT to explore this area.

Overall Center

Identified Overall Center Strengths

- Novel use of RF technologies in identifying new modalities (O)
- Deep technical work and strong interdisciplinary collaborations across the board (J)
- Good connection with CPs and good flow of new CPS entering the program (O)
- Good metrics to date: 33+ publications, patents, 2 startups (A)
- Good pipeline of new funding from NSF, NIH and other sources (A)
- Good institutional support (A)
- The mHealth (MHTI) training fellowship seems well liked by the participants (D)
- The potential to track trainee outcomes (using FlightTracker) may provide valuable data (D)
- Great team, good leadership, good organization, and collaboration across campuses. (A)
- Initial commercialization of some of the technologies developed at mDOT (J)
- Strong outcomes for students and postdocs, in terms of faculty and industry positions (D)

mDOT Center Response

We would like to thank the EAC for noting these strengths, and in the coming years hope to build upon them.

Identified Overall Center Weaknesses

6.a. Identification of key deliverables is not clear (D)

6.b. Dissemination of P41-developed resources not well itemized/addressed (D)

6.c. Website does not reflect the breadth of activities being undertaken (D)

6.d. Industry involvement is weak at the present time (O)

6.e. Privacy addressed at research level (IRB) but needs more for industry for tech adoption (J)

6.f. More tools that others can use or build on (D)

6.g. How will the SPs be incorporated (A)

mDOT Center Response

6.a. Key deliverables include Reference designs scalable RF sensing architectures, embedded programming libraries for biomarker.

6.b. We appreciate the EAC's attention to detail here. As mentioned above in Response 2b. we have consolidated all the dissemination core results and Center-related website & repository holdings within the Technical Training & Dissemination portion of the RPPR (Section B.5.) based on this recommendation.

6.c. We thank the EAC for this observation, we will revise the website to have descriptions of the resources and links to the GitHub pages that encapsulate our P41-developed resources.

6.d. Please see our response to Item 4.a above.

6.f. We also recognize this and, as referenced in Response 2e. above, the mDOT Center does have many repositories and tools that others in the mHealth community may benefit from. We will submit a comprehensive list of our websites and repositories as part of the RPPR, and the redesigned mDOT Center website in Year 4 will be the new central home for all other mDOT Center websites, tools, and repositories so that visitors can access all the resources in one centralized location.

6.g. This is a very good question. As many of the technologies co-developed with CP's are becoming more mature, we plan to engage with SPs in Year 4 to explore how to transition them so it can become an enabler.

Identified Overall Center Opportunities

- LLMs for modeling and generating synthetic data and for speeding up training of new models (J)
- More sharing of data sets and tools on website and a more streamlined website to clearly highlight what the Center provides (D)
- Getting MHTI participants and others to use data sets and tools in the classes they teach (J)
- Identifying existing mHealth companies to understand their privacy concerns and compliance issues (J)
- Getting industry integrated into the efforts of the Center
- Further expanding exciting new modalities in TRD3
- Having good Center milestones for the next 5 years and next 10 years (A)
- More widely impacting use cases (e.g., Early detection of Alzheimer's/Dementia)

mDOT Center Response

These are excellent opportunities identified by the EAC. We will pursue them, starting with our visioning workshop on October 30 that will bring several (established and startup) industry partners and health researchers in the areas of Alzheimer's and Dementia (from NIA-funded center).

Identified Overall Center Threats

7.a. Industry collaborations challenging, due to concerns about privacy, intellectual property.

7.b. Student tension of working at the intersection of research and translation.

7.c. Not getting funding renewed (A)

7.d. Insufficient training data or computing resources for their multi-modal foundation model research

mDOT Center Response

7.a. As rightly pointed out by the EAC, collaborations with industry does present a challenge in integrating them with the center. Successfully addressing these issues can bring outsized rewards as adoption of the center technology by the industry can magnify the center's impact by bringing our research advances to the real-life usage by a large number of users. We are trying several models for this including gifts to fund collaborations and having students intern with them where they can develop protected IP. Models that prove more successful will be adopted at more sites.

7.b. Having software staff (especially postdoctoral) has helped reduce this tension to some extent, but it also reduces opportunities for the students to gain hands-on experience that is useful to the students joining industry post-graduation. Hence, another strategy we are trying out is to put together teams of students that include those interested in system development and experiments with those interested in theory. Depending on how it works, we can adopt it at more sites.
7.c. Please see our response to Item 1.d.

7.d. It is a timely issue raised by the EAC. Models are becoming more powerful, but they are also becoming more data hungry. While a lot of training data exist for modalities that can be labeled by humans post data collection such as images, videos, text, and voices, sensor data can't be labeled post-facto. Therefore, the availability of labeled sensor data for multiple modalities is very slow. We plan to take steps in this direction by labeling and releasing multimodal sensor data collected from the field environment to accelerate model training and evaluation.

B.4. What opportunities for training and professional development has the project provided?

All personnel working on the project learn about their own domains and collaborating domains via regular communication and collaborative research activities. In addition, they learn critical team science skills via the interdisciplinary collaborations among the investigative teams as well as by working closely with the health research team from our collaborative projects (CP). They get unique opportunities to test their ideas out by developing working software, getting regular feedback from CP investigators and their staff, and then get to test their work in real-life deployment. All personnel also learn communication skills via regular presentations and discussions. Finally, they attend relevant conferences and professional meetings to communicate and network with other members of their research community.

Training in Professional Software Development - The software is designed to be extensible and usable by a variety of researchers including students and postdocs. Students who wish to contribute to the software platform reach out to the software team and we start a discussion to determine how we can best help each other. In general, this process includes the utilization of our repositories on GitHub for managing the software and Pivotal Tracker for handling bug reports and project planning.

Learning from Group Meetings - Minutes of teleconference calls as well as audio recordings are available for review by all team members. They help capture the content and context of discussions among mDOT Center team members and enable the team to keep up with what is going on outside their particular area of research. These are archived on the mDOT Center Google Drive which allow for easy access to information in a usable and consumable manner.

mHealth Awareness via mHealthHUB - The mHealthHUB website serves as a location where students and staff, as well as the general public, can find mHealth news aggregated. It includes a calendar of events, which also features submission deadlines for pertinent conferences and announcements of mDOT Center webinars. https://mhealth.md2k.org/

Sharing Publications - mDOT Center investigators have published or have submitted and under review 38 papers related to mDOT Center research. The papers have been readily available for team review to facilitate broader discussion.

Webinars - We have an archive of over 32 webinars and over 22 hours of training video content. Students and staff are encouraged to attend live, and webinars are posted to the mDOT Center YouTube channel and links are featured on the mHealthHUB. https://www.youtube.com/c/mdotcenter

Multidisciplinary Training - Each mDOT Center-affiliated graduate student has a faculty advisor to guide them in their studies and they get to work closely with students and investigators at other sites as well as from collaborative projects. This way, they learn to work in multidisciplinary teams.

mHealth Training Institute Lectures - All the presentations by the mHTI faculty are archived on mHealthHUB that mDOT personnel can watch at their convenience
https://mhealth.md2k.org/mhealth-training-institute

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Category	Explanation
Audio or video	https://www.tiktok.com/@mdotcenter The mDOT Center TikTok social media account.
Audio or video , Data or Databases , Educational aids or curricula , Research Material	https://mhealth.md2k.org/ The mHealthHUB is a service of the mHealth Center for Discovery, Optimization & Translation of Temporally-Precise Interventions (the mDOT Center). The mHealthHub is a virtual forum where technologists, researchers, and clinicians connect, learn, share, and innovate on mHealth tools to transform healthcare. Its mission is to create an innovation ecosystem that fosters the collaborative team science essential for mHealth and data science innovations. The mHealthHub collaboratory offers a “watering hole” where its members can: Develop a common vocabulary and a shared understating of the various facets of mHealth. Make connections across disciplinary silos, institutional constraints and geographic boundaries. Access content curated by mHealth thought leaders. Avail of tools and data sets developed by the various BD2K Centers. Participate in the mDOT Center’s training program. Crowdsource solutions for mHealth challenges. Share innovative ideas and develop the collaborations to actualize them. Learn about funding opportunities for mHealth research and products.
Educational aids or curricula	https://mhti.md2k.org/ The mHealth Training Institute Homepage. The mHTI is a national connector/incubator/facilitator for advancing mHealth researchers with the transdisciplinary expertise and networks for co-creating practical healthcare solutions with societal impact. Scholars develop a shared vocabulary and conceptual framework, acquire deep domain expertise in latest mHealth technologies and methodologies, and obtain

	the soft skills and team science abilities and connections essential for mHealth innovation.
Audio or video	https://www.youtube.com/c/mdotcenter The mDOT Center's YouTube library that archives the Center's webinars, lectures, and video media.
Evaluation Instruments , Software	https://github.com/mDOT-Center/pJITAI The pJITAI toolbox being developed in TR&D2 software and code repository. The repository serves as a centralized hub for storing, managing, and tracking the evolution of project code, scripts, and software tools. This facilitates seamless collaboration among project members, streamlining the process of code integration, debugging, and enhancement. The repository's branching and versioning capabilities enable the team to work concurrently on different aspects of the project without compromising code integrity. It ensures that changes are tracked, reviewed, and merged in a controlled manner, bolstering the project's overall reliability.
Models , Software	https://github.com/ SENSE-Lab-OSU/cardiac_gen_model To improve the performance of Machine Learning (ML) algorithms for Heart Rate, Hart Rate Variability prediction, and stress detection, OSU a Deep Learning framework dubbed as Cardiacgen for generating synthetic but physiologically plausible cardiac signals like ECG. This software can unlock the potential of using ML algorithms on limited datasets by creating synthetic training data by improving the performance of such Deep Learning (DL) models through data augmentation. We empirically show that in addition to having realistic physiological features, the synthetic data from CardiacGen can be used for data augmentation to improve the performance of Deep Learning-based classifiers.
Other	https://www.reddit.com/user/mDOT_Center/ The mDOT Center's Reddit used to disseminate information about the Center research activities and findings.
Other	https://twitter.com/mdot_center The mDOT Center's X, formerly known as Twitter, social media account used to disseminate upcoming webinars and Center activities.
Other	https://www.linkedin.com/in/mdotcenter/ The mDOT Center's LinkedIn page.
Other	https://www.reddit.com/user/mDOT_Center/

	The mDOT Center Reddit page used to disseminate Center activity and research.
Research Material	https://mdotcenter.org/ The mDOT Center's Homepage. Redesign of the mDOT Center website. This year, the mDOT Center website is undergoing a major redesign to enhance its online presence and engagement with its target audience. The redesign focuses on two key objectives: 1. Showcase Research Projects and Outcomes: By presenting research projects and outcomes in a more digestible way, the mDOT Center is making its work more accessible and understandable to a broader audience. This is crucial for advancing mHealth, as it allows not only researchers and clinicians but also stakeholders and the general public to comprehend the Center's contributions to the field. Clear communication of research findings can foster better understanding and support for mHealth initiatives and thus drive innovation. 2. Facilitate Engagement and Collaboration: Redesigning the website to make Center resources more accessible encourages researchers and clinicians to explore the Center's offerings in depth. The inclusion of call-to-actions that prompt collaboration inquiries can foster more direct and efficient communication between potential collaborators and the Center. This can lead to new partnerships with potential collaborative and service projects.
Software	https://github.com/nesl/neurosymbolic-tinyml To enable robust and efficient digital biomarkers on extremely resource-constrained devices, UCLA created and released TinyNS, the first platform-aware neurosymbolic architecture search framework for joint optimization of symbolic and neural operators. TinyNS addresses the problem that AI/ML-enabled digital biomarkers require neural models to be combined with symbolic reasoning and traditional algorithms to ensure interpretability and satisfy the underlying system rules and physics within the tight platform resource constraints is challenging. It provides recipes and parsers to automatically write microcontroller code for five types of neurosymbolic models, combining the context awareness and integrity of symbolic techniques with the robustness and performance of machine learning models.
Software	https://github.com/MD2Korg/ The mDOT Center's software and code repository.
Research Material , Software	https://moods.md2k.org/ The Mobile Open Observation of Daily Stressors (MOODS)

	study homepage. The purpose of the MOODS study is to understand what causes stress (i.e., what are the daily stressors) in daily life, focusing on those stress events that can be detected by smartwatches.

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Data or Databases	WristPrint: For privacy risk characterization, the source code of the WristPrint model is being released so that the research community can build upon it (see https://github.com/MD2Korg/wrist-print).
Data or Databases	SmokingOpp: Several new mHealth datastreams were computed for CP1 and CP5 resulting from the SmokingOpp work. They indicate the risk level from the GPS and wrist-worn accelerometry data for a newly abstinent smoker. In particular, they indicate proximity to microlocations where this individual used to smoke prior to quitting (called personal smoking spots) and where other smokers were detected to have regularly smoked (called public smoking spots). These information were combined with smoking allowance reports and cigarette availability to obtain a continuous measure of whether the location a newly abstinent smoker is currently in presents a low or high risk of smoking lapse. The source code for computing these new data streams are integrated in Cerebral Cortex and upon successful usage by CP1 and CP5 will be released for usage by relevant SPs.
Instruments or equipment	MotionSense HRV: Several technologies have been developed and released by TR&D3 in Year 1. They include the MotionSense HRV that are deployed in CP1 and CP5, creating an entirely new open-source stack based on Zeyphr RTOS (see github.com/SENSE-Lab-OSU), and a dual core version of MotionSense HRV. Both of these redesigns now enable the execution of ML algorithms for deriving micromarkers and biomarkers (in some cases) at the point of sensor data collection itself, reducing the need for frequent communication with a smartphone or cloud.
Models	BayesLDM: A toolbox for the specification and estimation of mechanistic models in the dynamic bayesian network family. This toolbox focuses on making it easier to specify probabilistic dynamical models for time series data and to perform Bayesian inference and imputation in the specified model given incomplete data as input.
Software	https://github.com/nesl/neurosymbolic-tinyml To enable robust and efficient digital biomarkers on extremely resource-constrained devices, UCLA created and released TinyNS, the first platform-aware neurosymbolic architecture search framework for joint optimization of symbolic and neural

	operators. TinyNS addresses the problem that AI/ML-enabled digital biomarkers require neural models to be combined with symbolic reasoning and traditional algorithms to ensure interpretability and satisfy the underlying system rules and physics within the tight platform resource constraints is challenging. It provides recipes and parsers to automatically write microcontroller code for five types of neurosymbolic models, combining the context awareness and integrity of symbolic techniques with the robustness and performance of machine learning models.
Software	https://github.com/ SENSE-Lab-OSU/cardiac_gen_model To improve the performance of Machine Learning (ML) algorithms for Heart Rate, Hart Rate Variability prediction, and stress detection, OSU a Deep Learning framework dubbed as Cardiacgen for generating synthetic but physiologically plausible cardiac signals like ECG. This software can unlock the potential of using ML algorithms on limited datasets by creating synthetic training data by improving the performance of such Deep Learning (DL) models through data augmentation. We empirically show that in addition to having realistic physiological features, the synthetic data from CardiacGen can be used for data augmentation to improve the performance of Deep Learning-based classifiers.
Software	https://github.com/MD2Korg/ The mDOT Center's software and code repository.
Software	Mobile Open Observation of Daily Stressors (MOODS): In conjunction with the mProv Collaborative Project (CP7), we have successfully deployed the Mobile Open Observation of Daily Stressors (MOODS) study with real-world participants and this study is ongoing with an expected completion date of Summer 2022. To reach this point, we had to get approvals from both of the major app stores (Google and Apple) for the MOODS app along with some specific customizations for Apple that they required us to implement. The participant enrollment process has been fully worked out with an initial screening survey link being sent out to various target groups as defined in the IRB procedures. Once participants complete this screening survey and are eligible, they are placed in a pool of candidates for our bi-weekly enrollment phase. Once a participant is selected, they are sent an invitation email with links to the app/play store mobile apps. The MOODS app contains the informed consent process and guides each participant through it. If the participants complete the consent process, we receive their personal information and can ship them one of the study watches, completing the enrollment process. Additionally, the MOODS app contains weekly surveys for the participants. As part of the participant engagement, we completed a visualization and explanation pipeline which compiles

	participant stress data into various graphical representations. These outputs are sent to each participant every week, prior to the survey, for them to review and comment on. The intention is to better educate participants about their stress patterns. Finally, we have developed some back-end data study monitoring tools that the researchers use to keep track of the study as a whole as well as each participant. These are especially helpful in diagnosing potential failures. The goal of this component is to ensure that actions can be taken quickly to help us collect the most complete dataset possible.
Software	https://github.com/mDOT-Center/pJITAI The pJITAI toolbox being developed in TR&D2 software and code repository. The repository serves as a centralized hub for storing, managing, and tracking the evolution of project code, scripts, and software tools. This facilitates seamless collaboration among project members, streamlining the process of code integration, debugging, and enhancement. The repository's branching and versioning capabilities enable the team to work concurrently on different aspects of the project without compromising code integrity. It ensures that changes are tracked, reviewed, and merged in a controlled manner, bolstering the project's overall reliability.
Software	Heteroscedastic Temporal Variational Autoencoder for Irregularly Sampled Time Series (HetVAE): HeTVAE is a deep learning framework for probabilistic interpolation of irregularly sampled or sparse time series data.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Component(s)	Country	SS
JINGYIGAN	N	Gan, Jingyi	PhD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	1.0	0.0	0.0		Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
HYLAI1	N	Lai, Hsin-Yu	PhD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	3.0	0.0	0.0		Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
YONGYIGUO	N	Guo, Yongyi	PhD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	2.0	0.0	0.0		Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
TWHNAT	N	Hnat, Timothy	BS,OTH,PHD	Staff scientist (Doctoral level)	1.0	0.0	0.0		Project-7965 (mDOT TR&D2 (Optimization):...ment Learning), Project-7966 (mDOT TR&D3 (Translation): ...plementations)		NA
SRATHNAM	N	Rathnam, Sarah	AB,MS	Graduate Student (research assistant)	3.0	0.0	0.0		Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
DAIQIGAO	N	Gao, Daiqi	BS,PHD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	1.0	0.0	0.0		Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
ZIPINGXU	N	Xu, Ziping		Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	1.0	0.0	0.0		Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
BRIANWANG	N	Wang, Brian	BS	Graduate Student (research assistant)	0.0	1.0	0.0		Project-7966 (mDOT TR&D3 (Translation): ...plementations)		NA
GFDONG	N	Dong, Gaofeng		Graduate Student (research assistant)	0.0	1.5	0.0		Project-7966 (mDOT TR&D3 (Translation): ...plementations)		NA

JBRISENO	N	de Gortari Briseno, Julian		Graduate Student (research assistant)	0.0	0.0	1.0		Project-7966 (mDOT TR&D3 (Translation): ...plementations)		NA
SKUMAR4	Y	Kumar, Santosh	PHD	PD/PI	0.0	2.3	0.8		Admin-7963 (mDOT Administrative Core), Project-7964 (mDOT TR&D1 (Discovery) - E...Risk Dynamics), Project-7965 (mDOT TR&D2 (Optimization):...ment Learning), Project-7966 (mDOT TR&D3 (Translation): ...plementations), Tech-7967 (mDOT Training and Dissemination)		NA
BMARLIN	N	Marlin, Benjamin M.	PhD	Co-Investigator	1.0	0.0	0.0		Admin-7963 (mDOT Administrative Core), Project-7964 (mDOT TR&D1 (Discovery) - E...Risk Dynamics), Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
SRIVASTAVA2	N	Srivastava, Mani	PHD,MS,OTH	Co-Investigator	0.0	0.0	0.5		Project-7966 (mDOT TR&D3 (Translation): ...plementations)		NA
ERTIN01	Y	Ertin, Emre	PHD	Co-Investigator	0.0	1.4	0.0		Admin-7963 (mDOT Administrative Core), Project-7966 (mDOT TR&D3 (Translation): ...plementations)		NA
SAMURPHY	Y	MURPHY, SUSAN A	PHD	Co-Investigator	1.2	0.0	0.0		Admin-7963 (mDOT Administrative Core), Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
J.REHG	Y	Rehg, James M.	PHD	Co-Investigator	1.2	0.0	0.0		Admin-7963 (mDOT Administrative Core), Project-7964 (mDOT TR&D1 (Discovery) - E...Risk Dynamics)		NA
SHETTY2	Y	SHETTY, VIVEK	DOTH,DDS	Co-Investigator	1.1	0.0	0.0		Admin-7963 (mDOT Administrative Core), Tech-7967 (mDOT Training and Dissemination)		NA
JWBGGERS	N	Biggers, Joseph	MS	Operations Director	2.0	0.0	0.0		Admin-7963 (mDOT Administrative Core)		NA
AZIMULLAH	N	Ullah, Md Azim	BS	Graduate Student (research assistant)	6.0	0.0	0.0		Project-7964 (mDOT TR&D1 (Discovery) - E...Risk Dynamics), Project-7965 (mDOT		NA

									TR&D2 (Optimization):...ment Learning)		
LDRUSH1	N	Tran, Lyndsey		Training Specialist	6.0	0.0	0.0		Tech-7967 (mDOT Training and Dissemination)		NA
JEONMJ	N	Jeon, Minjeong	PhD	Consultant	1.0	0.0	0.0		Tech-7967 (mDOT Training and Dissemination)		NA
MSAHA1	N	Saha, Mithun		Graduate Student (research assistant)	6.0	0.0	0.0		Project-7964 (mDOT TR&D1 (Discovery) - E...Risk Dynamics), Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
SAMEERNEUPANE	N	Neupane, Sameer	BS	Graduate Student (research assistant)	6.0	0.0	0.0		Project-7964 (mDOT TR&D1 (Discovery) - E...Risk Dynamics), Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
MXU870	N	Xu, Maxwell	Ph.D.	Graduate Student (research assistant)	0.0	0.0	3.0		Project-7964 (mDOT TR&D1 (Discovery) - E...Risk Dynamics)		NA
HUIWEI123	N	Wei, Hui	BS,MS,PHD	Graduate Student (research assistant)	6.0	0.0	0.0		Project-7964 (mDOT TR&D1 (Discovery) - E...Risk Dynamics), Project-7965 (mDOT TR&D2 (Optimization):...ment Learning)		NA
SSAMIEI	N	Samiei, Shahin		Research Coordinator	2.4	0.0	0.0		Admin-7963 (mDOT Administrative Core), Project-7964 (mDOT TR&D1 (Discovery) - E...Risk Dynamics), Project-7965 (mDOT TR&D2 (Optimization):...ment Learning), Project-7966 (mDOT TR&D3 (Translation): ...plementations), Tech-7967 (mDOT Training and Dissemination)		NA
TUSHAR_AGARWAL	N	Agarwal, Tushar	BS	Graduate Student (research assistant)	6.0	0.0	0.0		Project-7966 (mDOT TR&D3 (Translation): ...plementations)		NA
YUYI_CHANG	N	Chang, Yuyi		Graduate Student (research assistant)	6.0	0.0	0.0		Project-7966 (mDOT TR&D3 (Translation): ...plementations)		NA

NSUGAVANAM	N	Sugavanam, Nithin	BS,PHD	Sr. Research Engineer	0.5	0.0	0.0		Project-7966 (mDOT TR&D3 (Translation): ...plementations)		NA

Glossary of acronyms:
S/K - Senior/Key
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)

Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RS - Reentry Supplement
DS - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

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D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

F. OVERALL CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. OVERALL SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Sub-Project ID	Study ID	Study Title	Delayed Onset	Clinical Trial	NCT	NIH-Defined Phase 3	ACT
Project-002	330869	TR&D2: Dynamic Optimization of Continuously Adapting mHealth Interventions via Prudent, Statistically Efficient, and Coherent Reinforcement Learning	YES	NO			
Project-001	330867	TR&D1: Enabling the Discovery of Temporally-Precise Intervention Targets and Timing Triggers from mHealth Biomarkers via Uncertainty-Aware Modeling of Personalized	YES	NO			
Project-003	330868	TR&D3: Translation of Temporally Precise mHealth via Efficient and Embeddable Privacy-aware Biomarker Implementations	YES	NO			

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

Yes

Information Privacy Security (IPS): CITI training for Information Privacy Security (IPS) provides comprehensive instruction on best practices and compliance in safeguarding sensitive information to maintain data privacy and security.

Social and Behavioral Responsible Conduct of Research (SBRCR): CITI training for Social and Behavioral Responsible Conduct of Research (SBRCR) offers essential guidance on ethical principles and responsible conduct in social and behavioral research, ensuring the integrity of research practices in these fields.

Social & Behavioral Research Investigators (SBRI): CITI training for Social and Behavioral Responsible Conduct of Research (SBRCR) equips researchers with essential guidance on ethical principles and responsible conduct within the social and behavioral research domains, ensuring research integrity and compliance with ethical standards.

Daiqi Gao - CITI IPS, SBRCR, SBRI
Hsin-Yu Lai - CITI IPS, SBRCR, SBRI
Kyra Gan - CITI IPS, SBRCR, SBRI
Sarah Rathnam - CITI IPS, SBRBI, SBRC
Yongyi Guo - CITI IPS, SBRCR, SBRI
Ziping Xu - CITI IPS, SBRCR, SBRI

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name	UEI	Congressional District	Address
Primary: UNIVERSITY OF MEMPHIS	F2VSMAKDH8Z7	TN-009	UNIVERSITY OF MEMPHIS ADMINISTRATION 315 MEMPHIS, TN 381520001
President and Fellows of Harvard College	LN53LCFJFL45	MA-005	1033 Massachusetts Avenue, 5th Floor Cambridge, MA 02138
The Ohio State University	DLWBSLWAJWR1	OH-003	1960 Kenny Road Columbus, OH 43210

The Regents of the University of California	RN64EPNH8JC6	CA-033	10889 Wilshire Blvd Suite 700, Box 951406 Los Angeles, CA 90095
University of Illinois Urbana-Champaign	Y8CWNJRCNN91	IL-013	352 Henry Administration Building 506 S. Wright Street Urbana, IL 61801-362
University of Massachusetts Amherst	VGJHK59NMPK9	MA-002	101 University Drive, Suite B6 Amherst, MA 01002

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period? No

G.12 F&A COSTS

Not Applicable

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
330869	TR&D2: Dynamic Optimization of Continuously Adapting mHealth Interventions via Prudent, Statistically Efficient, and Coherent Reinforcement Learning	No	TRD2_Justification.pdf

Project Lead: Murphy, Susan Primary Investigator: Kumar, Santosh

Justification

TR&D2 will provide technology and support to active human subjects studies but will not be conducting research activities involving interaction with living human subjects. All TR&D2 activities involving human subjects data for research will be governed or otherwise overseen by Institutional Review Board (IRB) oversight, as appropriate. Each project that involves human subjects interactions for research or interaction with human subjects data for research will continue to follow the letter and the spirit of regulations protecting the rights and welfare of human subjects in research studies. All interactions with human subjects and/or their data are governed by both internal TR&D2 and institutional policies requiring Institutional Review Board oversight, exemption, or determination that human subjects research is not taking place. Any data involving human subjects collected in TR&D2 projects (e.g., via the CPs and SPs) will be governed by the data management plans of the respective projects. In addition, all human subject data collection will have explicit Institutional Review Board (IRB) approval. It is not known at this time, what human subject data will be collected using TR&D2 technologies, hosted by TR&D2, and used for technology development and testing by TR&D2.

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
330867	TR&D1: Enabling the Discovery of Temporally-Precise Intervention Targets and Timing Triggers from mHealth Biomarkers via Uncertainty-Aware Modeling of Personalized	No	TRD1_Justification.pdf

Project Lead: Rehg, Jim Primary Investigator: Kumar, Santosh

Justification

TR&D1 will provide technology and support to active human subjects studies but will not be conducting research activities involving interaction with living human subjects. All TR&D1 activities involving human subjects data for research will be governed or otherwise overseen by Institutional Review Board (IRB) oversight, as appropriate. Each project that involves human subjects interactions for research or interaction with human subjects data for research will continue to follow the letter and the spirit of regulations protecting the rights and welfare of human subjects in research studies. All interactions with human subjects and/or their data are governed by both internal TR&D1 and institutional policies requiring Institutional Review Board oversight, exemption, or determination that human subjects research is not taking place. Any data involving human subjects collected in TR&D1 projects (e.g., via the CPs and SPs) will be governed by the data management plans of the respective projects. In addition, all human subject data collection will have explicit Institutional Review Board (IRB) approval. It is not known at this time, what human subject data will be collected using TR&D1 technologies, hosted by TR&D1, and used for technology development and testing by TR&D1.

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
330868	TR&D3: Translation of Temporally Precise mHealth via Efficient and Embeddable Privacy-aware Biomarker Implementations	No	TRD3_Justification.pdf

Project Lead: Ertin, Emre Primary Investigator: Kumar, Santosh

Justification

TR&D3 will provide technology and support to active human subjects studies but will not be conducting research activities involving interaction with living human subjects. All TR&D3 activities involving human subjects data for research will be governed or otherwise overseen by Institutional Review Board (IRB) oversight, as appropriate. Each project that involves human subjects interactions for research or interaction with human subjects data for research will continue to follow the letter and the spirit of regulations protecting the rights and welfare of human subjects in research studies. All interactions with human subjects and/or their data are governed by both internal TR&D3 and institutional policies requiring Institutional Review Board oversight, exemption, or determination that human subjects research is not taking place. Any data involving human subjects collected in TR&D3 projects (e.g., via the CPs and SPs) will be governed by the data management plans of the respective projects. In addition, all human subject data collection will have explicit Institutional Review Board (IRB) approval. It is not known at this time, what human subject data will be collected using TR&D3 technologies, hosted by TR&D3, and used for technology development and testing by TR&D3.

A. COMPONENT COVER PAGE

Project Title: mDOT Administrative Core
Component Project Lead Information: Kumar, Santosh

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The mHealth Center for Discovery, Optimization & Translation of Temporally-Precise Interventions (the mDOT Center) will enable a new paradigm of temporally-precise medicine to maintain health and manage the growing burden of chronic diseases. The mDOT Center will develop and disseminate the methods, tools, and infrastructure necessary for researchers to pursue the discovery, optimization, and translation of temporally-precise mHealth interventions. Such interventions, when dynamically personalized to the moment-to-moment biopsychosocial-environmental context of each individual, will precipitate a much-needed transformation in healthcare by enabling patients to initiate and sustain the healthy lifestyle choices necessary for directly managing, treating, and in some cases even preventing the development of medical conditions. Organized around three Technology Research & Development (TR&D) projects, mDOT represents a unique national resource that will develop multiple technological innovations and support their translation into research and
practice by the mHealth community in the form of easily deployable wearables, apps for wearables and smartphones, and a companion mHealth cloud system, all open-source.

To execute its research, development, collaboration, training, and dissemination goals, the mDOT Center builds on central operations infrastructure developed through the successful administration of the NIH Center of Excellence for Mobile Sensor Data-to-Knowledge (MD2K). MD2K involves 70 investigators, students, postdoctoral fellows, software engineers, and administrative staff, distributed across 13 universities. In addition, MD2K leads or participates in 13 concurrently active research grants from NIH, NSF, and other federal agencies. The mDOT Center takes advantage of an experienced, multidisciplinary team of investigators and technical staff from MD2K. This expertise includes program operations, business management, data management, marketing and communication, study coordination, training coordination, and outreach. The overall goal is to implement an operational structure that facilitates the discovery, optimization, and translation of temporally-precise mHealth interventions to advance health research and improve health outcomes.

The mDOT Center is organized into an Administration Core, a Technology, Training and Dissemination Core (TT&D), and three Technology Research and Development (TR&D) Projects: TR&D1 (Intervention Discovery); TR&D2 (Intervention Optimization), and TR&D3 (Intervention Translation). PI/PD Kumar will serve as the mDOT Center Director, responsible for overseeing all project-related activities, and will also lead the Administration Core. He will work with an Executive Committee, the mDOT Center Operations Office, and the External Advisory Committee to carry out this role. The Administration Core will facilitate interactions among the TR&D Researchers and their external collaborators from collaborating and service projects; coordinate the activities of the TT&D Core to enable both targeted and broad-based training and dissemination of methods, tools, and research findings developed through mDOT Center activities; assess the productivity and impact of Center activities; and provide ongoing management, oversight, and planning related to Center funds, resources, and operations. Drawing on its prior leadership experience at the NIH-funded MD2K National Center of Excellence, the Administration Core will provide the managerial and operational structures through which the mDOT Center will achieve its research, development, collaboration, training, and dissemination goals. The Administration Core has five specific aims:

Aim 1: Establish an organizational structure, coordinating procedures, and managerial practices that effectively facilitate coordination, communication, and collaboration among team members, collaborative and service projects, and the broader research community.

Aim 2: Establish operating procedures to successfully work with collaborative projects (CPs) and service projects (SPs), including criteria and mechanisms to receive, review, approve, and facilitate the use of mDOT Center resources by CPs and SPs, and establish criteria for prioritizing and selecting CPs and SPs.

Aim 3: Recruit, assemble, and manage an external advisory committee (EAC) of eminent scholars with diverse and complementary expertise to obtain feedback and guidance on research directions, software development, selection of CPs and SPs, as well in the overall structure and operations of the mDOT Center.

Aim 4: Acquire, manage, and leverage institutional support to successfully accomplish the goals of the mDOT Center.

Aim 5: Develop quantifiable measures and implement systems to monitor, assess, and evaluate the quality and utility of mDOT Center products, and continuously improve the long-term impact of Center activities on biomedical research by systematically securing feedback from collaborators and community stakeholders.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Publications, Talks, & Presentations: mDOT Center investigators have published or have submitted and under review a total of 33 papers related to mDOT Center research for project Year 3. In addition, mDOT Center investigators have participated in 168 talks and presentations at 152 global meetings since the Center’s inception.

The mDOT Center disseminates information to communities of interest via its website, mdotcenter.org (more than 19,500 page views since launch on July 1, 2020).

Recordings of webinars are posted to the mDOT Center’s YouTube channel, where they are accessible by the general public; 40 mDOT Center-hosted webinars in the series have been released to date. More than 260 videos posted on the mDOT Center’s YouTube channel have been viewed a total of more than 50,500 times on the channel, which now has 360 subscribers and more than 4,400 hours of watch time.

A second website, mHealthHUB, serves as a portal for the greater mHealth community (more than 52,400 unique users and more than 172,600 page views since its November 2015 launch).

A third website, mhti.md2k.org, exists for the purpose of providing information about the NIH mHealth Summer Training Institute and has received 17,300 users and over 59,200 page views through September 2023.
The mDOT Center runs, maintains, and disseminates information on the following websites:

mDOTCenter.org: https://mdotcenter.org/

mHealthHUB: https://mhealth.md2k.org/

mHealth Training Institute: https://mhti.md2k.org/

Mobile Open Observation of Daily Stressors (MOODS): https://github.com/MD2Korg/moods

Social Media Channels
mDOT Center YouTube Channel: https://www.youtube.com/c/mdotcenter

mDOT Center LinkedIn: https://www.linkedin.com/in/mdotcenter/

mDOT Center Reddit: https://www.reddit.com/user/mDOT_Center/

mDOT Center TikTok: https://www.tiktok.com/@mdotcenter

Repositories
Tools Repository: https://colab.research.google.com/drive/1hjYdqVUFThpZtV7sagQdhFZudTUsuIXU?usp=sharing

mDOT Center GitHub Repository: https://github.com/MD2Korg/

mDOT Center pJITAI Toolbox: https://github.com/mDOT-Center/pJITAI

CardiacGen: https://github.com/ SENSE-Lab-OSU/cardiac_gen_model

TinyNS: https://github.com/nesl/neurosymbolic-tinym

WristPrint: https://github.com/MD2Korg/wrist-print

Auritus: https://github.com/nesl/auritus

TinyOdom: https://github.com/nesl/tinyodom

MotionSenseHRV: https://github.com/SENSE-Lab-OSU/MotionSenseHRV_v3

Cerebral Cortex: https://github.com/MD2Korg/CerebralCortex

mCerebrum: https://github.com/MD2Korg/mCerebrum

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Admin: The Admin Core will continue to provide administrative, managerial, and infrastructure support to enable the mDOT Center to accomplish its Year 4 goals in research, training, and dissemination activities. In addition to continuing its successful strategies for communication and management, the mDOT Center plans to do several activities in Year 4 tied to the Administration Core Aims:

Aim 1 - Administratively Manage The Center
Annual Meeting: The mDOT Center will look to host its next annual meeting with all Center investigators in attendance.
Student Exchange: The mDOT Center will continue to facilitate and enhance scholar exchanges between subsites/CPs/SPs as much as possible (virtually or in-person).
Award: The administration team will again look to receive, process, and execute all grant subcontracts for the Year 4 award and provide assistance to collaborating institutions with their process.
Renewal: The administration team will spearhead and coordinate the Center's renewal efforts as the team transitions into a phase of focus on renewed funding.

Aim 2 - CP and SP Coordination & Expansion

Appraisal: The mDOT Center team, in conjunction with the Executive Board and the External Advisory Committee, will finalize CP and SP inclusion and review criteria, paying attention to aligning new projects to TR&D aims.
Expansion: The mDOT Center team intends to expand the number of CPs and SPs and onboard new CPs and SPs as needed.
Facilitate: The mDOT Center administration team will continue coordinating relevant CP and SP meetings tailored to the push/pull relationship and research.

Aim 3 - Executive Advisory Committee Engagement
Evaluate: The mDOT Center will look to convene (in-person if feasible) the Executive Advisory Committee, using its new evaluation model, for its annual evaluation meeting to review the current progress and future direction of the mDOT Center. The EAC's formal reviews will be included in the Year 5 RPPR.
Integrate: The mDOT Center will look to enhance its engagement with the Executive Advisory Committee throughout Year 4 and include EAC members in relevant meetings and discussions to utilize their expertise and advise mDOT Center stakeholders.
Improve: The administration core will review and utilize the feedback given by the EAC during their Year 3 review to improve all facets of the mDOT Center research agenda and center operations and implement strategies for a successful renewal.
Rotation: The mDOT Center's Executive Leadership team will look to rotate out EAC members whose term is expiring and replace those members with new advisors whose expertise and experience will help guide the Center toward wider adoption and renewal.

Aim 4 - Leveraging Institutional Support for the mDOT Center
Staff: The Admin Operations team will look to retain and cross-train our current staff to efficiently and fiscally responsibly operate the Center in Year 4 while utilizing in-kind positions and resources given by the University of Memphis.
Annual Meeting: The Admin Core will secure University spaces, institutional facilities, and enterprise-level video conferencing tools and technology to host an in-person annual meeting with the goal of bringing together relevant mDOT Center stakeholders for charting the Center's future research agenda and successful renewal.
Websites, Data, & Servers: The mDOT Center Software and Admin team will continue to leverage, and modify as needed, the established collaborative infrastructure and computational resources developed through the Center's previous years and other projects at the University of Memphis, inclusive of hosting and storage of digital resources and data.
Data Sharing: The mDOT Center will continue to utilize Memphis IRB oversight and data sharing agreements to facilitate the accessibility of meaningful and timely data to enhance CP & SP research partnerships in Year 4.

Aim 5 - Progress Monitoring & Reporting
Reporting: In year 4, the admin team will compile and submit the required annual report to NIH for programmatic review.
Communication: The Admin Core staff will continue upholding the standards of responsive, thoughtful communication to sustain the collaborative culture of the mDOT Center throughout Year 4.
Tracking: Utilization of current best practices for tracking goals and progress will be used by the Admin Core to create and provide a detailed, concise snapshot of mDOT Center advancement throughout Year 4 to internal members, institution officials, and external stakeholders.
Improvement: For continuous improvement in the mDOT Center technologies, its training activities, dissemination channels (e.g., website structure and content), and administrative procedures, feedback will be regularly sought from mDOT Center team members, NIH program officers, mDOT Center affiliates, and the community stakeholders.

Transitioning hosting of the pJITAI project to the University of Michigan (CP8): The hosting of the pJITAI project will be handed off to the University of Michigan. The decision to transfer the project to Michigan is based on the fact that the development will be located with the same teams that are currently co-developing and will be the first adopters using the service, resulting in a more cohesive and impactful product.
Previously, it made sense to keep the project in Memphis and utilize the staff of software engineers available. However, over the past year, as the project has expanded and engineers at Memphis have departed, it was deemed necessary to transfer the project to Michigan where resources and personnel are available.
To accomplish this hand-off, we will collaborate with TR&D2, CP1, and CP3 to provide advice and context to the pJITAI codebase for a local software engineer at the University of Michigan (CP8). This advice will include architecture designs explaining how and why the system was built in a way that allows for easy extensibility, suitable for data scientists or

statisticians to add and modify algorithms.
Furthermore, we will ensure that the algorithms are easily accessible for behavioral scientists utilizing pJITAI through a common API interface with appropriate libraries in relevant languages. This will enable them to effectively utilize the platform. We will also provide detailed explanations of what our team did in the code and offer a general understanding of how the project was built. This will aid the local software engineer in managing and maintaining the project. Additionally, we will give general advice on how they should proceed with the project. This guidance will help them make informed decisions and ensure a smooth transition.
Once the transfer is underway and the University of Michigan has created a copy of the running system, we will shut down the Memphis-based cloud server that currently hosts pJITAI. This step will mark the complete transfer of the pJITAI project to Michigan. To assist in the transfer, we plan to engage Dr. Timothy Hnat, our former Chief Software Architect and designer of the pJITAI project, in a consulting capacity. His expertise and knowledge will be valuable in ensuring a successful hand-off.

Once the hand-off is complete and the project is set up in Michigan, it is expected that a pilot study could happen with the pJITAI within the project Year 4 timeframe.

Principal Investigator: Kumar, Santosh

mDOT Center ADMINISTRATION

B.2 What was accomplished under these goals?

In Year 3, the Administration core undertook a variety of activities (as described below) to fulfill its goals.

B.2.1. Major Activities

Activity 1.1. Visioning Workshop on Generative mHealth Interventions on Emerging Wearables. The mDOT Center is putting together a full-day visioning workshop to delve into the impact of generative mHealth interventions on emerging wearables. Held in conjunction with the mDOT Center Annual Meeting on the campus of Harvard University in Boston, MA, the mDOT Center leadership brought together researchers and stakeholders from industry, academia, and medicine to discuss both the significant opportunity that the conjunction of generative AI and novel wearables represent in the mobile health space, and the significant scientific and socio-technical challenges that need to be overcome to ensure that resulting approaches are safe, efficacious, ethical, contextually appropriate, engaging and adaptive. With about 40 attendees, the workshop's core objective is to chart out a research agenda for the next 5-10 years to explore how generative AI and emerging wearables can lead to innovative mHealth interventions.

Activity 1.2. Year 3 Annual Meeting. This year the Admin team is hosting the Year 3 mDOT Center Annual Meeting at Harvard University (home site of TR&D2 Lead Susan Murphy) in Boston, MA. It will bring together all mDOT Center investigators, students, EAC members, and other stakeholders so they can discuss research, strategies, brainstorm, and network in person. This is the first time the center's annual meeting is being held outside of Memphis (where the Admin team is located) and planning from afar provided a new wrinkle to this year's preparation.

Activity 1.3. Scheduling and Collaborative Tools. Each TR&D holds its own separate monthly telecons among investigators and students. In addition, there are various calls involving all the leads of the TR&Ds and their respective CP and SP teams. The mDOT Center students and postdocs hold weekly meetings within their own team sites to present recent research on topics of interest and to discuss progress and solicit feedback from other team members. An agenda is developed prior to each call and minutes and action items are noted during the call. All of this happens using the collaborative power of Google Docs so that all participants can jointly edit these documents in real-time or after the call.

Activity 1.4. Systematic Feedback. The creation of vetted administrative procedures in Year 1 ensured commitment to shared protocols with respect to virtual interactions. Regular feedback, both formal (kick-off meeting session) and informal (emails, chats, correspondence), is solicited from the team throughout the year and used to review and revise the communication plan, helping to streamline the procedure and make communication more effective.

Activity 1.5. Institutional Review Board approvals for data collection and analysis from CPs. When appropriate, the mDOT Center's admin team helps to facilitate appropriate research review and oversight for compliance purposes, ensuring that CP & SP research partnerships involving human subjects research activities where data collected are being stored in our cloud servers, i.e., involving interactions with human subjects or their identifiable data, can proceed. For example, the mDOT Center works closely with the University of Memphis (UofM) Institutional Review Board to facilitate appropriate reviews, such as reliance agreements, across sites performing human subjects research. Additionally, the Institutional Review Board (IRB) and the UofM Office of Sponsored Programs support the review and execution of data-sharing agreements to further facilitate research activities while also ensuring appropriate chain-of-custody for shared human subjects data across research sites. The mDOT Center also coordinates IRB activities across sites to ensure appropriate documentation from the institution(s) of record are recorded and transmitted to sites performing various levels of research, including activities involving living human subjects, identifiable data from living human subjects, or data that are coded, de-identified, and/or used for secondary analyses. The mDOT Center's experience in facilitating data sharing across different categories and institutions is rooted in years of crafting policies and reviewing different institutional procedures from the MD2K Center of Excellence project to the present date.

In Year 3, the mDOT Center continued these activities to ensure the flow of study data between CP sites to allow for research coordination, management, analyses, and writing of scientific papers.

Activity 1.6. Authorized data access procedures of research data from CPs by TR&D investigators. Via the ongoing execution of our mDOT data management plan, mDOT administrative staff were both proactive and responsive to data access queries and needs across Center constituents. Investigators with a need-to-know for data from requisite research studies have been considered in the formulation of protocols and informed consent documents for those studies. The consideration for other (i.e., external) investigators to access study data has also been considered, with additional procedures proactively built in place such as IRB reliance agreements, institutional data sharing agreements, de-identification, and other mechanisms to protect the privacy and confidentiality of human subjects data used for research. Our years of experience in managing these needs – the flow of data across investigators and the careful attention to data access procedures – has allowed for a balance between these sometimes competing interests and allows for rapid and reflexive consideration of best practices to best allow for the research and data sharing needs to be appropriately met.

Activity 1.7. Major Revisions to the Executive Advisory Committee review process. The mDOT Center investigators and EAC convened last Fall and determined that both wanted to change the current process of the formal Executive Advisory Committee review that is submitted as part of the RPPR. It was decided that instead of multiple, individual presentations to EAC members that are tailored to their expertise, the EAC will review the entirety of the Center as a group in a 3-hour block, allowing for a clearer, overall picture of the Center's progress and facilitating the EAC to play off of each other's comments and advice. The new process has the Admin team presenting a preliminary version of relevant portions of the RPPR) to the EAC members a week in advance of the review. This gives each EAC member a foundational understanding of where the mDOT Center and each of its components are currently and an idea of what they are looking to accomplish going forward. This also allows the investigators to prime the EAC with discussion topics for their respective review blocks and provides the EAC members an avenue to let the investigators know in advance any questions they may have prior to the review. On the day of the review, the expectation is that the EAC members have read the technical review, submitted any questions for discussion to the mDOT Center team in advance, and are aware of the discussion topics proposed by the investigators leading into the review. Each TR&D Lead, the Center Director (representing the Admin Core), and the Training Core Lead, each have a dedicated session where they give a brief summary of achievements over the past year, provide a roadmap for the upcoming year, but utilize the bulk of their time to have a future-thinking discussion with the EAC, as opposed to the report-based presentation method that was previously employed. A final portion of the block is a closed session to let the EAC talk among themselves, compile their thoughts, and create their report at the conclusion of the review day. The report that is created is submitted to the RPPR along with our responses.

Principal Investigator: Kumar, Santosh

Activity 1.8. Leveraging Institutional Support. The mDOT Center administrative team successfully retained and employed institutional support for the project, securing dedicated space, staff assistance, and operational funding crucial for achieving the research goals set by the investigating team. The University of Memphis played a pivotal role, offering substantial resources to ensure the smooth functioning of the mDOT Center. Housed within the University's FedEx Institute of Technology, the Center's Administration Core and operations hub occupied a dedicated office suite and included a student research lab. Supplementary to the Administration Core budget, non-federal funds were allocated by the University to cover salaries and benefits for professionals handling business management, administration, training, and communications, all deeply committed to driving Center activities. Despite limited direct grant funding, the mDOT Center successfully garnered institutional support to secure full-time engagement of essential personnel like operations directors, software staff, training specialists, and research coordinators. This cohesive administrative team was instrumental in effectively engaging and supporting numerous CPs and SPs, investigators, and student researchers. Furthermore, the Center enjoyed access to a range of centrally provided services including grants accounting, research development, research compliance staff, as well as expertise in legal matters, technology transfer, and human resources – collectively enhancing the efficiency of operations and overall project success.

Activity 1.9. Impact Measurement and Evaluation. To have maximum scientific and societal impact, the mDOT Center has developed quantifiable measures and implemented systems to monitor, assess, and evaluate the quality and utility of mDOT Center products, and continuously improve by systematically securing feedback from collaborators and community stakeholders. Leveraging the successful approach of other large-scale and center-level projects, each core has its own specific set of metrics. Metrics for measuring administrative tasks include the number of telecons scheduled, the number of documents produced, and number of in-person meetings organized. Administrative efficiency metrics typically include satisfaction with administrative support services and processes, collected informally throughout the year and via a dedicated session during the annual meeting. Another important metric tracked by the Administration Core is personnel advancement. Placement of graduate students, tenure & promotion, and important awards received by mDOT Center personnel, as well as its affiliate members, are also reported in Section G of the RPPR.

Activity 1.10. mHTI administration. The primary offering of the training core was the hosting of the weeklong mHealth Training Institute (mHTI) in-person boot camp in Los Angeles, CA in July 2023 combined with a virtual session in the preceding two months. The mHTI scholars were presented with an all-virtual didactic core consisting of pre-institute lectures, webinars, and mentored sandboxes. The Memphis team was instrumental in the hosting, setup, and backend administration of the virtual portions of the institute. This entailed the creation and deployment of a team collaborative spaces (Google Drive), a comprehensive, online application management system (SmarterSelect), a Lecture and Media Library (YouTube), and an informative and dynamic home page for the event participants (mHTI.md2k.org). In addition to the event management and virtual setup, the Memphis team was responsible for scheduling and communication for both scholars and faculty, collaborative environment setup (Zoom rooms, Google Drive Folders, Document Archive creation, etc.), and providing live, responsive technical support and troubleshooting support. The virtual portion 2023 mHTI was conducted between April 10 and June 26, 2023. (https://mhti.md2k.org/index.php/program/2023-program).

Activity 1.11. New Service Projects (SPs). The mDOT Center added two new Service Projects in Year 3. Our process for vetting and admitting a new CP/SP was rigorous to ensure “fit” within the mDOT Center research mission and need within the temporally-precise mHealth intervention community. Our TR&D2 Lead, Dr. Susan Murphy, recognized a synergy with a recently awarded R01 and a clinical trial using digital health interventions that were headed by former research colleagues at Northwestern University and Harvard University respectively. A one-page proposal for each potential SP was introduced by Dr. Murphy to the mDOT Center Executive Committee. The Executive Committee, consisting of Center Leadership, reviewed the merits of the potential collaborations.

After vetting from the mDOT Center Executive Committee it was determined that both would be good candidates for an SP spot. From there, the SP proposals were brought by the Center Director to the Executive Advisory Committee (EAC) for their review and final recommendation and upon their approval, submitted to the NIH program officer for her review and final approval.

Project Title	PI Name	Affiliation	Grant Number	Contact Info
SP7 - Toward Optimizing Digital Mental Health Interventions: A Clinical Trial Aimed at Understanding What Drives Patient Engagement	Dr. Jessica M. Lipschitz	Harvard University; Brigham and Women's Hospital	K23MH120324; NIH/NIMH; 4/9/2020 – 3/31/2025	jlipschitz@bwh.havard.edu
SP8 - A Micro-Randomized Trial to Optimize Just-in-Time Adaptive Intervention for Binge Eating & Weight-related Behaviors	Dr. Andrea K. Graham	Northwestern University; Feinberg School of Medicine	R01DK133300; NIH/NIDDK; 8/1/2022 – 5/31/2027	andrea.graham@northwestern.edu

Activity 1.12. Successful Transfer of Grant Sub Award. In Project Year 3, the Admin Team undertook the pivotal task of transferring the sub award from one academic institution to another. There was a performance site change from Georgia Institute of Technology to the University of Illinois Urbana-Champaign (UIUC) in the middle of the project period when TR&D1 Lead and Deputy Center Director Dr. James Rehg accepted a new position at UIUC as a Founder Professor with joint faculty appointments in the Departments of Computer Science and Industrial & Enterprise Systems Engineering and the new director of the Health Care Engineering Systems Center (HCESC). The retention of Dr. Rehg and the relocation to the UIUC as a performance site ensured a seamless transition of his current research responsibilities and mitigated any negative impact on mDOT Center collaborations and progress. Throughout the process, the Admin Team thoroughly reviewed the grant agreement, opened channels of communication between the Prime Institution (Memphis), Georgia Tech, and UIUC, and facilitated discussions to create a collaborative atmosphere, ensuring that all stakeholders were aligned in their objectives. The transfer of funds, project data, and personnel records was handled with precision. Administrative hurdles were expertly navigated, and the bureaucratic hurdles were streamlined to avoid any disruptions. Throughout the transition, the Administration Team served as a resource for researchers and staff involved, providing guidance and support, addressing concerns, and facilitating a smooth transition process.

There were challenges with the timely execution of some sub agreements in Year 3 due mostly in part to residual pandemic-related staffing gaps at the administrative levels at the various institutions. The mDOT Center requested a change in responsibilities at the institutional level while amending its own internal procedures to help facilitate a more responsive process to deliver the promptest service from our team in future scenarios.

B.2.2. Specific Objectives

Principal Investigator: Kumar, Santosh

The objective of the Administration Core is to provide the managerial and operational structures through which the mDOT Center will achieve its research, training, and dissemination goals. As described above, these objectives are articulated in the five specific aims.

B.2.3. Significant Results

Institutional Support. In the first three years, University of Memphis (the prime awardee) has invested over half a million (+$560,000) towards the operation of the mDOT Center that includes staff salaries, honorariums for the Executive Advisory Committee (EAC), and hosting of the annual meeting, among others.

New Service Projects (SP7 & SP). We expanded the service projects for the mDOT Center by two in Year 3 and will enhance their research being done through the work being done in TR&2. SP7 - Toward Optimizing Digital Mental Health Interventions: A Clinical Trial Aimed at Understanding What Drives Patient Engagement is led by Dr. Jessica M. Lipschitz at Harvard University and funded by NIMH through 2025. The focus of this project is to investigate strategies to enhance patient engagement in digital mental health interventions for individuals with depression and anxiety while testing the effectiveness of automated motivational push messaging and light-touch human coach support and the impact of their delivery frequency and context. SP7 is interested in the personalization algorithms proposed by TR&D2, in particular, the use of these stochastic algorithms to determine the randomization probabilities in the MRT. Further SP7 is very interested in using the pJITAI toolbox when fully developed. If the TR&D algorithms are demonstrated to be robust, SP7 would be potentially interested in including extra participants to conduct a feasibility study for use in informing SP7's future research.

SP8 - A Micro-Randomized Trial to Optimize Just-in-Time Adaptive Intervention for Binge Eating & Weight-related Behaviors is led by Dr. Andrea K. Graham at Northwestern University and funded by an NIDDK R01 through 2027. The focus of this project, called "FoodSteps", is to be the first intervention for both obesity and binge eating, delivered by a mobile device to increase scalability with integrated key mechanisms of behavioral and psychological treatments and provide a personalized medicine approach that intervenes on five evidence-based treatment targets. SP7 is interested in the algorithms proposed by TR&D2, in particular, the pJITAI toolbox when ready as well. If the TR&D algorithms are demonstrated to be robust, then SP7 would be potentially interested in delivering the pJITAI to participants in the trial, as applied to the MRT that is the focus of the trial or another MRT that we could design and implement within the trial to enhance engagement and completion of behavioral strategies (e.g., prompts to users to document in the app when they practice skills), for use in informing the SP7's future research.

B.2.4. Key Outcomes & Other Achievements

Mobile Open Observation of Daily Stressors (MOODS) Study: We completed several rounds of data collection using the MOODS software platform, developed by the mDOT Center in Year 2. With appropriate IRB oversight, we enrolled and successfully onboarded 136 participants in this all-virtual study. To date, we have collected approximately 65,000 hours of sensor data. Accompanying these sensor data are 26,732 total annotated stress/non-stress events, with 11,222 total stressors recorded by participants. Included in these participant descriptive statistics, in 2023 we implemented a sub-cohort of participants to participate in a modified MOODS protocol that did not present certain stress information in the study app, allowing us to further examine how stress and stressor detection may inform bias or interventional response to participating in an observational study of this type. We are preparing several manuscripts for publication from this study, and expect the disseminated results to be impactful across several scientific domains, including behavioral, mHealth interventional, and computational science.

Software Support for the MOODS Study: The Memphis team provided essential technical support for the all-virtual MOODS study. The team focused on troubleshooting, development enhancements, and bug fixes to ensure the app's smooth performance. Troubleshooting involved identifying and addressing technical challenges on the fly, guaranteeing uninterrupted user experiences. We delved into intricate software components to maintain functionality, including upgrading the SDK versions and libraries to be compliant with App and Play stores.

Development support efforts included refining existing features and optimizing overall performance to align with evolving research needs. Bug fixes were rigorously executed through meticulous examination of user feedback and error logs. Our systematic testing and validation processes significantly improved app stability.

MOODS Software Licensing. In Year 3, an intellectual property agreement was filed with the University of Memphis Office of Technology Transfer regarding the MOODS software that consists of a Wear OS smartwatch app, a cross-platform smartphone app, and cloud services. This application governed the intellectual property resulting from the software development, testing, and deployment used in the MOODS study.

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mDOT Center Personnel Status & Acknowledgements

INVESTIGATOR	CHANGE IN STATUS/RECOGNITION	DATE
Dr. Tim Hnat	Went on to co-found and become Chief Technical Officer for the mHealth startup CuesHub	February 2023
Dr. Anand Tirtha	Joined a health startup Thalamus GME	July 2023
Dr. Nasir Ali	Joined Apple as a software engineer	April 2023

Principal Investigator: Kumar, Santosh

mDOT Center ADMINISTRATION

B.4. What opportunities for training and professional development has the project provided?

All personnel working on the project learn about their own domains and collaborating domains via regular communication and collaborative research activities. In addition, they learn critical team science skills via the interdisciplinary collaborations among the investigative teams as well as by working closely with the health research team from our collaborative projects (CP). They get unique opportunities to test their ideas out by developing working software, getting regular feedback from CP investigators and their staff, and then getting to test their work in real-life deployment. All personnel also learn communication skills via regular presentations and discussions. Finally, they attend relevant conferences and professional meetings to communicate and network with other members of their research community.

As part of her on-the-job training, our training specialist is learning website development, HTML, and Joomla as part of the ongoing homepage redesign. This expansion of her skillset will ensure the cross training of the administration staff.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Other	An invention disclosure application was filed in Year 3 pertaining to the MOODS study software platform.

D. COMPONENT PARTICIPANTS

Not applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

A. COMPONENT COVER PAGE

Project Title: mDOT TR&D1 (Discovery) - Enabling the Discovery of Temporally-Precise Intervention Targets and Timing Triggers from mHealth Biomarkers via Uncertainty-Aware Modeling of Personalized Risk Dynamics	
Component Project Lead Information: Rehg, James M.	

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The past decade has seen tremendous advances in the ability to compute a diverse array of mobile sensor-based biomarkers in order to passively estimate health states, activities, and associated contexts (e.g. physical activity, sleep, smoking, mood, craving, stress, and geospatial context). Researchers are now engaged in the conduct of both observational and interventional field studies of increasing complexity and length that leverage mHealth sensor and biomarker technologies combined with the collection of measures of disease progression and other outcomes. As a result of the expansion of the set of available mHealth biomarkers and the push toward long-term, real-world deployment of mHealth technologies, a new set of critical gaps has emerged that were previously obscured by the focus of the field on smaller-scale proof-of-concept studies and the investigation of single biomarkers in isolation.

First, the issue of missing sensor and biomarker data in mHealth field studies has quickly become a critical problem that directly and significantly impacts many of our CPs. Issues including intermittent wireless dropouts, wearables and smartphones running out of battery power, participants forgetting to carry or wear devices, and participants exercising privacy controls can all contribute to complex patterns of missing data that significantly complicate data analysis and limit the effectiveness of sensor-informed mHealth interventions. Second, with increasing interest in the use of reinforcement learning methods to provide online adaptation of interventions for every individual, there is an urgent need for high-quality, compact and interpretable feature representations that can enable more effective learning under strict budgets on the number of interactions with patients. Finally, as in other areas that are leveraging machine learning methods to drive scientific discovery and support decision-making, mHealth needs methods that can be used to derive high-level knowledge and support causal hypothesis generation based on complex, non-linear models fit to biomarker time series data. TR&D1 will address these challenges via three specific aims:

Aim 1: Model and represent uncertainty in mHealth biomarkers to account for multifaceted uncertainty during momentary decision-making in selecting, adapting, and delivering temporally-precise mHealth interventions. This research will address the fundamental problem of missing sensor data by developing state-of-the-art deep probabilistic neural network imputation models for both raw sensor data and derived biomarkers. We will focus on developing reference imputation model architectures for widely used sensor data modalities including IMU, PPG, RIP, GPS, and key biomarkers including stress, steps, and cigarette smoking.

Aim 2: Derive uncertainty-aware composite risk scores to identify timing triggers for delivering temporally-precise interventions. This research will focus on compressing multiple biomarkers that serve as risk factors into personalized composite risk scores using novel recurrent neural network models that correctly account for biomarker uncertainty. We will develop methods for learning personalized risk models for a range of adverse events including smoking lapse, sedentary behavior, alert fatigue, and intervention disengagement. In conjunction with TR&D2, these novel risk scores will be used to drive temporally-precise adaptive interventions.

Aim 3: Model the time-varying dynamic relationships between personalized drivers of momentary risk and disease progression to identify targets of temporally-precise interventions. This research will begin to address the critical issue of providing model-based tools for identifying which potential risk factors actually impact risk in different contexts for different individuals, in order to support intervention design. To this end, we will develop methods and tools for introspecting the time-varying and contextual relationships between risk factors and risk scores learned by complex, non-linear risk-scoring models developed under Aim 2.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The primary mechanisms of dissemination have been technical papers and seminar talks.

Modeling uncertainty in irregularly sampled and incomplete multivariate time series - Our work on the BayesLDM toolbox was presented at the IEEE/ACM Conference on Connected Health Applications, Systems and Engineering Technologies (CHASE).

Two talks (one at Depression grand challenge workshop and another at mHealth Training Institute) covered the challenges and recent findings on improving the detection of stress from sensor data collected in the noisy field environment.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In Year 4, we will follow the following research thrusts:

● Towards fulfilling Specific Aim 1, we will submit a first manuscript on imputation methods for the All of Us research project data. This will include methods that address multi-time scale temporal dependencies. We will also release the source code for creating the benchmark data set we have built, which is not exposed by the All of Us research project cohort builder tool. We will subsequently investigate scaling the initial model to larger subsets of data and will investigate the extent to which the resulting models can generalize to new data sets, specifically, the HeartSteps II data set collected by CP3. We will begin working on imputation with uncertainty modeling in hierarchical biomarker computation graphs.

● Towards fulfilling Specific Aim 2, we will begin the development of composite risk scores for sedentary behavior and smoking lapse by leveraging advances in modeling the personalized drivers of risk factors and methods for improved uncertainty quantification.

● Towards fulfilling Specific Aim 3, we will submit a manuscript on personalized drivers of momentary stress. We plan to use the large-scale labeled data collected from field setting in the MOODS study to develop new models for stress detection that are more robust for the field settings, where prior field studies have shown marginal than chance performance. We will also develop new models to identify stressors upon the detection of stress.

● We will submit a manuscript on personalized drivers of momentary stress and a second manuscript on imputation-drive self-supervised learning of mHealth signal representations. We will explore uncertainty quantification methods. We will also explore the use of self-supervised learning to significantly improve the accuracy of risk prediction tasks related to momentary stress and smoking cessation. We will benchmark the potential to use large scale unlabeled waveform data to improve performance on mHealth applications.

Component Lead: Rehg, James

mDOT Center TR&D1 (Discovery):

Enabling the Discovery of Temporally-Precise Intervention Targets and Timing Triggers from mHealth Biomarkers via Uncertainty-Aware Modeling of Personalized Risk Dynamics

B.2 What was accomplished under these goals?

In Year 3, the TR&D1 undertook a variety of activities (as described below) to fulfill its goals.

Activity 1.1: ***Modeling uncertainty in irregularly sampled and incomplete multivariate time series***: Our goal in Aim 1 is to model and represent uncertainty in mHealth biomarkers to account for multifaceted uncertainty during momentary decision-making in selecting, adapting, and delivering temporally-precise mHealth interventions. In this period, we continued our work on modeling and imputing missing mHealth biomarkers. Our current focus is on the imputation of step count data at the hourly level as produced by ubiquitous off-the-shelf wearables including Fitbit devices. This work began with the analysis of missing step count data for the participants in CP3's HeartSteps II trial. We have since expanded this work to include data from the All of Us Research Project (SP1). This work has included setting up a project within the All of Us data enclave, processing the minute-level Fitbit data for over 10,000 All of Us participants, extracting an initial experimental cohort of 100 individuals and over 3,000,000 hourly step count observations. To date we have produced step count imputation results for multiple baseline methods including mean imputation, median imputation, forward filling, backward filling, linear regression imputation, K-nearest neighbor imputation, and multiple imputation by chained equations. We have also developed a custom self-attention-based model that outperforms all of these baselines and that we are continuing to refine with the goal of submitting an article describing this work by October 2023. Our plan is to close the loop with the data collected in CP3 by studying the ability of the model trained on the All of Us cohort to generalize to the HeartSteps II cohort. We expect that similar to Large Language Models, we may be able to learn a generalizable foundation model for step count imputation and forecasting if the training of the proposed model can be extended to the complete set of All of Us participants that have contributed Fitbit data.

- Vadera, Meet P; Samplawski, Colin; Marlin, Benjamin M: Uncertainty Quantification Using Query-Based Object Detectors. In: Computer Vision–ECCV 2022 Workshops, Part VIII, pp. 78–93, 2023.

Activity 1.2: ***Imputing Quasiperiodic Biophysical Signals***: In support of our Aim 1 goal we conducted additional investigation of the use of deep learning-based transformer models to perform imputation of pulsative biophysical signals such as ECG and PPG, which are defined by a quasiperiodic morphology. Using the PulseImpute dataset we created in Year 2, we conducted an investigation into the incorporation of uncertainty modeling into our Bottleneck Dilated Convolutional (BDC) architecture which has the highest imputation accuracy among competing methods but lacks the ability to quantify the uncertainty associated with imputation. We explored the incorporation of architectural elements from the Heteroscedastic Temporal Variational Autoencoder (HeTVAE), which represents input uncertainty via a sparsity-award layer in the encoder and decoder. We then investigated the self-attention weights within the BDC model as we observed empirically and mathematically that these weights exhibit characteristic patterns related to the sparsity pattern in the input signal. These investigations led us to develop a novel self-supervised approach to representation learning in Activity 3.2. Further development of uncertainty modeling in the context of hierarchical computation graphs is on-going.

- Xu, Maxwell, Alexander Moreno, Supriya Nagesh, Varol Aydemir, David Wetter, Santosh Kumar, and James M. Rehg. "PulseImpute: A Novel Benchmark Task for Pulsative Physiological Signal Imputation." Advances in Neural Information Processing Systems 35 (2022): 26874-26888.

Component Lead: Rehg, James

Activity 1.3: ***Self-Supervised Learning of Pulsative Signal Representations****:* A key challenge in model development is the sparsity of labels for mHealth signal data. While the quantity of available mHealth signal data continues to grow, the ability to collect large quantities of labeled examples of health outcomes is inherently limited, creating challenges for representation learning. We are developing a novel approach to self-supervised representation learning which leverages reconstruction error in imputation as a metric to identify positive and negative examples in a contrastive learning framework. We extract clips of pulsative waveforms and use the error metric to identify clips that are more or less similar. Training an embedding function using this similarity metric produces a feature representation that is surprisingly effective for downstream tasks. These findings are captured in a manuscript which will be submitted in October 2023.

Activity 1.4: ***Personalized Drivers of Momentary Stress (i.e., Stressors)****:* Our goal in Aim 3 is to understand the dynamic relationships between personalized drivers of momentary risk and disease progression to identify targets of temporally-precise interventions. This year, we completed the MOODS study with 122 participants who wore a study-provided Fossil Sport smartwatch with our MOODS app, installed our MOODS app on their personal smartphones, and used both apps for 100 days. They rated their stress 3-4 times daily and described the stressor for events they rated as stressful. They received new visualizations of their data each week. We analyzed the impact of the study on self-reported stress ratings and the diversity in stressors reported by the participants.

- Neupane, S., Saha, M., Ali, N., Hnat, T., Nandagudi, A., Samiei, S., Almeida, D., and Kumar, S., (Under Review) Momentary Stressor Logging and Reflective Visualizations: Implications for Stress Management with Wearables. ACM CHI 2024.

Summary of Push-Pull Activities with CPs:

CP1 (Nahum-Shani) & CP5 (Lam/Wetter): The CP1 and CP5 teams are specifically interested in risk prediction problems based on mobile sensors and EMA data to support novel interventions for smoking cessation. Rehg continued to work closely with the CP5 team on representation learning methods for pulsative signals as a means to address missing sensor data and learn effective representations for risk prediction in Activities 1.2 and 3.2.

- Chow, Sy-Miin; Nahum-Shani, Inbal; Baker, Justin T; Spruijt-Metz, Donna; Allen, Nicholas B; Auerbach, Randy P; Dunton, Genevieve F; Friedman, Naomi P; Intille, Stephen S; Klasnja, Predrag; others: The ILHBN: challenges, opportunities, and solutions from harmonizing data under heterogeneous study designs, target populations, and measurement protocols. In: Translational Behavioral Medicine, vol. 13, no. 1, pp. 7–16, 2023.
- Yang, M.J., Sutton, S.K., Hernandez, L.M., Jones, S.R., Wetter, D.W., Kumar, S. and Vinci, C., 2023. A Just-In-Time Adaptive intervention (JITAI) for smoking cessation: Feasibility and acceptability findings. Addictive behaviors, 136, p.107467.

CP3 (Klasnja): We are working closely with the CP3 team on learning missing data imputation models for FitBit step data (Activity 1.1). TR&D1 is continuing to provide modeling tools and inference results to further CP3's data analysis goals.

- Karine, Karine; Klasnja, Predrag; Murphy, Susan; Marlin, Benjamin: Assessing the Impact of Context Inference Error and Partial Observability on RL Methods for Just-In-Time Adaptive Interventions. In: Conference on Uncertainty in Artificial Intelligence (To Appear), 2023.

CP4 (Rivera): Marlin continued to work closely with the CP4 team to deploy the BayesLDM toolbox developed under TR&D1 in control systems-based data analytic workflows. The team collaborated on the development of an ARX model estimation method that uses multiple imputations provided by Bayes LDM, as well as an approach for estimating uncertainty in ARX step response functions due to both data scarcity and data missingness. The team is currently revising a manuscript describing this work.

- Tung, Karine; Torre, Steven De La; Mistiri, Mohamed El; Braganca, Rebecca Braga De; Hekler, Eric; Pavel, Misha; Rivera, Daniel; Klasnja, Pedja; Spruijt-Metz, Donna; Marlin, Benjamin M: BayesLDM: A Domain-specific Modeling Language for Probabilistic Modeling of Longitudinal Data. In: 2022 IEEE/ACM Conference on Connected Health: Applications, Systems and Engineering Technologies (CHASE), pp. 78–90, IEEE 2022.

CP8 (Nahum-Shani): We are working with CP8 to analyze and perform imputation for patterns of missingness associated with EMA data. We are developing standard software implementations of imputation methods for dissemination to the community and benchmarking them against standard methods.

B.2.2. Specific Objectives

Based on the research conducted under the above aims, TR&D1 will produce toolboxes and cloud-based data analysis tools for missing data modeling and imputation, uncertainty-aware personalized risk scoring, and introspection of complex risk scoring models. These tools will address critical gaps in the current mHealth technology landscape and will provide transformative capabilities for both advancing the understanding of health and behavior and for supporting the design of temporally-precise, sensor-based mHealth interventions.

B.2.3. Significant Results (inlcuding major findings, developments, or conclusions both positive and negative)

UMASS

Activity 1.1: *Modeling uncertainty in irregularly sampled and incomplete multivariate time series* - The UMass team has constructed a new large-scale testbed for mHealth imputation research leveraging Fitbit data from the All of Us research project. The team is currently using a 100-participant, 3,000,000-hour subset of these data to support model development and plans to expand to use all of the data over the coming year.

GT/UIUC

Activity 1.2: *Self-Supervised Learning of Pulsative Signal Representations*: We have developed a novel approach to contrastive learning for pulsative mHealth signal types such as ECG and PPG. In domains such as image analysis, the adoption of self-supervised learning has provided a major breakthrough making it possible to learn effective representations without massive amounts of labeled examples. The translation of these approaches to the analysis of time series data has proved to be challenging. Our approach leveraging imputation error as a similarity measure provides a novel approach to self-supervised learning which could lead to more effective representation learning and risk prediction models.

Component Lead: Rehg, James

Memphis

Activity 1.4: ***Personalized Drivers of Momentary Stress (Stressors)****:* We analyzed 26,521 self-reports of stress ratings and 11,222 stressors collected in the MOODS study. We report several findings from our analysis. First, we found substantial diversity in reported stressors. Despite having 80 stressors (from the literature) to select from, participants reported over 1,000 new stressors. Second, we found that self-reflection by the act of logging their stressors and visualizing patterns in their self-reported stress and stressors each week led to a significant reduction in stress from pre-study to post-study along with both reported severity of stress and the weekly reports of the frequency of stressful events. Third, we found that self-reflection resulted in increasing the awareness of participants to identify their dominant stressors, time, and place. Fourth, we found that increased awareness led many participants to self-initiate changes in their daily behaviors and develop new coping mechanisms. The actions that participants took led to a reduction in their stress, confirmed by their data using interrupted time series analysis. Fifth, we find a wide diversity in the actions undertaken by the participants to reduce their stress. It implies a need to expand the diversity in interventions for stress and a need to match the intervention to the source of stress. Finally, the study showed a high utility of such mHealth technologies that can allow participants to log and reflect on their own data. In contrast with a 30-day retention rate of 3.3% in mental health apps, the MOODS study had a 30-day retention rate of 81% despite the participants having to use an old smartwatch with 6 hours of battery life. These findings were submitted to ACM CHI'24.

B.2.4. Key Outcomes & Other Achievements

- Our work with the All of Us research project data was awarded $5,000 in Google Cloud credits to support the conduct of the research with Google Cloud-based the All of Us research project data enclave.

mDOT Center Personnel Status & Acknowledgements

INVESTIGATOR	CHANGE IN STATUS/RECOGNITION	DATE
Dr. Md Azim Ullah (Memphis)	Graduated with PhD; Joined Amazon as an Applied Scientist with the AWS Pinpoint Data & Machine Learning Team	May 2023
Dr. Sayma Akther (Memphis)	Graduated with PhD; Joined San Jose State University as an Assistant Professor in the Department of Computer Science	July 2023

TR&D1 - Discovery	Books	Papers	Abstracts
Number Published	0	10	0
Number in Press	0	7	0
Number in Submission/Review	0	3	0

Component Lead: Rehg, James

mDOT Center TR&D1 (Discovery):
Enabling the Discovery of Temporally-Precise Intervention Targets and Timing Triggers from mHealth Biomarkers via Uncertainty-Aware Modeling of Personalized Risk Dynamics

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B.4. What opportunities for training and professional development has the project provided?

At UMass Amherst, one student received training in the development of machine learning methods for incomplete and irregularly sampled data. This student participated in telecons with CP3 and CP4 investigators as well as in mDOT Center telecons. At Georgia Tech, one Ph.D. student and one undergraduate student received training in the development of machine learning methods for mHealth data. The student participated in meetings with CP5 investigators as well as center meetings and telecons. In Memphis, in addition to growing their core computational skills via weekly group meetings and presentations, two graduate students received training in multidisciplinary collaboration by engaging with experts in stress and stressors research from Penn State.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Software	https://moods.md2k.org/ For the MOODS study, a Wear OS app for smartwatches, a cross-platform smartphone app, and a cloud service was developed and deployed. It was used by 122 participants for up to 173 days.
Research Material	https://moods.md2k.org/ For the MOODS study, a Wear OS app for smartwatches, a cross-platform smartphone app, and a cloud service was developed and deployed. It was used by 122 participants for up to 173 days.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. COMPONENT PARTICIPANTS

Not applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

A. COMPONENT COVER PAGE

Project Title: mDOT TR&D2 (Optimization): Dynamic Optimization of Continuously Adapting mHealth Interventions via Prudent, Statistically Efficient, and Coherent Reinforcement Learning
Component Project Lead Information: MURPHY, SUSAN A

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Mobile health (mHealth) interventions have typically used hand-crafted decision rules that map from biomarkers of an individual's state to the selection of interventions. Recently, reinforcement learning (RL) has emerged as a promising approach for online optimization of decision rules. Continuous, passive detection of the individual's state using mHealth biomarkers enables dynamic deployment of decision rules at the right moment, i.e., as and when events of interest are detected from sensors. RL-based optimization methods that leverage this new capability created by sensor-based biomarkers, can enable the development and optimization of temporally-precise mHealth interventions, overcoming the significant limitations of static, one-size-fits-all decision rules. Such next-generation interventions have the potential to lead to greater treatment efficacy and improved long-term engagement.

However, there exist several critical challenges to the realization of effective, real-world RL-based interventions including the need to learn efficiently based on limited interactions with an individual while accounting for longer-term effects of intervention decisions, (i.e., to avoid habituation and ensure continued engagement), and accommodating multiple intervention components operating at different time scales and targeting different outcomes. As a result, the use of RL in mHealth interventions has mostly been limited to very few studies using basic RL methods.

To address these critical challenges, TR&D2 will build on more precise biomarkers of context, including TR&D1 risk and engagement scores, to develop, evaluate, and disseminate robust and data-efficient RL methods and tools. These methods will continually personalize the selection, adaptation and delivery timing decision rules for core intervention components so as to maximize long-term therapeutic efficacy and engagement for every individual. TR&D2 will address these challenges via the following three specific aims:

Aim 1: Accounting for delayed treatment effects via prudent learning of decision rules. Generalize current myopic Bandit RL methods to enable learning non-myopic decision rules that account for delayed intervention effects. A particular focus is delayed effects due to intervention burden.

Aim 2: Efficient personalization via optimizing data sharing across users. Develop RL methods that personalize decision rules for every individual by optimally leveraging data across a population or cohort to accelerate learning. We will further develop RL methods to facilitate the analysis of the resulting data, taking into account the additional correlation structure that results from partial between-person sharing of data during learning.

Aim 3: Coherent learning of decision rules across intervention components operating at different time scales and with different objectives. Increasingly, mobile interventions include multiple components targeting different outcomes (e.g., stress, inactivity) and time scales (e.g., within day, daily). We will develop approaches to use distal health outcomes to guide learning for these multiple components, so as to minimize negative interactions.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File Uploaded : B.2. - TR&D2 YEAR 3 RPPR.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File Uploaded : B.4. - TR&D2 YEAR 3 RPPR.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The primary mechanisms of dissemination have been technical papers and seminar talks.

pJITAI Website development: https://github.com/mDOT-Center/pJITAI. The establishment of a dedicated website for the pJITAI project stands as a significant milestone in our efforts to move the project forward, disseminate findings, and foster collaboration within the research community. Throughout Year 3, bug fixes were made to the pJITAI platform, enhancements were made to the user interface, and new features were added to the website based on user feedback. Primary among these new features was displaying the calculated probability of delivering an intervention based on the parameters used for the study. In addition, the pJITAI backend was further developed to collect and analyze data based on the parameters configured for the user study. Other notable features include support for the client to upload data, validation of that data, and multiple RL algorithms; executing the algorithm periodically (configured from the study) for updating the model on new data; and an exposed API so that the client can pass parameters and query the algorithm for the intervention probability. As it stands, the present version of the pJITAI website is ready for an internal user study. Once a proposed transition from the Memphis-based cloud server is handed off to the University of Michigan, then a pilot study is scheduled to be launched in project Year 4.

pJITAI Library development: https://github.com/mDOT-Center/pJITAI. The initiation of a dedicated GitHub repository marks a pivotal step in fostering collaborative development and version control for the pJITAI project. The repository serves as a centralized hub for storing, managing, and tracking the evolution of project code, scripts, and software tools. This facilitates seamless collaboration among project members, streamlining the process of code integration, debugging, and enhancement. The repository's branching and versioning capabilities enable the team to work concurrently on different aspects of the project without compromising code integrity. It ensures that changes are tracked, reviewed, and merged in a controlled manner, bolstering the project's overall reliability. Furthermore, establishing the library underscores our commitment to transparent and efficient research development practices. By providing a structured environment for code sharing and collaboration, it empowers our team to collectively drive the project forward while maintaining a robust foundation for future innovation.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In Year 4, we will focus on the following research thrusts:

In Year 4, CP2 and CP8 will run clinical trials deploying our RL algorithms. These RL algorithms will pool data (Aim 2) across individuals to personalize intervention delivery. Further, both algorithms will be using approaches developed under Aim 1 to allow the RL algorithm to account for delayed effects. These trials will allow for the first real-life evaluations of the RL algorithmic research conducted under Aims 1,2. We aim to complete a Python and R package to provide confidence intervals and standard errors for use in primary data analyses conducted after the clinical trial is over. This package will be used by the Oralytics team. Further, because the MiWaves RL algorithm uses a mixed effects model, we need to generalize our prior work on standard error development for use in the primary analyses for MiWaves.

Motivated by both the Oralytics RL project and the MiWaves project, we aim to finish the development of an online RL monitoring system that will act as a template for other researchers.

We will continue to work (in collaboration with Drs. Klasnja and Nahum-Shani) on the toolbox. CP3 will conduct a user study that will then allow us to refine the toolbox. This toolbox will allow us to disseminate our RL algorithm developments more effectively. We aim to have a first version for use by health scientists and in particular our SPs this year.

We aim to start making greater progress on Aim 3, particularly with regard to the use of intermediate outcomes of treatments by the RL algorithm. This work will also involve generalizing RL algorithms to be able to accommodate both delayed observations of state and reward.

We will continue to work on integrating research themes from TR&D1 into TR&D2 by studying the effects of uncertainty on RL. The next step for the JITAI simulation environment that supports this work is to enhance the environment to model individuals with different characteristics. Further, we will shift focus from the study of classical RL algorithms that do not have realistic limits on total interactions with study participants to sample efficient algorithms based on enhanced versions of Thompson sampling that account for delayed effects.

Using the data collected in the MOODS study, we will develop a tool that study designers can use to select parameters necessary to optimize the number of prompts needed to catch participants in (high or low-stress) moments to test the efficacy of delivering various candidate JITAI's.

Component Lead: Murphy, Susan

mDOT Center TR&D2 (Optimization):
Dynamic Optimization of Continuously Adapting mHealth Interventions via Prudent, Statistically Efficient, and Coherent Reinforcement Learning

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B.2 What was accomplished under these goals?

B.2.1 Major Activities (include push-pull activities with CPs): In Year 3, the TR&D2 undertook a variety of activities (as described below) to fulfill its goals.

B.2.1.1. ***Activity 1: RL Algorithm***

<u>Development of RL algorithms (Aims 1,2) and inference from an MRT employing an RL algorithm (Aim 2)</u>: As was the case last year this research was motivated by and spurred on by our collaborations with CP2 and CP8. In particular, CP2 is now deploying our developed RL algorithm (Trella et al. 2023[1]) for improving dental health in the pilot phase. The full Oralytics trial is scheduled to start in this fall. The Oralytics RL algorithm includes the use of a reward function developed in Trella et al. (2023) with the goal of speeding up the personalization by the RL algorithm (Aim 1). We have submitted the trial design paper (Nahum-Shani et al., under review)[2]; this collaboration motivated us to develop a template for how RL designers can update the RL algorithm based on pilot data and RL designers can prospectively report their RL design in a clinical trial protocol[3].

As discussed last year, the Oralytics RL algorithm autonomously pools data across individuals to personalize the mHealth intervention to each individual. This pooling of data by the RL algorithm produces dependence between individuals (called "adaptive sampling"). To assess treatment effects in after study analyses we need a method for adjusting for this dependence. We developed statistical methods that adjust for this dependence; these methods provide confidence intervals for, and hypothesis testing concerning, treatment effects (Zhang et al[3]); this work is under review by a statistical venue.

This year we have been developing the MiWaves RL algorithm for cannabis reduction (CP8); this algorithm uses a more flexible approach to pooling data across participants. In particular, this new RL algorithm pools data across participants only to the extent that the participants respond similarly, thus if the accruing data indicates high heterogeneity between participants, then the algorithm will minimally pool their data in order to learn which intervention option to provide. To accomplish this, the MiWaves RL algorithm uses a classical tool from statistics (mixed effects models). The MiWaves trial is scheduled to be piloted in October 2023.

Also this year we have made the very first steps toward developing an RL algorithm for dyads (Li, et al)[4] (Aim 3). This is a very exciting new research direction. This work is motivated by our collaboration with CP8. In this case, the dyad is composed of a target person (here an adolescent/young adult who had a bone marrow transplant) and their care partner. In this setting, there are different sets of intervention options corresponding to whether the intervention option is for the target person or the care partner or, quite interestingly, for improving the social connection between the target person and care partner. These different sets of intervention options operate at different time scales (some over a week, others daily). To tackle this problem, we are using ideas from hierarchical RL.

Component Lead: Murphy, Susan

B.2.1.2. ***Activity 2: pJITAI Toolbox***

Designing an mDOT Center toolbox that health scientists can use to design their RL algorithm for use in conducting their mHealth study (All Aims; Dissemination): As discussed last year, this work is in collaboration with CP3 (physical activity). A beta version of the health scientist web interface is now complete, and we have IRB approval to begin conducting user studies (in this case the users are behavioral health scientists who are interested in using RL to personalize in a clinical trial). This work requires high-quality communication between students and postdocs in HCI & engineering as well as with software engineers. Furthermore, translating very technical ideas (methods for constructing RL algorithms) into language and guidelines that can be used by behavioral health scientists turns out to be very challenging. These communication challenges along with departures by the software engineering team made for slow progress. We are now in the initial stages of transferring the pJITAI toolbox to a University of Michigan consortium composed of CP3 & CP8 teams.

This work has motivated a collaboration with CP3 in which we have a draft paper for behavioral health scientists. This paper introduces the term "pJITAI" (aka, personalizing JITAI) and discusses at length the first RL algorithm that will be in the toolbox. This "Thompson-Sampling" algorithm is very popular in industry (e.g., personalization of ad placement, and recommendations). We aim to submit this paper to a behavioral science journal soon.

B.2.1.3. ***Activity 3: Stress-guided prompts***

Designing a new capability to decide when to trigger stress-related EMA's and Interventions (Aim 2): Using the data collected in the MOODS study conducted in collaboration with CP7, we are developing new methods and tools to guide the timing of when to generate prompts for stress-related interventions and EMA's in micro-randomized trials of stress interventions. Interventions for several health targets (such as stress management, smoking cessation, unhealthy eating, etc.) aim to deliver (low-effort) interventions at times of high stress and (capacity-building) interventions at times of low stress. But, these prompts are largely based on random or pre-scheduled prompts that ask participants to report their stress state and decide which intervention to deliver with what probability depending on their response. In the MOODS study, prompts were generated based on the detection of physiological events. Analysis of data collected in this 100-day study completed with 122 participants showed that using the likelihood with which our AI algorithm estimates the event to be stressful can reduce the number of prompts needed to catch participants in a stressful moment from 6 to 2 per day. We have initiated a new collaboration with stress experts at Penn State (Dr. David Almeida and Dr. Marty Silwinski) to develop a method and a tool using which future studies can decide a prompting schedule and probabilities to minimize the number of prompts needed to catch participants in high and low-stress moments. We are preparing a new submission to npj Digital Medicine.

Summary of Push Pull Activities with CPs:

CP2 (Shetty): We are extensively collaborating on the Oralytics trial (see above under B.2 Activity 1). This collaboration has resulted in one publication and four submitted papers. We also submitted an NIH grant application and we are waiting to hear about funding.

- A. Trella, K. Zhang, I. Nahum-Shani, V. Shetty, F. Doshi-Velez, and S. Murphy. Reward Design For An Online Reinforcement Learning Algorithm Supporting Oral Self-Care. *Accepted at IAAI 2023*
- I. Nahum-Shani, Z. M. Greer, A. L. Trella, K. W. Zhang, S. M. Carpenter, D. Ruenger, D. Elashoff, S. A. Murphy, V. Shetty (2023). Optimizing an adaptive digital oral health intervention for promoting oral self-care behaviors: Micro-randomized trial protocol. (Submitted)
- Carpenter S.M., Greer Z.M., Newman, R., Murphy, S.A., Shetty, V., I. Nahum- Shani. Engaging Racial and Ethnic Minorities in Digital Oral Self-Care Interventions: A Formative Research into Messaging Strategies. (Submitted)

Component Lead: Murphy, Susan

The following two papers are theoretical and focus on problems that arose in the development of the RL algorithm for Oralytics. In the first paper (Guo and Murphy) we consider the setting in which a prediction (i.e, in Oralytics this would be a prediction of future engagement) is used to assist in describing the state of a participant. In the second paper (Gan et al.) we consider the setting in which the participant needs to take "pro-treatment actions." These are behaviors that provide information needed by the RL algorithm to make decisions. In the context of Oralytics, due to budgetary constraints, if the participant does not open up the app then the cloud server cannot deliver the treatment decisions for the next day. As a result, the scientific team has a protocol whereby staff members contact participants if they have not opened the app for a pre-specified period of time.

- Guo, Y., S. Murphy. Online Learning in Bandits with Predicted Context. (Submitted)
- Gan, K., Keyvanshokooh, E., Liu, X., S. Murphy. Contextual Bandits with Budgeted Information Reveal. (Submitted)

CP3 (Klasnja): Collaborations with CP3 have occurred across multiple areas. In close collaboration with CP3 PI Klasnja, Marlin and Murphy worked on the development of a JITAI simulation environment inspired by components of the HeartSteps II intervention. The simulation environment models steps as a measure of physical activity. It includes habituation and disengagement risk variables, which are hypothesized to have important impacts on the efficacy of the HeartSteps intervention, but that were not assessed in the HeartSteps II trial. Inspired by aspects of the Sense2Stop intervention (PI Spring), the simulation environment also models a noisy machine learning-based binary stress state classifier. Similar to the Sense2Stop intervention, the simulated output of the stress classifier is used as the primary tailoring variable for a simulated messaging-based intervention. Four actions are modeled: do not send a message, send a non-tailored message, send a message tailored to the stress state, and send a message tailored to the no-stress state.

This simulation environment was designed to support the assessment of the impact of machine learning-based state estimation error and uncertainty on the ability for reinforcement learning methods to learn performant JITAI intervention option selection policies. It was also designed to study the impact of latent variables on reinforcement learning algorithms by selecting whether or not habituation and disengagement risk are observed. In (Karine et al), we present the results of multiple experiments using this simulation environment. We quantify the decrease in policy performance as state estimation uncertainty is increased and we further show that this drop in performance can be partially mitigated by conditioning policy learning directly on state probabilities instead of most likely states. Further, we show that state-action value function-based reinforcement learning methods are significantly outperformed by policy gradient methods under partial state observability.

Further, motivated by our use of an RL algorithm across multiple HeartSteps studies, we developed a variety of "post-mortem" analyses (Ghosh et al.) aimed at a close inspection of the implemented RL algorithm. These methods can be used to reduce false claims of personalization as well as used between studies to help inform revisions to the RL algorithm. In the following two papers we develop methods for analyzing data resulting from the use of an RL algorithm. A second paper (Saengkyongam et al) develops causal inference approaches to learning when an RL algorithm implemented on one population might be useful in warm-starting an RL algorithm for another population. This work was motivated by the fact that earlier HeartSteps studies involved individuals newly diagnosed with stage 1 hypertension whereas CP3 is using HeartSteps on individuals who are obese.

We also submitted an NIH grant application which received an excellent score. If funded, we will be able to add a new CP.

- K. Karine, P. Klasnja, S. Murphy and B. Marlin Assessing the Impact of Context Inference Error and Partial Observability on RL Methods for Just-In-Time Adaptive Interventions. Accepted at UAI 2023
- Ghosh, S., Kim, R., Chhabria, P., Dwivedi, R., Klasnja, P., Liao, P., Zhang, K., S. Murphy Did we personalize? Assessing personalization by an online reinforcement learning algorithm using resampling. (Submitted)

Component Lead: Murphy, Susan

- Saengkyongam S., Pfister N., Klasnja P., Murphy S., Peters J. (2023). Effect-Invariant Mechanisms for Policy Generalization. (Submitted)

CP4 (Rivera): Marlin continued to collaborate closely with PI Rivera's group on CP4, as well as through CP3 where Rivera is also an investigator. This collaboration has resulted in the integration of methods from the BayesLDM toolbox into several parts of PI Rivera's work. His team investigated integrating model-based missing data imputation methods into the the Just Walk intervention and have also integrated model-based imputation methods into control system engineering-based analysis procedures including ARX model order estimation and the computation of ARX model step response functions. A paper on these methods is currently under revision.

CP8 (Nahum-Shani): We are extensively collaborating on the MiWaves trial (see above under B.2 Activity 1).

- L. Collins, I. Nahum-Shani, K. Guastaferro, J. Strayhorn, D. Vanness, S. A. Murphy (2023). Intervention optimization: A paradigm shift and its potential implications for clinical psychology. (Submitted)
- S. Li, L. Salvat Niell, S. Choi, I. Nahum-Shani, G. Shani, S. Murphy (2023). Dyadic Reinforcement Learning. (Submitted)

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1. A. Trella, K. Zhang, I. Nahum-Shani, V. Shetty, F. Doshi-Velez, and S. Murphy Reward Design For An Online Reinforcement Learning Algorithm Supporting Oral Self-Care. Accepted at IAAI 2023
2. I. Nahum-Shani, Z. M. Greer, A. L. Trella, K. W. Zhang, S. M. Carpenter, D. Ruenger, D. Elashoff, S. A. Murphy, V. Shetty (2023). Optimizing an adaptive digital oral health intervention for promoting oral self-care behaviors: Micro-randomized trial protocol. (Submitted)
3. K. Zhang, L. Janson, S. Murphy Statistical Inference After Adaptive Sampling for Longitudinal Data. (Submitted)
4. S. Li, L. Salvat Niell, S. Choi, I. Nahum-Shani, G. Shani, S. Murphy (2023). Dyadic Reinforcement Learning. (Submitted)

B.2.2. Specific Objectives

TR&D2 will address three key limitations of current online reinforcement learning (RL) when applied to personalize mobile interventions to individuals. Two of these limitations are related to the need to increase efficacy and reduce negative delayed intervention burden effects leading to disengagement. The third looks to future needs involving the personalization of multiple intervention components each operating at a different time scale. In particular, the mDOT Center will accommodate the ever-present mobile health challenge of user disengagement by developing a continuum of approaches between RL algorithms that ignore delayed intervention effects and RL algorithms that attempt to capture noisy delayed intervention effects over a more distant future. Second, the mDOT Center will increase the rate at which personalization occurs via optimally leveraging data across time and across users to more quickly personalize the interventions to each user. Third, the mDOT Center will develop the first RL approaches to coherently personalize multiple intervention components holistically. In addition, to enhance impact and dissemination, the methods will be developed in close collaboration with designated collaborative projects (CPs) with an emphasis on model interpretability. TR&D2 will create a toolkit for online intervention optimization that will include cloud-based modules for personalizing adaptation rules as well as smartphone modules implementing real-time intervention selection. TR&D2 will also produce a reference tutorial for use of the online intervention optimization toolkit. Both tools will be implemented within the mDOT Center software framework and will enable a broad segment of the mHealth research community to continuously optimize mHealth intervention rules, to achieve optimal efficacy and engagement for individuals despite dynamic variations in the physical, behavioral, social, & environmental states.

Component Lead: Murphy, Susan

B.2.3. Significant Results (including major findings, developments, or conclusions both positive and negative)

HARV

- Our most significant result has been the completed Oralytics RL algorithm. This work has led to a number of templates that our lab can use and (in the case of MiWaves) is using to enhance the replicability and stability of online, real-time use of RL in clinical trials for personalizing mHealth interventions. Moreover, we made critical first steps on methods for post-mortem analyses to enhance truth-in-advertising when an RL algorithm is used for personalization.

UMASS

- Our recent simulation study on assessing the impact of context inference error and uncertainty on classical RL algorithms has provided one of the first links between the performance of machine learning-based state estimation methods and the performance of RL policies learned using estimated state. Our results suggest that constructing JITAI policies that directly condition on state probability distributions instead of most likely inferred states can help to mitigate the otherwise negative effects of noisy state estimates.

Memphis

- We completed the MOODS study with 122 participants in which participants wore a study-provided Fossil Sport smartwatch with our MOODS app, installed our MOODS app on their personal smartphones, and used both apps for 100 days. They rated their stress 3-4 times daily and described the stressor for events they rated as stressful. Using 26,521 self-reports of stress ratings, we have found that using the stress likelihood produced by the MOODS smartwatch app, the number of prompts needed to catch participants in a stressful moment can be reduced from 6 to 2 per day. The description of methods and tools to design a prompting schedule is being prepared for submission to npj Digital Medicine journal.

B.2.4. Key Outcomes & Other Achievements

Susan Murphy	Graduate student Kelly Zhang has graduated and has taken up a postdoctoral position at Columbia Business School	8/1/2023	
Susan Murphy	Postdoc Kyra Gan left to take up an assistant professorship at Cornell Tech	7/1/2023	
Susan Murphy	Postdoc Yongyi Guo left to take up an assistant professorship at UW-Madison	8/15/2023	
Susan Murphy	Postdoc Raaz Dwivedi left the lab to take up an assistant professorship at Cornell	8/17/2023	
Susan Murphy	Postdoc Ziping Xu joined the lab	8/1/2023	
Susan Murphy	Postdoc Daiqi Gao joined the lab	8/1/2023	
Susan Murphy	grad student Nowell Closser joined the lab	6/1/2023	
Benjamin Marlin	Marlin gave the opening keynote at the Machine Learning for Health Conference on the topic of Uncertainty and Adaptive Interventions.	8/10/2023	

Component Lead: Murphy, Susan

TR&D2 - Optimization	**Books**	**Papers**	**Abstracts**
Number Published	**0**	**21**	**0**
Number in Press	**0**	**5**	**0**
Number in Submission/Review	**0**	**16**	**0**

Component Lead: Murphy, Susan

mDOT Center TR&D2 (Optimization):

Dynamic Optimization of Continuously Adapting mHealth Interventions via Prudent, Statistically Efficient, and Coherent Reinforcement Learning

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B.4. What opportunities for training and professional development has the project provided?

Murphy runs weekly brainstorming sessions through her lab at Harvard. At these brainstorming sessions, a postdoc or graduate student in the lab presents a research idea and everyone in the lab brainstorms about how to help that person. Brainstorming sessions are also run with health scientists. An important aspect of the brainstorming is that attendees learn to present their ideas concisely and to communicate across disciplinary boundaries. Attendees include computer scientists, electrical engineers, operations research scientists, statisticians and health scientists. Further, Murphy and two of her postdocs taught a summer course in RL for mHealth at the StatML CDT Summer School in England. Murphy also presented in the mHealth Training Institute 2023 (see mHealth Training Institute - 2023 Program (md2k.org)).

Marlin and Murphy are also jointly mentoring one student at UMass Amherst who is working on Activity 3 listed under section B.2. They meet with the student biweekly along with CP3 PI, Klasnja. These opportunities provide the student with training in RL applied to behavioral science as well as diverse exposure to behavioral theory and modeling. In addition, Marlin meets regularly with the CP3 team as an MPI on that project and has been working closely with other CP3 students to disseminate TRD2 research.

In Memphis, in addition to growing their core computational skills via weekly group meetings and presentations, two graduate students received training in multidisciplinary collaboration by engaging with experts in stress and stressors research from Penn State.

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Vigorous research activity in mHealth has resulted in an ever-growing list of physiological and behavioral markers. However, the translation of these biomarkers into real-time intervention lagged behind the observational research studies that led to their development due to computation, storage, and communication bottlenecks faced by wearables and smartphone platforms. Further, the next generation of wearables is emerging with the ability to sample data from multiple sensors at rates several orders of magnitude higher than current-generation devices, exacerbating the computational and communication bottleneck. They can image structure, motion, and function, to provide visibility into physiology previously possible only in clinics.

Traditionally, such imaging sensors use post-processing algorithms for feature identification, co-registration, alignment, and enhancement. However, high-frequency high-volume imaging data from wearables cannot be transported to cloud computing for post-processing. Finally, researchers have shown that the high-dimensionality sensor data needed to compute biomarkers presents immense privacy risks. Advances in machine learning are leading to an ever-growing list of surprising inferences about user identity and activities that can be made from seemingly innocuous sensors, particularly when data are captured over long durations. Simplistic methods such as stripping personally identifiable information and addition of noise that focus on anonymizing the data have been ineffective for mHealth, both from privacy and utility perspectives, particularly with the availability of vast amounts of side information (e.g. metadata), computational power, and advanced algorithms.

To address these growing challenges, we propose a hierarchical computing framework that reduces the data into minimal modular abstractions called Micromarkers computed at the edge devices. Micromarkers can be used directly as features in new biomarker inferences or can be adapted to support legacy algorithms. TR&D3 will develop hardware, software, and computational techniques to implement privacy-aware, efficient, and embedded intelligence support into wearables. They will enable continuous, high-throughput, low-latency biomarker captures across wearable, mobile, and cloud platforms to support large-scale and long-term research studies and eventual real-life rollout. TR&D3 will pursue the following specific aims:

Aim 1: Develop modular and reusable micromarker abstractions to enable resource-efficient concurrent computation of a growing collection of biomarkers: Develop hierarchical computing methods and tools to support scalable, low-latency, power-efficient computation of current and emerging biomarkers. Modular Micromarker abstractions will be used to compress information relevant to biomarker computations at the edge devices while stripping nuisance variables such as hardware biases/drifts and background levels that are not pertinent to inference.

Aim 2: Create signal processing architectures combining Compressive Sensing and Machine Learning algorithms to support biomarker computations on resource-constrained high data rate sensor arrays: Develop and disseminate configurable sensor hardware prototypes and data-driven methods for resource-efficient denoising, signal reconstruction, and deblurring to enable real-time computation of biomarkers from the next generation of sensor modalities employing sensor arrays.

Aim 3: Enable optimization of privacy-utility tradeoffs in biomarker computations via cross-layer mechanism design: Create computational mechanisms and a general biomarker privacy framework to enable participant control over the privacy-utility tradeoffs during study design, data collection, and sharing of collected mHealth data for third-party research when data cross trust domains.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The primary mechanisms of dissemination have been technical papers, seminars, and other invited talks related to TR&D3 research. Srivastava gave keynote talks that related to activities and findings from project research at (i) ACM SenSys 2022, the top conference in mobile and wireless sensing; (ii) ACM/IEEE CPS-IoT Week 2023, the top conference in CYber-Physical Systems and the Internet of Things; (iii) IEEE WoWMoM; and (iv) Croucher Foundation Advanced Study Institute 2023 on AI for Internet of Things. Ertin gave one of the plenary talks at the IEEE Conference on SP and Comm. Applications.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In Year 4, we will follow the following research thrusts:

For the RF bio imaging thrust, we will build on our invertible neural network work to create stochastic estimates that can sample from the posterior of the data. In subcutaneous imaging, we are working in a low signal-to-noise ratio regime and therefore many multilayer profiles can potentially explain the measurements, yet the majority of deep learning approaches generate only a single solution. We will consider invertible neural networks as a way to establish normalizing flows from stochastic inputs to posterior images. This will allow us to have uncertainty measures on the derived quantities such as estimates of liquid water.

We will work on creating generative models of radio frequency biosensor data based on our previous work with multi-resolution GANs (generative adversarial networks). These models will enable researchers to extrapolate (in frequency domain) images captured by low-cost narrow-band sensors for better-resolved images and to augment existing BioRF datasets so they can be used in training machine learning-based data-intensive methods of biomarker discovery.

For the privacy activity, based on the feedback from EAC, we plan to conduct an interview-based user study to understand privacy concerns encountered in mHealth applications deployed in the industry. This will help us elicit privacy concerns and compliance issues, to help pave the way for the adoption of mDOT Center methods and technologies in the long term.

Additionally, to make the insights and methods resulting from our privacy work more easily accessible, we will create on the mDOT Center website a section describing recommended privacy best practices for health science studies that employ mobile sensing, as well as tools that we have developed. The goal is to create a central resource for the research community.

We will also build upon our previously reported work on UWB RF-based remote respiration waveform morphology sensing in a new health science collaboration involving the use of breathing exercises and yoga in the context of health management.

Component Lead: Ertin, Emre

mDOT Center TR&D3 (Translation):
Translation of Temporally Precise mHealth via Efficient and Embeddable Privacy-aware Biomarker Implementations

B.1 What are the major goals of the project?

Vigorous research activity in mHealth has resulted in an ever-growing list of physiological and behavioral markers. However, the translation of these biomarkers into real-time intervention lagged behind the observational research studies that led to their development due to computation, storage, and communication bottlenecks faced by wearables and smartphone platforms. Further, the next generation of wearables is emerging with the ability to sample data from multiple sensors at rates several orders of magnitude higher than current-generation devices, exacerbating the computational and communication bottleneck. They can image structure, motion, and function, to provide visibility into physiology previously possible only in clinics.

Traditionally, such imaging sensors use post-processing algorithms for feature identification, co-registration, alignment, and enhancement. However, high-frequency high-volume imaging data from wearables cannot be transported to cloud computing for post-processing. Finally, researchers have shown that the high-dimensionality sensor data needed to compute biomarkers presents immense privacy risks. Advances in machine learning are leading to an ever-growing list of surprising inferences about user identity and activities that can be made from seemingly innocuous sensors, particularly when data are captured over long durations. Simplistic methods such as stripping personally identifiable information and addition of noise that focus on anonymizing the data have been ineffective for mHealth, both from privacy and utility perspectives, particularly with the availability of vast amounts of side information (e.g. metadata), computational power, and advanced algorithms.

To address these growing challenges, we propose a hierarchical computing framework that reduces the data into minimal modular abstractions called Micromarkers computed at the edge devices. Micromarkers can be used directly as features in new biomarker inferences or can be adapted to support legacy algorithms. TR&D3 will develop hardware, software, and computational techniques to implement privacy-aware, efficient, and embedded intelligence support into wearables. They will enable continuous, high-throughput, low-latency biomarker captures across wearable, mobile, and cloud platforms to support large-scale and long-term research studies and eventual real-life rollout. TR&D3 will pursue the following specific aims:

Aim 1: Develop modular and reusable micromarker abstractions to enable resource-efficient concurrent computation of a growing collection of biomarkers: Develop hierarchical computing methods and tools to support scalable, low-latency, power-efficient computation of current and emerging biomarkers. Modular Micromarker abstractions will be used to compress information relevant to biomarker computations at the edge devices while stripping nuisance variables such as hardware biases/drifts and background levels that are not pertinent to inference.

Aim 2: Create signal processing architectures combining Compressive Sensing and Machine Learning algorithms to support biomarker computations on resource-constrained high data rate sensor arrays: Develop and disseminate configurable sensor hardware prototypes and data-driven methods for resource-efficient denoising, signal reconstruction, and deblurring to enable real-time computation of biomarkers from the next generation of sensor modalities employing sensor arrays.

Aim 3: Enable optimization of privacy-utility tradeoffs in biomarker computations via cross-layer mechanism design: Create computational mechanisms and a general biomarker privacy framework to enable participant control over the

Component Lead: Ertin, Emre

privacy-utility tradeoffs during study design, data collection, and sharing of collected mHealth data for third-party research when data cross trust domains.

B.1.a. Have the major goals changed since the initial competing award or previous report?

No

B.2 What was accomplished under these goals?

In Year 3, the TR&D3 undertook a variety of activities (as described below) to fulfill its goals.

B.2.1. Major Activities (include push-pull activities with CPs)

Activity 1.1: (Aim 1) CardiacGen: A Hierarchical Deep Generative Model for Cardiac Signals. There are many Machine Learning (ML) algorithms that use physiological signals like Electrocardiogram (ECG) for useful inference tasks such as biometrics, Heart-Rate prediction, and stress detection. However, the publicly available datasets are limited in size, especially in training large-scale data-driven Artificial Neural Networks (ANN) models. Moreover, collecting data at abnormal physiological conditions such as extreme heart rates and Stress has practical limitations since most people usually have normal physiological conditions. Therefore, there is a potential for creating synthetic training data to improve the performance of such Deep Learning (DL) models through data augmentation. Alternatively, data augmentation can be interpreted as an indirect method to incorporate domain knowledge into the learning process through this synthetic data. We developed a Deep Learning framework dubbed as CardiacGen for generating synthetic but physiologically plausible cardiac signals like ECG. Based on the physiology of cardiovascular system function, we propose a modular hierarchical generative model and impose explicit regularizing constraints for training each module using multi-objective loss functions. The model comprises 2 modules, an HRV module focused on producing realistic Heart-Rate-Variability characteristics and a Morphology module focused on generating realistic signal mor- morphologies for different modalities. We empirically show that in addition to having realistic physiological features, the synthetic data from CardiacGen can be used for data augmentation to improve the performance of Deep learning-based classifiers. CardiacGen code is available at [https://github.com/ SENSE-Lab-OSU/cardiac_gen_model](https://github.com/SENSE-Lab-OSU/cardiac_gen_model).

- T. Agarwal and E. Ertin, "CardiacGen: A Hierarchical Deep Generative Model for Cardiac Signals," Extended Abstract at Machine Learning for Health (ML4H) symposium, Nov 2022.

Activity 1.2: (Aim 2) Scalable Radio Frequency Sensor Arrays for Subcutaneous Fluid Detection. In this period we worked on the design of scalable radio frequency (RF) array and are developing deep-learning models to solve the inversion problem of estimating subcutaneous fluid content of layered tissue from backscattered measurements. The scalable RF array consists of the transceiver front-end, flexible antenna design and a central processor that controls the module, samples the backscattered signal, and implements the learning methods to estimate the tissue edema levels. The transceiver front-end which comprises of the phase-locked loops for synthesizing agile waveform for illuminating the area of interest, an RF mixer, and filter to demodulate the reflected signal, and an analog-to-digital converter (ADC) to digitize the signal has been designed and the performance metrics such as RF budget analysis, cascaded gain, noise-figure, input 3rd order intercept point (IIP3), and 1dB compression point (P1dB) has been utilized for characterizing the proposed design. The RF budget analysis for the transceiver module is utilized to choose the amplifier and attenuator blocks to ensure the signal amplitude matches the ADC dynamic range. The cascaded gain of the RF system is designed to ensure the required sensitivity for assessing minor differences in the backscatter signal (>9dB), while maintaining a low noise figure of 1.7 dB. The microstrip lines and the RF vias are designed to minimize mismatch losses between the source and the antenna. The design is validated using Ansys HFSS (high-frequency structure simulator) simulations. We are currently manufacturing a prototype array to support a pilot research program on lymphedema detection, towards a potential new CP.

Activity 1.3: (Aim 2): Calibration of RF sensor arrays using invertible neural networks. Ultrawideband (UWB) radar sensors are an emerging biosensing modality that can be used to assess the dielectric properties of internal tissues. Antenna effects, including antenna body interactions, limit the sensor's ability to isolate the weak returns from the internal tissues. In this work, we developed a data-driven calibration method for recovering Green's function of the multilayered media model of the tissue profiles using an Invertible Neural Network (INN). The proposed INN structure resembles a series of multilayered perceptron layers but is fully invertible between input and output, and the model is trained to invert the antenna transfer function to form estimates of Green's function modeling returns from internal tissues. A synthetic multilayered media antenna measurement dataset was generated using plane wave propagation model and antenna transfer functions collected from an actual antenna. We use simulation experiments to assess the effectiveness of the trained INN in antenna transfer function inversion. Our empirical results show that the INN can successfully recover Green's function of previously unseen multilayer profiles in the test set from noisy measurements.

- Y. Chang, N. Sugavanam, and E. Ertin, "Removing antenna effects using an invertible neural network for improved estimation of multilayered tissue profiles using uwb radar," in 2023 IEEE International Symposium on Antennas and Propagation and USNC-URSI Radio Science Meeting (AP-S/URSI). IEEE, 2023, pp. 53–54.

Activity 1.4: (Aim 2): Antenna optimization for Subcutaneous Imaging. The Antenna used in BioRF sensors has to be optimized for directing energy into the body. Our design focuses on a meander-line antenna because it offers a set of design parameters that can be optimized to produce antenna characteristics for a wide variety of applications. Typically, the tissues attenuate the RF signals at higher frequencies beyond 2 GHz and frequencies below 2 GHz penetrate deeper tissues. This phenomenon is utilized as a design principle for optimizing the antenna geometry. We maximize the RF power coupled to the deeper tissue layers at lower frequencies and further match the antenna by minimizing mismatched reflections in the low-frequency band. To this end, we found designs that are suited for lung-fluid detection and lymphedema detection. Furthermore, we optimize the thickness of a matching medium with known electrical characteristics to maximize the RF power coupled to the tissue layers.

Activity 1.5 (Aim 1): Unsupervised Siamese Adaptation for Robust and Performance Biomarkers Under Person-to-Person Variations. The aim of this activity is to develop methods by which digital biomarkers computed from sensor data (particularly motion sensor data) can be made robust to person-to-person variations. Such variations – caused by factors such as differences in biomechanical characteristics, sensor characteristics, and sensor placement – make it difficult for machine learning algorithms trained on a subpopulation of individuals to work well on new individuals that are out of the distribution of individuals in the training subpopulation - a problem that is commonly referred to as that of *domain shift*. Moreover, the problem is more severe with neural networks which have become popular with their higher accuracy since to fit them in resource-constrained wearable devices the models are often compressed using methods such as pruning and quantization that retain the performance on the validation set but at the cost of reduced robustness to domain shifts. The common approach of fine-tuning the model to a new individual by seeking more labeled data is extremely disruptive, particularly given the difficulty of labeling while engaged in daily activities of life. To overcome the shortcomings of the current supervised adaptation approach, we have developed a new unsupervised approach that is inspired by online learning and domain adaptation. It calibrates the model to a new individual via an unsupervised Siamese adversarial learning method that requires no intervention by the individual. We utilize an unsupervised domain adversarial neural network to match the embeddings of the unlabeled data collected from the new individual with the embeddings of the labeled data from the original training subpopulation. We optimized the domain discriminator with Siamese contrastive training so it works for hundreds of domains (each domain corresponds to a different individual in the training subpopulation). To validate the efficacy of our approach particularly for biomarkers involving subtle motion features, we implemented in collaboration with researchers from the University of Virginia an end-to-end system for off-the-shelf Android smartwatches to classify finger movements (a proxy for biomarkers) and conducted an offline ablation study, a real-time system evaluation, and a user experience study with 134 volunteers. The results of the user study indicate that our unsupervised method is more convenient and user-friendly than supervised adaptation while providing robustness to deployment variations, such as different hand shapes, finger activity strengths, and smartwatch positions on the wrist. A key aspect of our Siamese domain adversarial neural network approach is that the model adapts over time as it is updated on a daily basis using unlabeled data. The updating process is executed at night on cloud servers, and in our study, the accuracies for 20 previously unseen users evolved for seven days as 90.1%, 95.2%, 96.4%, 96.8%, 96.7%, 97.2%, and 97.1%, respectively. This effectively demonstrates that the approach adapts the model to specific users. The accuracy then showed slight improvements over the following week. Particularly for some previously unknown users, performance has improved significantly, such as from 65% to 95% for one of the users. A paper reporting this work has been accepted at the ACM Symposium on User Interface Software and Technology (UIST), and we are currently applying the Siamese domain adversarial neural network approach to various motion and non-motion biomarker computations.

- Chen, Wenqiang, Ziqi Wang, Pengrui Quang, Zhencan Peng, Shupei Lin, Mani Srivastava, Wojciech Matusik, John Stankovic. "Robust Finger Interactions with COTS Smartwatches via Unsupervised Siamese Adaptation." ACM Symposium on User Interface Software and Technology (2023). Accepted.

Activity 1.6 (Aim 1): Platform-Aware Neurosymbolic Auto Tiny Machine Learning. Last year we reported our work on THIN-Bayes, an open-source software tool developed in collaboration with Arm for neural architecture search for wearable devices employing resource-constrained microcontrollers. This allowed us to create neural models for tasks such as human activity classification and head-pose estimation using wearable sensors, and for tracking motion in 3D space, all of which are essential building blocks for a variety of motion-related biomarkers. However, real-life sensor-based biomarker implementations require not just neural models but also symbolic computation-performing algorithms for feature extraction and post-processing. To meet energy, memory, latency, and biomarker accuracy requirements, co-optimization of neural and symbolic components of the overall system is necessary. For example, if the output of the neural model is fed to the Kalman tracker to get a reliable estimate, it becomes important that the parameters of the two be co-optimized. Towards this objective, we developed TinyNS, the first platform-aware neurosymbolic architecture search framework for joint optimization of symbolic and neural operators. TinyNS provides recipes and parsers to automatically write microcontroller code for five types of neurosymbolic models, combining the context awareness and integrity of symbolic techniques with the robustness and performance of machine learning models. TinyNS uses a fast, gradient-free, black-box Bayesian optimizer over discontinuous, conditional, numeric, and categorical search spaces to find the best synergy of symbolic code and neural networks within the hardware resource budget. To guarantee deployability, TinyNS talks to the target hardware during the optimization process. We showcase the utility of TinyNS by deploying microcontroller-class neurosymbolic models through several case studies. In all use cases, TinyNS outperforms purely neural or purely symbolic approaches while guaranteeing execution on real hardware. We have applied TinyNS for implementations of select human motion activity-related biomarkers where the neural model has symbolic pre- and post-processing. A paper describing TinyNS was recently published in the *ACM Transactions on Embedded Computing Systems*.

- Saha, Swapnil Sayan, Sandeep Singh Sandha, Mohit Aggarwal, Brian Wang, Liying Han, Julian de Gortari Briseno, and Mani Srivastava. "TinyNS: Platform-Aware Neurosymbolic Auto Tiny Machine Learning." ACM Transactions on Embedded Computing Systems (2023).

Activity 1.7 (Aim 3): LLM-assisted Privacy Regulation of Sensory Information Flows. Digital biomarkers rely on measurements from wearable and ambient sensors, and in the process, these sensors capture privacy-sensitive information about the subject or patient, as well as other individuals they engage with or are near. The current paradigm for privacy management is that of informed consent which drives the capture and processing of the sensor information.

Component Lead: Ertin, Emre

However, truly informed consent by the data subjects is often not possible: of the absence of channels to communicate informed consent, low technological sophistication, inadequate understanding of privacy risks, language barriers, etc. While efforts such as privacy nutrition label attempt to improve understanding of risks, the fundamental challenge of lack of proper consent remain, and the challenges are amplified as laws, regulations, and norms vary with context, and the sensor capabilities continually evolve. In the absence of effective consent mechanisms, the theory of Contextual Integrity (CI) offers a framework for managing privacy. Key to this framework is a knowledge base specifying social, ethical, and legal norms that govern the privacy-appropriate flows of information. In this activity, we have proposed the use of Large Language Models (LLMs), which have been trained on large corpora of texts from law, medicine, and ethics. We harness LLMs to validate new sensor informational flows against privacy norms. The main contribution of this work, PrivacyOracle, is an LLM-based privacy firewall for regulating flows of sensory information in environments where consent is challenging to obtain. We design several prompt engineering strategies and structured interfaces based on CI informational flows. We evaluate performance on several tasks: validation of informational flows involving 1st/3rd party data subjects under HIPAA, agreement with social norms of informational flows, and providing recommendations for sensor deployments under varying knowledge of privacy risks. A paper with preliminary findings from this work is currently under submission.

Summary of Push-Pull Activities with CPs:

- **CP1 (Nahum-Shani):** The Mobile-Assistance for Regulating Smoking (MARS) investigators are now analyzing the data and exploring the use of MotionSense sensor data to assess the smoking state and HRV as a measure of self-regulatory capacity. We attended MARS group meetings and provided information on timing data to unravel HRV information.

- **CP6 (Inan):** We have exchanged ideas with Prof Inan, on complementing their ballistography-based sensor system with the RF scalable sensor for assessing the contractility of the heart. We will continue the discussion when the RF sensor array prototype is available.

B.2.2. Specific Objectives

TR&D3 will provide the research community with 1) mDOT Center applications and software development kits (SDK) on popular wearables, personal devices, and smartphones with embedded micromarker-based implementation of biomarkers of stress, fatigue, speaking, smoking, craving, eating, brushing, and new biomarkers from CPs; 2) Reference design and prototypes of mDOT Center radio-frequency (RF) Patch sensors, modular hardware modules and embedded software cores to power wearable sensor arrays; 3) Toolbox for exploring privacy implications of sensor and biomarker choices and enabling run-time control over privacy-utility trade-off in biomarker implementations. These tools will enable continuous, high throughput, low-latency capture of current and emerging biomarker streams to support large-scale, long-term research studies that provide privacy management at the entire lifecycle, including study design, data collection, and data sharing.

B.2.3. Significant Results (including major findings, developments, or conclusions both positive and negative)

<u>OSU</u>

- Our findings from the activity **CardiacGen: A Hierarchical Deep Generative Model for Cardiac Signals** show that the generative model is able to produce physiologically plausible signals as well as its ability to augment datasets.

Component Lead: Ertin, Emre

We have shown that the tachogram of the signals deviates from the actual tachograms at an error rate of less than 30 ms in RMSE (root mean square error). We have shown that data augmentation with CardiacGen improved the emotion and identity recognition performance from ECG signals by 30% and 82% respectively.

- Our findings from the activity **on Scalable Radio Frequency Sensor Arrays for Subcutaneous Fluid Detection** have shown that the RF array can effectively detect subcutaneous liquid using multiple snapshots captured axially on the forearm, potentially informing of the status of early-stage lymphedema. Simulation studies have shown the same array can be used to capture and characterize cardiac motion.

- Our findings from the activity **Calibration of RF sensor arrays using invertible neural networks** that the proposed invertible neural network structure can successfully recover Green's function of previously unseen multilayer profiles in the test set from noisy measurements. Determination of the Green function is the first step in the imaging algorithm. We note that a feed-forward convolutional neural network is unable to solve the calibration problem as the optimization criteria lack terms of the implied forward problem.

UCLA

- Our findings from the activity on ***Unsupervised Siamese Adaptation for Robust and Performance Biomarkers Under Person-to-Person Variations*** indicate that the Siamese domain adversarial neural network approach to adapting the ML model in the presence of domain shift is an effective approach to achieving high performance with new individuals in the face of high person-to-person variability. In our example study, which was for motion-related biomarkers, the average accuracy on a cohort of 20 new individuals, a model originally trained on a set of 134 individuals evolved for seven days as 90.1%, 95.2%, 96.4%, 96.8%, 96.7%, 97.2%, and 97.1%, respectively. Notably, this improvement did not require any new labeled data from the individuals and is thus entirely burden-free.

- Our findings from the activity on ***Platform-Aware Neurosymbolic Auto Tiny Machine Learning*** indicate that the TinyNS tool for automatically generating neurosymbolic code (and as a special subcase neural-only code) for biomarkers on microcontroller class devices is highly effective and produces solutions that are far superior to those reported in literature based on considerable manual tuning. Indeed, solutions generated by TinyNS are often significantly better in both accuracy and memory footprint. For more details, we refer to the recently published journal paper (TinyNS: Platform-Aware Neurosymbolic Auto Tiny Machine Learning, Saha et al., 2023).

- Our initial findings from the activity on ***LLM-assisted Privacy Regulation of Sensory Information Flows*** suggest that LLMs can be very effective tools for privacy management by allowing validation of informational flows involving 1st/3rd party data subjects under HIPAA, agreement with social norms of informational flows, and providing recommendations for sensor deployments under varying knowledge of privacy risks. The work takes one step closer to a future where information is automatically configured and regulated with respect to privacy norms and regulations, thus enabling the privacy of sensory information to flow in settings where truly informed consent is challenging to obtain.

Component Lead: Ertin, Emre

TR&D3 - Translation	Books	Papers	Abstracts
Number Published	0	5	1
Number in Press	0	3	1
Number in Submission/Review	0	2	0

B.2.4. Key Outcomes & Other Achievements

- To enable robust and efficient digital biomarkers on extremely resource-constrained devices, UCLA created and released TinyNS, the first platform-aware neurosymbolic architecture search framework for joint optimization of symbolic and neural operators. TinyNS addresses the problem that AI/ML-enabled digital biomarkers require neural models to be combined with symbolic reasoning and traditional algorithms to ensure interpretability and satisfy the underlying system rules and physics within the tight platform resource constraints is challenging. It provides recipes and parsers to automatically write microcontroller code for five types of neurosymbolic models, combining the context awareness and integrity of symbolic techniques with the robustness and performance of machine learning models. The code has been released at https://github.com/nesl/neurosymbolic-tinyml and has already been applied not only to biomarkers (for both humans and sea animals) but also in agriculture.

- To improve the performance of Machine Learning (ML) algorithms for Heart Rate, Hart Rate Variability prediction, and stress detection, OSU a Deep Learning framework dubbed as Cardiacgen for generating synthetic but physiologically plausible cardiac signals like ECG. This software can unlock the potential of using ML algorithms on limited datasets by creating synthetic training data by improving the performance of such Deep Learning (DL) models through data augmentation. We empirically show that in addition to having realistic physiological features, the synthetic data from CardiacGen can be used for data augmentation to improve the performance of Deep Learning-based classifiers. CardiacGen code is available at https://github.com/ SENSE-Lab-OSU/cardiac_gen_model.

Component Lead: Ertin, Emre

mDOT Center TR&D3 (Translation):
Translation of Temporally Precise mHealth via Efficient and Embeddable Privacy-aware Biomarker Implementations

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B.4. What opportunities for training and professional development has the project provided?

OSU: Two OSU graduate research assistants (Chang Yuyi and Soumobrata Ghosh), one undergraduate student (Devan Mallory) and a postdoctoral researcher (Nithin Sugavanam) were supported by the Grant this year. The project gave the students the opportunity to work on an interdisciplinary project that combines elements of sensor hardware design, machine learning algorithm development, and embedded computing. Furthermore, a design project and examples from RF-based biomedical sensing and design projects have been incorporated into a senior-level undergraduate course providing training to 25 students in the ECE and CS departments. A graduate student trained under this funding in deep learning methods and models is now part of the technical staff at Qualcomm developing methods for audio signal analysis and synthesis.

UCLA: Due to the significantly delayed arrival of funding from the U. Memphis to UCLA - the new Y3 funding and the approval for Y2 carryover transpired in July 2023 - we were unable to engage students and/or professional development support thus far. The research activities reported above were conducted through other projects. As the funds became available only recently, we are in the process of re-engaging one student and one post-doc directly on this project starting Fall.). The project will further their educational training by giving them hands-on experience in various facets of sensor information processing towards biomarker computation on resource-constrained wearable devices, and on quantifying and mitigating privacy risks. Beyond the direct engagement of researchers, the project also provided training and professional development to students via courses and other educational vehicles. For example, a group of nine students in UCLA's Masters of Engineering Program in IoT conducted two capstone projects exploring the use of a new electrostatic sensing modality called Qvar that has emerged in microcontrollers from ST Microelectronics for breathing waveform sensing and muscle and finger movements. These projects were actively mentored by ST Microelectronics. Additionally, through Srivastava's graduate course, a group of 30+ CE and CS were trained in foundational concepts for digital biomarker technology development.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Models Software	https://github.com/ SENSE-Lab-OSU/cardiac_gen_model To improve the performance of Machine Learning (ML) algorithms for Heart Rate, Hart Rate Variability prediction, and stress detection, OSU a Deep Learning framework dubbed as Cardiacgen for generating synthetic but physiologically plausible cardiac signals like ECG. This software can unlock the potential of using ML algorithms on limited datasets by creating synthetic training data by improving the performance of such Deep Learning (DL) models through data augmentation. We empirically show that in addition to having realistic physiological features, the synthetic data from CardiacGen can be used for data augmentation to improve the performance of Deep Learning-based classifiers.
Software	https://github.com/nesl/neurosymbolic-tinyml To enable robust and efficient digital biomarkers on extremely resource-constrained devices, UCLA created and released TinyNS, the first platform-aware neurosymbolic architecture search framework for joint optimization of symbolic and neural operators. TinyNS addresses the problem that AI/ML-enabled digital biomarkers require neural models to be combined with symbolic reasoning and traditional algorithms to ensure interpretability and satisfy the underlying system rules and physics within the tight platform resource constraints is challenging. It provides recipes and parsers to automatically write microcontroller code for five types of neurosymbolic models, combining the context awareness and integrity of symbolic techniques with the robustness and performance of machine learning models.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. COMPONENT PARTICIPANTS

Not applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

A. COMPONENT COVER PAGE

Project Title: mDOT Training and Dissemination	
Component Project Lead Information: SHETTY, VIVEK	

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The mHealth Center for Discovery, Optimization & Translation of Temporally-Precise Interventions (the mDOT Center) will enable the new paradigm of temporally-precise medicine to maintain health and manage the growing burden of chronic diseases. The mDOT Center will develop and disseminate the methods, tools, and infrastructure necessary for researchers to pursue the discovery, optimization, and translation of temporally precise mHealth interventions. Such interventions, when dynamically personalized to the moment-to-moment biopsychosocial-environmental context of each individual, will precipitate a much-needed transformation in healthcare by enabling patients to initiate and sustain the healthy lifestyle choices necessary for directly managing, treating, and preventing medical conditions. Organized around three Technology Research and Development (TR&D) projects, the mDOT Center will generate multiple technological innovations and translate them into a unique national technological resource for the mHealth community in the form of easily deployable wearables, apps for wearables and smartphones, and companion mHealth cloud system, all open-source.

Given that the inherently transdisciplinary, team-based nature of mHealth research requires scientists to cross-disciplinary and institutional boundaries, training and dissemination in mHealth technologies require a team-science approach. The mDOT Center will leverage our established and mature infrastructure, widely visible mHealthHUB platform, and an experienced team to develop training and dissemination activities that extend beyond the CPs and SPs to involve new research groups with little or no technological expertise. By reducing access barriers, we seek to reduce the growing disparity among various research groups in using the latest mHealth sensing, biomarker, and analytics technology in their research. The main goals of the mDOT Center's Technology Training and Dissemination (TT&D) Core are two-fold: (a) improve the general understanding and uptake of the mDOT Center technologies and methods by the mHealth research communities; (b) develop a perpetuating cadre of transdisciplinary researchers conversant with the mDOT Center technologies and able to effectively apply them in their research programs. Envisioned as a national resource, the dissemination activities of the mDOT Center will focus on informing the scientific community about the tools and processes developed by the mDOT Center and facilitate broad distribution and optimized use of the mDOT Center technologies. The mDOT Center will use the Theory of Action (described below) as an organizing framework for its key training and dissemination activities to achieve the outcome objectives of the TT&D Core. Training efforts will reach beyond mDOT Center affiliates to include mentorships, a scholar exchange program, and a visiting scholar residency program. Our annual mHealth Training Institute (mHTI) and other group courses and workshops are common forums that will blend the mDOT Center's dissemination with direct training activities. Planned dissemination activities include the hosting of our community website (mHealthHUB; https://mhealth.md2k.org/), the development of user application documentation, delivery of virtual seminars, publication of research methods and findings, development of the user community, and technology transfer. The TT&D core will pursue the following specific aims:

Aim 1: [Training] Provide direct training activities that leverage annual workshops, conferences, and meetings of professional societies, and conduct an annual mHealth training institute to develop a perpetuating cadre of outside researchers well-equipped to apply the mDOT Center's technologies and methods.

Aim 2: [Dissemination] Provide "light-touch" outreach using web portals with "heavy-touch" outreach activities including training sessions, workshops, and conferences to inform the scientific community about the technical capabilities and accomplishments of the mDOT Center, and to both promote and enable a broader use of the mDOT Center's methods and technologies.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File Uploaded : B.2. - TRAINING & DISSEMINATION YEAR 3 RPPR.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Research Results: The results of the advanced quantitative methods studying the formation of transdisciplinary teams and the development of team processes are being readied for publication in two peer-reviewed open-access scientific journals with a high impact factor (a) Journal of Clinical and Translational Science, and (b) PLOS One.

Publications, Talks, & Presentations: mDOT Center investigators have published or have submitted and under review a total of 33 papers related to mDOT Center research for project Year 3. In addition, mDOT Center investigators have participated in 168 talks and presentations at 152 global meetings since the Center’s inception.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

mHTI: We will continue to make significant strides in advancing team science through the analysis and publication of the 2023 mHTI findings. The results will provide invaluable insights into multidisciplinary healthcare innovation. Plans are already in place to conduct the 2024 mHTI, with the goal of expanding on these discoveries and fostering enhanced collaboration.

Webinar Series: Our commitment to education and knowledge-sharing continues with the monthly mDOT webinars, providing regular interactive sessions on cutting-edge topics. The engagement and feedback have been overwhelmingly positive, encouraging further development of these digital resources.

FlightTracker: Furthermore, we are actively tracking the career trajectories of our scholars using the Flight Tracker. The data generated from this tool offers a clear view of their growth paths and achievements, further emphasizing the impact of our programs. The ongoing monitoring supports our drive to refine and adapt our offerings, ensuring we meet the ever-evolving needs of our scholars.

Redesign of the mDOT Center Website: In line with the Center’s dissemination goals and galvanized by the Executive Advisory Committee’s annual review, the mDOT Center website will undergo a major redesign to enhance its online presence and engagement with its target audience. The redesign will focus on a few key objectives:

Showcase Research Publications and Outcomes: Each TR&D page will undergo a redesign with a primary focus on prominently featuring the latest publications and research outcomes linked to their current work. This redesign aims to enhance accessibility and comprehensibility of the Center's work for a broader audience. Visitors will be able to access a concise overview of publications, GitHub repositories, and datasets associated with each TR&D, with the flexibility to delve deeper based on their specific interests. This will be achieved by structuring research outcomes into tabular toggles, organized according to research objectives. Each publication will have a relevant graphic and key information to allow visitors to quickly navigate to the content that is most relevant to them. This is crucial for advancing mHealth, as it allows not only researchers and clinicians but also stakeholders and the general public to more clearly see the Center's contributions to the field. Effective communication of research findings can foster better understanding and support for mHealth initiatives and thus drive innovation.

Showcase Collaboration and Service Projects: Each of the Collaboration and Service Projects will be showcased in a gallery with individual graphics to provide a snapshot of relevant information as well as tags to allow individuals to quickly navigate to the CP or SP that is of most interest to them. Each CP and SP will have their own page that will be built to prominently display the publications associated with their collaboration with specific TR&Ds.

Showcase mDOT Center Websites & Tools: The mDOT Center website will be the new central home for all other mDOT Center websites, tools, and repositories so that visitors can access all the resources at

Facilitate Engagement and Collaboration: The mDOT Center website will be redesigned to make Center resources more accessible and to encourage researchers and clinicians to explore the Center's offerings in depth. The inclusion of a Collaboration Interest Form as well as call-to-actions that prompt collaboration inquiries can foster more direct and efficient communication between potential collaborators and the Center. This can lead to new partnerships with potential collaborative and service projects.

Increase Search Engine Visibility: A Search Engine Optimization (SEO) plug-in will be utilized in order to increase visibility and organic traffic. Additionally, the plug-in will generate an XML sitemap allowing search engines to crawl and index the website. Doing so will enable the website to rank higher in search engines, increasing our audience over time.

Social Media Campaign: Once the mDOT Center site redesign is implemented, we will post a series of stories on LinkedIn and X (formerly Twitter) that describe recent mDOT Center publications, news, and offerings (i.e. datasets, tools, etc.). Additionally, YouTube shorts and TikToks will be shared that not only distill recent publications into easily digestible formats but also encourage website visits and help audiences connect the mDOT Center with its valuable resources and offerings, potentially drawing in a wider audience.

Collaboration and Service Project Newsletter: After the mDOT Center site redesign is implemented, we will initiate a newsletter campaign aimed at recruiting new CPs and SPs. This newsletter will describe novel technologies that have been recently developed for which we are actively seeking collaborators. Included in the newsletter will be a link to a user-friendly form on the mDOT Center website, enabling potential collaborators to establish contact with us.

Component Lead: Vivek, Shetty

mDOT Center TRAINING & DISSEMINATION

B.1 What are the major goals of the project?

The mHealth Center for Discovery, Optimization & Translation of Temporally-Precise Interventions (the mDOT Center) will enable the new paradigm of temporally-precise medicine to maintain health and manage the growing burden of chronic diseases. The mDOT Center will develop and disseminate the methods, tools, and infrastructure necessary for researchers to pursue the discovery, optimization, and translation of temporally precise mHealth interventions. Such interventions, when dynamically personalized to the moment-to-moment biopsychosocial-environmental context of each individual, will precipitate a much-needed transformation in healthcare by enabling patients to initiate and sustain the healthy lifestyle choices necessary for directly managing, treating, and preventing medical conditions. Organized around three Technology Research and Development (TR&D) projects, the mDOT Center will generate multiple technological innovations and translate them into a unique national technological resource for the mHealth community in the form of easily deployable wearables, apps for wearables and smartphones, and companion mHealth cloud system, all open-source.

Given that the inherently transdisciplinary, team-based nature of mHealth research requires scientists to cross-disciplinary and institutional boundaries, training and dissemination in mHealth technologies require a team-science approach. The mDOT Center will leverage our established and mature infrastructure, widely visible mHealthHUB platform, and an experienced team to develop training and dissemination activities that extend beyond the CPs and SPs to involve new research groups with little or no technological expertise. By reducing access barriers, we seek to reduce the growing disparity among various research groups in using the latest mHealth sensing, biomarker, and analytics technology in their research. The main goals of the mDOT Center's Technology Training and Dissemination (TT&D) Core are two-fold: (a) improve the general understanding and uptake of the mDOT Center technologies and methods by the mHealth research communities; (b) develop a perpetuating cadre of transdisciplinary researchers conversant with the mDOT Center technologies and able to effectively apply them in their research programs. Envisioned as a national resource, the dissemination activities of the mDOT Center will focus on informing the scientific community about the tools and processes developed by the mDOT Center and facilitate broad distribution and optimized use of the mDOT Center technologies. The mDOT Center will use the Theory of Action (described below) as an organizing framework for its key training and dissemination activities to achieve the outcome objectives of the TT&D Core. Training efforts will reach beyond mDOT Center affiliates to include mentorships, a scholar exchange program, and a visiting scholar residency program. Our annual mHealth Training Institute (mHTI) and other group courses and workshops are common forums that will blend the mDOT Center's dissemination with direct training activities. Planned dissemination activities include the hosting of our community website (mHealthHUB; https://mhealth.md2k.org/), the development of user application documentation, delivery of virtual seminars, publication of research methods and findings, development of the user community, and technology transfer. The TT&D core will pursue the following specific aims:

Aim 1: [Training] Provide direct training activities that leverage annual workshops, conferences, and meetings of professional societies, and conduct an annual mHealth training institute to develop a perpetuating cadre of outside researchers well-equipped to apply the mDOT Center's technologies and methods.

Aim 2: [Dissemination] Provide "light-touch" outreach using web portals with "heavy-touch" outreach activities including training sessions, workshops, and conferences to inform the scientific community about the technical capabilities and accomplishments of the mDOT Center, and to both promote and enable a broader use of the mDOT Center's methods and technologies.

Component Lead: Vivek, Shetty

B.1. Have the major goals changed since the initial competing award or previous report?

No

B.2 What was accomplished under these goals?

In Year 3, the Training and Dissemination Core undertook a variety of activities (as described below) to fulfill its goals.

B.2.1. Major Activities

Activity 1: Training: The main focus of the training was the development and conduct of the 2023 mHealth Training Institute (mHTI). This entailed the development of a comprehensive, online application management system (SmarterSelect). The call for applications was released in December 2022 with a deadline of January 15, 2023. A team of evaluators from the mHTI faculty and NIH program officers were put together to evaluate the applications. From a pool of 131 applicants, 30 were chosen as scholars for the 2023 mHTI (2023 mHTI Scholars). The selected scholars were notified by April 10, 2023. A corresponding group of faculty, comprising both academics and NIH Program Officers (2023 mHTI Faculty), was recruited to serve as faculty. The hybrid 2023 mHTI, incorporating both virtual and in-person components, was conducted between April 10 and July 20, 2023 (2023 mHTI Program). It started with 15 pre-recorded lectures from prior mHTI's to be viewed in three sessions between May 1st and June 2nd. It was followed by five live lectures on May 1st and three live lectures on May 15. After the lectures, two mentored sandboxes were organized, where each team of scholars met with their mentors for three hours each day (on June 5 and June 26) to formulate their project. All scholars and faculty then arrived on the UCLA campus on July 16 for the in-person training. Six more interactive lectures were held on the mornings, followed by mentored sessions prior to lunch, and team work in the afternoons. On the final day (July 20), each team presented their project and received feedback from the faculty. Each scholar filled out a survey prior to their departure about the institute whose results were analyzed.

FlightTracker: Furthermore, we are actively tracking the career trajectories of our scholars using the Flight Tracker. The data generated from this tool offers a clear view of their growth paths and achievements, further emphasizing the impact of our programs. The ongoing monitoring supports our drive to refine and adapt our offerings, ensuring we meet the ever-evolving needs of our scholars. A short-term evaluation of educational effectiveness was conducted by the evaluation team; a long-term evaluation of post-mHTI career trajectories is being tracked by the Flight Tracker software.

Activity 2: Dissemination: In addition to scientific publications and presentations, dissemination were conducted via mHealthHUB, live webinars, social media, websites, and repositories. They are described below.

mHealthHUB: The mHealthHUB, the mDOT's primary platform for training and dissemination, was comprehensively reconfigured to develop a more versatile training and dissemination portal. The remodel was aimed at promoting a wider dissemination of information and facilitating the conduct of webinars. A dedicated webinar platform was integrated into the interface to streamline online training sessions, allowing for seamless communication, live discussions, and the sharing of multimedia content. Additionally, improved navigation features and advanced search options were implemented to aid in the broad dissemination of information. These enhancements aimed to provide a more user-friendly and efficient resource for all mHTI users, enabling them to access relevant training resources and stay up to date with the latest mHealth trends and discussions. The redesign also incorporated analytics and tracking features to monitor and analyze engagement metrics, allowing continuous improvement in delivering training content. Notable highlights of this overhaul include the following key components:

Component Lead: Vivek, Shetty

- **Training Content (Lectures & Webinars):** mHTI lectures and mDOT webinars were consolidated into a centralized training repository. Videos were categorized and tagged for easy searchability, allowing users to access content based on year or specific topics.
- **Digital Toolbox:** A digital toolbox was created as a one-stop-shop for researchers seeking access to open-source tools and datasets. To enhance usability, we introduced categories and tags, enabling researchers to locate tools and datasets aligned with their specific needs. Furthermore, we incorporated counters to provide quick, at-a-glance statistics, such as the total hours of sensor data or days of data collection, offering valuable insights to researchers.
- **IRB Resources:** An IRB Resources section was created to provide novice researchers with templates and sample materials to serve as a framework to get started. The templates include descriptions and sample language that can be readily incorporated into research protocols. In addition, sample materials from the ROBAS and MOODS studies, e.g., study protocol, informed consent form, and recruitment flyer, were added to provide researchers with concrete examples that can be tailored to their specific studies.

Webinars: The center regularly conducts webinars with a wide viewership both in real-time and in post-webinar viewing. In Year 3, the center conducted 6 webinars, with 3 more scheduled for Year 3. In addition, 8 webinars were conducted as part of the mHTI. Videos of all webinars are archived on the center's YouTube channel. To date 43 mDOT webinars have been recorded and curated for asynchronous access. In addition, the mHealthHUB now hosts 120 mHTI-recorded lectures and talks so that all training content can be accessed in one central location.

Social Media: A concerted effort was made to explore the reach of social media dissemination in Year 3. Stories were posted on LinkedIn and X (formerly Twitter) to promote specific webinars and lectures, thus fostering a more effective connection with the target audience and the content available on the mHealthHUB. Additionally, YouTube Shorts and TikToks were created to boost awareness of both upcoming webinars and newly accessible webinars on the mHealthHUB.

Websites and Repositories: As listed in C.2, the center maintains four websites, four social media channels, and eleven repositories of models, source codes, and data.

B.2.2. Specific Objectives

- Train a cadre of transdisciplinary mHealth scientists to develop national capacity.
- To answer a series of the process (or implementation) and outcome (or impact) questions relative to the 2023 mHTI. The process evaluation questions investigate aspects of the design and implementation of the mHTI, and outcome evaluation questions focus on the extent to which intended goals were achieved.
- Use the mHTI as a testbed to apply advanced quantitative methods to study the formation of transdisciplinary teams and the development of team processes central to the effective functioning of highly diverse teams.

Component Lead: Vivek, Shetty

B.2.3. Significant Results

Activity 1: Training: We present the details about the scholars and an evaluation from their reviews.

<u>Sociodemographics</u>

Table Demographic Background Characteristics of 2023 Scholars

	N	%
Race/Ethnicity (participants could select multiple)	28	100
White/Caucasian	12	43
Asian	8	29
Hispanic/Latino/Latina	4	14
Black/African American	3	11
Prefer not to state	1	4
Gender	28	100
Female	18	64
Male	9	32
Prefer not to state	1	4
Region	28	100
Northeast	6	21
Midwest	2	7
Southeast	10	36
Southwest	3	11
West	4	14
International (not from the U.S.)	3	11
Institution Type	28	100
University	22	79

Component Lead: Vivek, Shetty

Research Center	5	18
Other	1	3
Discipline	28	100
CS/Engineering/Data Science	6	21
Medicine/Nursing	5	18
Psychology	13	46
Public Health/Others	4	14

1. Key summaries of evaluation:
   a. The majority of the participants responded that the 2023 virtual mHTI was "extremely worthwhile" [mean score = 6.61 (out of 7) with SD of 0.88 (N=28)].

   b. Graphs from 2023 evals

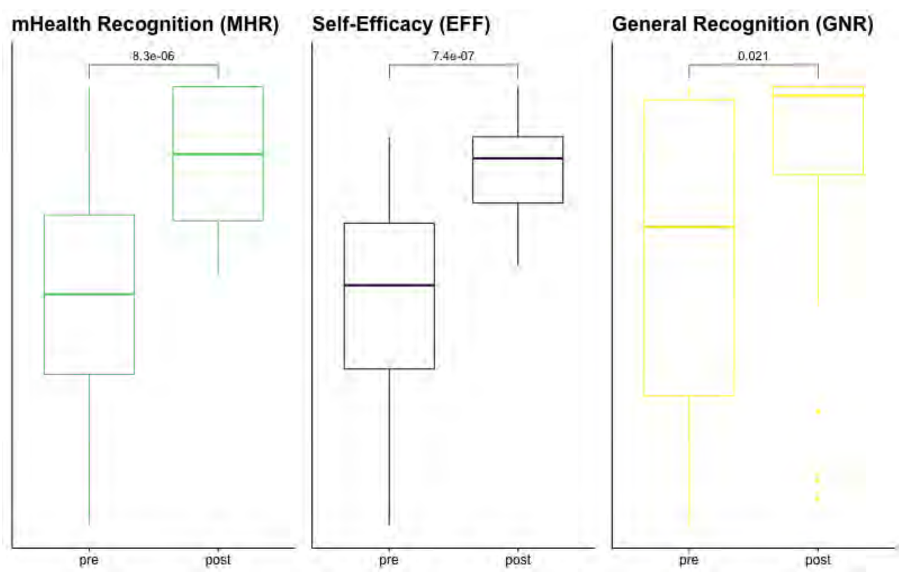

Figure. mHealth Institute Impacts on Scholars' mHealth research recognition, self-efficacy and general cross-disciplinary research recognition. The value is the p-value for the t-test of the differences in the means of the pre-and post-institute scores. The effect size for mHealth Recognition, Self-Efficacy, and General Recognition towards cross-disciplinary research was 1.65, 1.85, and 0.70, indicating a large and statistically significant impact of the program on scholars' major learning outcomes.

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Table Comfort with Key mHealth Concepts, Methods, Techniques and Practices After Didactic Core

Didactic Core Lectures	Before	After	Effect Size	*p*-value
Considerations for Preparation, Optimization, and Evaluation of Digital Therapeutics	3.04	4	1.06	0.00
Deep Learning Approaches in mHealth	2.46	3	0.43	0.00
Developing and Adopting Digital Biomarkers in mHealth Research	2.53	3.7	1.12	0.00
Experimental Design and Analytic Strategies for Adaptive Behavioral Intervention	3	4.18	1.37	0.00
Learning Algorithms to Personalize Digital Interventions in Real Time	2.62	3.93	1.16	0.00
Maintaining Behavior Change in Digital Interventions	3.29	4.07	0.86	0.00
Passive Monitoring and Relapse Risk Prediction in Behavioral Health	3.15	4	1.16	0.00
Understanding Engagement Strategies in Digital Behavioral Interventions	3.36	4.14	0.96	0.00

Note: Effect size (Cohen's d) around 0.5 represents a medium effect size, effect size around and greater than 0.8 represents a large effect size. *p*-value less than 0.05 indicates statistical significance of the difference.

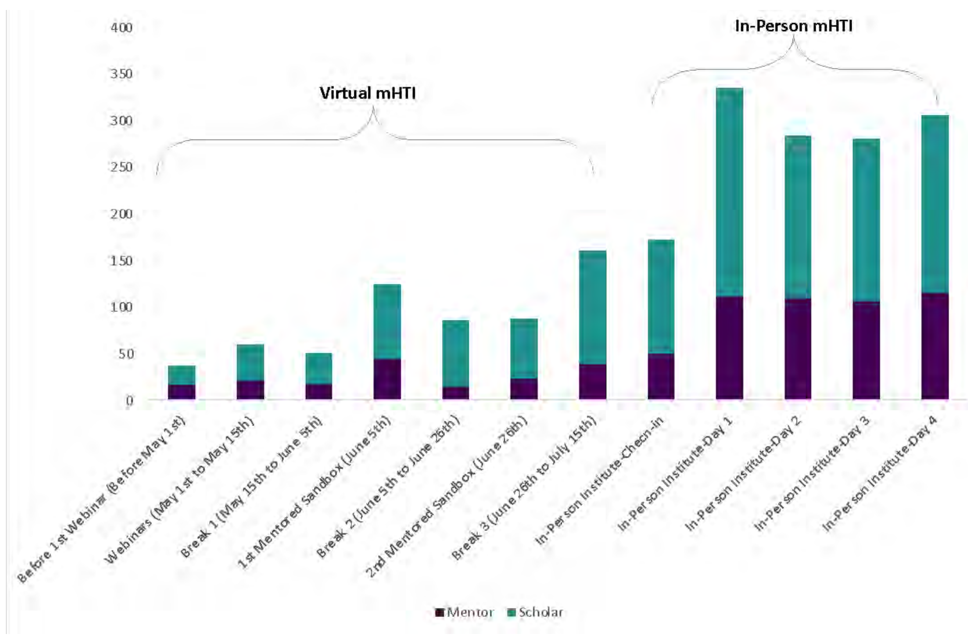

Figure. Conversations between scholars and mentors during mHealth Institute-bar graph. Purple indicates conversations between scholars and mentors, and green indicates conversations between scholars.

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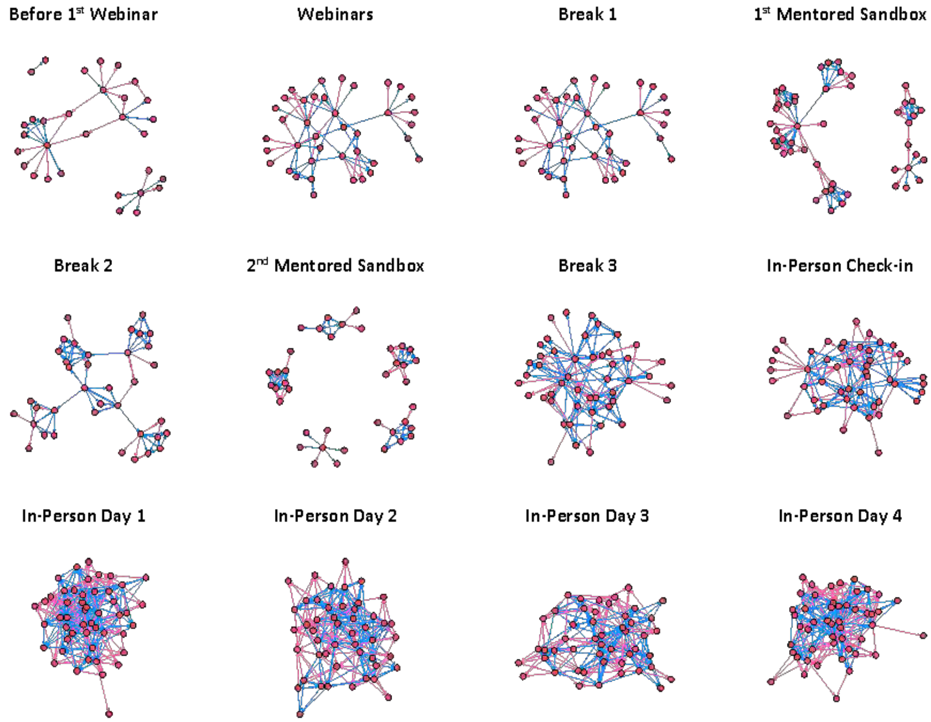

Figure. Conversations between scholars and mentors during mHealth Institute-Networks. Red ties indicate conversations between scholars and mentors, and blue ties indicate conversations between scholars.

c. Most of the participants had extremely positive views of the 2023 mHTI as an opportunity to

i. Apply material from the didactic core
ii. To get to know other scholars
iii. To get to know faculty members
iv. learn about transdisciplinary mHealth project development
v. To learn about working on a multidisciplinary team.
vi. Develop a project that will continue beyond the end of the institute

The mean of each question above was larger than 4.2 (out of 5.0, extremely positive).

d. Most of the participants strongly agreed that for the eight didactic core lectures

vii. Session speakers were informative and engaging.
viii. The session provided exposure to new content, perspectives, or disciplines related to mHealth.
ix. The speakers presented the content clearly and effectively.

The mean of each question above was larger than 4.2 (out of 5.0, extremely positive). The mean of the ratings for each speaker is 4.75 (out of 5.0, excellent).

Component Lead: Vivek, Shetty

Activity 2: Dissemination

The mDOT Center website, **mdotcenter.org** garnered more than 19,500 page views.

Recordings of webinars are posted to the **mDOT Center's YouTube channel**, where they are accessible by the general public; 40 mDOT Center-hosted webinars in the series have been released to date. More than 260 videos posted on the mDOT Center's YouTube channel have been viewed a total of more than 50,500 times on the channel, which now has 360 subscribers and more than 4,400 hours of watch time.

mHealthHUB which serves as a portal for the greater mHealth community garnered more than 52,400 unique users and more than 172,600 page views.

The training website, **mhti.md2k.org**, exists for the purpose of providing information about the NIH mHealth Summer Training Institute and has received 17,300 users and over 59,200 page views.

mDOT Social Media Channels

- The mDOT Center LinkedIn has 169 followers with 33 posts, 217 engagements, and 12,000 impressions over the past year.
- The mDOT Center X (formerly Twitter) has 361 followers with a total of 44 posts, 496 engagements, and 10,988 impressions over the past year.
- The mDOT Center TikTok has 6 unique videos (9 posts overall) with a total of 546 views.

B.2.4. Key Outcomes & Other Achievements

The educational consultant (Dr. Jeon) used the mHTI to conduct a longitudinal social network analysis of scholars' communications during the 2017-2019 mHTI programs. Their findings have been summarized by a paper that was recently accepted by the *Journal of Clinical and Translational Science*, a top-tier journal in the team science field. This paper employed separable temporal exponential random graph models (STERMGs) and other descriptive social network analyses techniques (SNA) to analyze scholars' project-based and fun-based communication networks from the previous mHTIs. Fig. 1 below visualizes the structures of the communication networks analyzed in the paper. Among others, we found that scholars from different disciplines or career stages were equally likely to speak to one another as those from the same disciplines or career stages.

Component Lead: Vivek, Shetty

Fig. 1 Network visualizations of team homophily for project-based conversations. Circles indicate scholars, sizes of circles represent the level of scholar's activeness (outdegree) in the network, and arrows represent conversation ties. Colors in circles indicate team membership; pink for team 1, green for team 2, yellow for team 3, red for team 4, sky blue for team 5.

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mDOT Center TRAINING & DISSEMINATION

B.4. What opportunities for training and professional development has the project provided?

In addition to the 30 scholars, the 2023 mHTI also provided an opportunity to 2 graduate students in the UCLA School of Education to conduct advanced social network analyses that will inform the growing field of team science.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. COMPONENT PARTICIPANTS

Not applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable
G.12 F&A COSTS Not Applicable