A. OVERALL COVER PAGE

Project Title: mHealth Center for Discovery, Optimization, and Translation of Temporally-Precise Interventions (mDOT)	
Grant Number: 5P41EB028242-02	**Project/Grant Period:** 07/15/2020 - 11/30/2025
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Change of Contact PD/PI: NA	
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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?

mDOT disseminates information to communities of interest via its website, mdot.md2k.org, which is updated on a regular basis and also when events warrant (7,523 page views since launch on July 1, 2020).

Recordings of webinars are posted to the center's YouTube channel, where they are accessible by the general public; more than 110 hours of training videos have been released. 152 videos posted on the Center's YouTube channel have been viewed a total of more than 38,500 times on the channel, which now has 268 subscribers and over 3,200 hours of watch time.

A second website, mhti.md2k.org, exists for the purpose of providing information about the upcoming NIH mHealth Summer Training Institute and has received 5,523 users and over 17,710 page views through September 2021, despite the cancellation of the 2020 mHTI event.

A third website, mHealthHUB, serves as a portal for the greater mHealth community (43,438 unique users and 153,977 page views since its November 2015 launch).
mDOT investigators have published or have submitted and under review 21 papers related to mDOT research. A full list of these publications by mDOT investigators can be found in section G.1.

In addition, MD2K investigators have participated in 56 talks and presentations at 31 global meetings.

mDOT.org: https:/mdot.md2k.org

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

mHealthHub: https://mhealth.md2k.org/

MD2K GitHub Repository: https://github.com/MD2Korg/

YouTube Channel: https://www.youtube.com/c/MD2KCenter

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

TR&D1
• We will complete the development of a diverse set of benchmarks and tasks for learning from incomplete and irregularly sampled time series including both publicly available datasets and data sets from selected CPs.
• We will continue the development of imputation methods for biophysical signals by developing missingness models that reflect real-life patterns of data missingness in mHealth applications.
• We will complete our development of continuous-time attention mechanisms for irregularly sampled longitudinal data by establishing the theoretical properties of the deformed kernel exponential family models and obtaining benchmark results on standard datasets.
• We plan to continue working on developing the mRisk method with CP1 and CP5 to estimate the momentary risk of lapse from mHealth biomarkers time series data.
• We plan to produce the relevant new mHealth biomarkers that estimate and characterize the lapse risk in the smoking cessation dataset of CP1 and CP5.
• We plan to implement the new biomarkers emerging from the mRisk model and apply them to the dataset of CP1 and CP5 so they can be used by our collaborating health researchers in pursuing their publication towards the design and development of new mHealth interventions.

TR&D2
• We will construct a hierarchical algorithm to account for delayed effects (Aim 1).
• We will continue building up a causal model to underpin the manager algorithm
• We will continue to collaborate with all 3 CPs.
• We will finish our methods development for analyzing MRT data in which the outcome is trivariate and time-varying (motivated by MRTs that we conducted under the prior MD2K grant).
• We will finish both of the papers in conjunctions with CP3.
• We will look to effectively incorporate uncertainty due to TR&D1 predictions into an RL algorithm.

TR&D3
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TR&D2
• We will write up and publish the analysis of the mHTI to advance Team Science
• We will organize and conduct the 2022 mHTI
• Reorganize the mHealthHUB portal
• Resume the online webinars by mDOT (currently on hold due to Zoom fatigue!)

Admin
• Software: Complete and publish the reinforcement learning module on the respective library repositories for both platforms.
• mDOT will look to host, hopefully in-person, it's next annual meeting with all Center investigators in attendance.
• We will look to expand the utility of the mDOT website by providing informative updates about new publications, software resources, and current center progress.
• The mDOT team intends to expand the number of CPs and SPs and onboard new CPs and SPs as needed.
• mDOT will look to enhance its engagement with the Executive Advisory Committee throughout Year 2 and include EAC members in relevant meetings and discussions to utilize their expertise and advise with mDOT stakeholders.
• mDOT 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 2.
• The admin team will compile and submit the required annual report to NIH for programmatic review.
• For continuous improvement in the mDOT technologies, its training activities, dissemination channels (e.g., website structure and content), and its administrative procedures, feedback will be regularly sought from mDOT team members, NIH program officers, mDOT affiliates, and the community stakeholders.

Principal Investigator: Kumar, Santosh

B.2 What was accomplished under these goals?

TR&D1 - DISCOVERY

In Year 1, the TR&D1 undertook a variety of activities (as described below) to fulfill its goals. In this period, we have focused on the fundamental problem of developing deep learning models for sparse, irregularly sampled, and incomplete time series data. We developed a novel approach for this problem that we refer to as Multi-Time Attention Networks. This model family generalizes past approaches to modeling irregularly sampled and incomplete time series data by enabling the learning of temporal similarity functions both within and across different dimensions of a time series using a novel attention-based layer that can operate directly over incomplete and irregularly sampled time series. Using this model class as a building block, we are exploring both its ability to reflect input uncertainty due to significant missing data and are developing modeling extensions to accommodate the hierarchical classification/imputation setting.

In additional work, we have explored a deep learning approach to the imputation of biophysical signals which exhibit a quasi-periodic signal structure in the form of “beats” resulting from the physiology of the cardiovascular and cardiopulmonary systems.

Recent work is providing an additional approach to developing continuous-time attention models which provide a flexible means to address irregularly sampled longitudinal data via attention densities. We are building on a recent formulation of continuous-time attention that has been shown to generalize the popular transformer architecture for learning discrete attention representations. Our work generalizes the standard approach, which is based on unimodal attention densities to encompass multimodal attention densities based on exponential and deformed exponential family distributions.

We have also explored the interaction of the varying internal and external risk factors/stimuli for developing a computational model to predict the imminent risk (in the form of a composite risk score) of impulsive behavior. Estimation of the continuous risk state may be critical for delivering temporally-precise interventions and treatment adaptations in cessation programs. For data analysis, we plan to work with CP1 (Novel Use of mHealth Data to Identify States of Vulnerability and Receptivity to JITAIs). Furthermore, once the model is developed, we aim to coordinate with CP5 (Affective Science and Smoking Cessation: Real-time Real-world Assessment) for its incorporation into the study.

Finally, we have developed a transformer-based deep learning architecture for predicting nonresponse given a history of past EMA responses in conjunction with demographic and contextual data. Our novel approach outperforms classical machine learning methods on this task.

TR&D2 - OPTIMIZATION

In Year 1, the TR&D2 undertook a variety of activities (as described below) to fulfill its goals. We developed the first method for inference of confidence intervals or bias in the case of estimation when the use of RL algorithms results in “adaptively sampled” data. We also developed a statistical inferential weighting method that permits the most common approaches to inference. This work will be used to inform how to design RL algorithms that both allow within user personalization as well as facilitate experiment learning (facilitate the building of scientific knowledge via after experiment data analyses). We completed work on methods for analyzing adaptive sampled data when there is no sharing of data among users. We also developed an efficient computational approach to hyperparameter tuning when the RL algorithm uses a mixed-effects model with data from multiple users to personalize intervention delivery for a particular user.

In another activity, we are developing a method for conditional forecasting of user state estimated from sensors. In

particular, we are using the stress assessment produced by wrist-worn PPG sensors in the context of smoking cessation from CP1. WIth CP3, we wrote a paper on methods for analyzing binary longitudinal outcomes from an MRT (here the outcome was whether the user monitored their weight each day) and a second paper on approaches for pooling data across individuals in after-study analyses in mobile health. We completed and presented a workshop paper on flexible modeling strategies for MRT data as well.

TR&D3 - TRANSLATION

In Year 1, the TR&D3 undertook a variety of activities (as described below) to fulfill its goals. We are deriving micromarker abstractions for PPG signals for heart rate and heart rate variability assessment using task-specific autoencoders through developing hierarchical computing methods to support scalable, low-latency, power-efficient computation of biomarker computations. We use a multichannel autoencoder structure paired with a tachogram estimation based on convolutional neural networks as an end-to-end trainable algorithm using a task-specific error metric that penalizes deviations from the actual tachogram signal derived from an ECG sensor during training. Then we use the latent codes learned in the autoencoder framework as the micromarker representations of the heart rate signal that are tailored for tachogram estimation. In future work, we will assess the utility of these micromarkers in a stress inference task.

We have developed a dual-core version of our wristband and rewrote the software stack from the ground up to support common machine learning abstractions often encountered in bio/micro marker implementations. This concrete implementation based on current industry standards will allow us to explore power, latency, data rate tradeoffs in real-time biomarker computations. We also seek to recover the characteristic properties, including permittivity, conductivity, and thickness, of the target tissues illuminated by a BIoRF sensor for the development of biomarkers for RF sensing of internal tissues.

Finally, we worked on the development of computational mechanisms for sharing clinical time-series data to assure privacy while retaining utility by creating computational mechanisms and a general biomarker privacy framework to enable participant control over the privacy-utility trade-offs during study design, data collection, and sharing of collected mHealth data for third-party research when data cross trust domains.

SOFTWARE

An overall software architecture was developed based on multiple rounds of discussion with all TR&D projects. To provide reusable software to the community, we previously developed modularized software that included mCerebrum as a collection of apps for smartphones so that one can pick and choose the suite of apps to meet the data collection needs of a specific research study. This platform included provisions for handling many diverse sensor modalities and real-time signal processing algorithms such as smoking or stress detection. Commercial wearable devices were unable to meet the data demands of our studies and we created the MotionSense platform to get access to wrist-based data. mCerebrum was complemented with a cloud-based big-data companion system called Cerebral Cortex, designed to accept all the data from field participants and further process the information for the purposes of accelerating research in the mHealth domain. For modularity, we made it a containerized cloud-based service. While these software suites were successfully deployed in a wide variety of research studies, they all required heavy involvement from our team.

What we learned over the years is that researchers want a high degree of control in their study and we were always modifying and augmenting the platform to suit their needs. So much so that each study nearly became a custom solution. To better accommodate these requirements, our approach has shifted from a modular, configurable hosted solution, which is not scalable to the 20+ projects involved in mDOT, to one where the team produces reusable modules

Principal Investigator: Kumar, Santosh

that embed our research innovations into cross-platform mobile libraries which are coupled with cloud-based containers. This approach will significantly reduce the overhead for anyone wishing to leverage the mDOT software modules in their own mHealth solutions. We see the primary users of these modules falling into two categories: 1) Software developers working with mHealth research groups that will directly support their data collection in research studies and 2) industry groups that are looking for software implementation of cutting edge mHealth technologies being developed by TR&D projects in the mDOT Center. To have a fully working production software system to test each developed software module, we have implemented and deployed a fully functional software system for the MOODS study in collaboration with CP7. As described in more detail in Section B.2.3., it includes computation of the stress biomarker on a commercial smartwatch (Fossil Sport), remote recruitment of participants, deployment of software on both wearable and participants' own smartphones via respective app stores, and collection and analysis of mHealth biomarkers.

TRAINING & DISSEMINATION

Due to the COVID pandemic, the training activities made a hard pivot to virtual training. The main focus of the training was the development and conduct of a virtual version of the annual mHealth Training Institute (mHTI). This entailed deployment of a virtual events platform (vFairs) and a comprehensive, online application management system (SmarterSelect). From a pool of 280 applicants, 35 were chosen as scholars for the 2021 mHTI . A corresponding group of faculty, comprising both academics and NIH Program Officers, was also recruited. The virtual 2021 mHTI was conducted between May 10 and July 30, 2021.

To allow the didactic content of the 2021 mHTI to be broadly accessible, 13 webinars were recorded and curated on the mHTI's website as well as our mHealthHUB platform.

ADMINISTRATION CORE

The mDOT Center Operations Office, housed in Memphis, Tenn., is the main hub for mDOT 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. The Director of Operations (Joe Biggers) reports to Center Director Kumar and is responsible for supervising all Administration Core staff, developing and implementing policies and practices related to Center record-keeping, activity planning, and monitoring, and acts as liaison to each partner site's designated contact to ensure seamless support for investigators at all sites. The Director of Center Operations established a close working relationship with the TR&D Leads as a means to facilitate effective day-to-day operation of all center activities.

Through the administrative core, the mDOT Center organized and hosted an all-virtual kick-off meeting event on Monday, September 28, 2020. Participants included all mDOT Team members, students, and various CP and SP lead. The goal of the kick-off meeting was to brainstorm about research, collaboration, training, and outreach as well as set the formal research agenda for the upcoming year.

The mDOT Center assembled a high-profile External Advisory Committee (EAB) that includes 5 thought leaders representing Center research expertise. Recruitment was deliberate to further ensure a diversity of perspectives and experiences. The EAC provided the high-level guidance, oversight, and review of progress towards research and training goals and the efficacy of Center operating structures and policies for Year 1. 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.

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

Managing and Mentoring - The software, mCerebrum and Cerebral Cortex, 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 PivitolTracker for handling bug report and project planning.

Archive - 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 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 Google Drive and PivotalTracker which allow for easy access to information in a usable and consumable manner.

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 webinars.
https://mhealth.md2k.org/

Publication Reviews - mDOT investigators have published or have submitted and under review 21 papers related to mDOT research. The papers have been readily available for team review to facilitate broader discussion.

Webinars - We have an archive of over 150 webinars and over 110 hours of training video content. Students and staff are encouraged to attend live, and webinars are posted to the MD2K YouTube channel and links are featured on the mHealthHUB. https://www.youtube.com/c/MD2KCenter

Student Mentoring - Each mDOT-affiliated graduate student has a faculty advisor to guide them in their studies and is available for discussions about coursework and research.

mHealth Training Institute - All the presentations by the mHTI faculty are archived on mHealthHUB.
https://mhealth.md2k.org/mhealth-training-institute

mDOT Website -
https://mdot.md2k.org

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

Webinars -
https://www.youtube.com/c/MD2KCenter

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 (see table below of recent talks and presentations).

- On December 13, 2020, we conducted a workshop at the 31st Annual Meeting of the American Association of Addiction Psychiatry entitled, "Trials and Tribulations in Optimizing mHealth Interventions in Addictions." This workshop provided training in MRT design and three addiction health scientists presented their MRTs.

- On December 16 and 18, 2020, we conducted virtual brainstorming sessions for health scientists who have conducted an MRT (first session) or are designing an MRT (second session). The first session was with scientists who conducted an MRT with the Drink Less app in the U.K. and the second session was with a health scientist developing dialectical behavior therapy for individuals in distress. Attendees included health scientists working on MRTs including exercise for cancer patients (Harvard Dana Farber Cancer Institute), smoking (Johns Hopkins, National Institute on Minority Health and Health Disparities, the University of Texas at Austin), physical activity (UC Berkeley), suicide prevention (Harvard Psychology), cancer prevention (Harvard Mass General), addiction (Univ of New Mexico, McLean Hospital), immunosuppressant medication adherence among adolescents and young adults (Johns Hopkins), mental health (Northwestern Univ., Brigham and Women's Hospital), ADHD (George Washington Univ. School of Medicine), postpartum risky drinking (Partnership to End Addiction), stress management (UCSF Department of Psychiatry and Behavioral Sciences), engagement (University Michigan) as well as data scientists from Harvard, Univ. Michigan, UC Irvine, Apple, and the University of Wisconsin. It was very exciting!

- On January 6,7,8, 2021 we ran a workshop at the Winter School AI4Health (Paris, virtual); this 6-hour workshop targets data scientists (CS, Eng, Stat) who are interested in machine learning for designing interventions in mobile health.

- In June 2021 we ran two virtual brainstorming sessions. The first session was with behavioral scientists who are designing an MRT for suicide prevention (M. Nock, Harvard Univ). In the second S. Dauber (Partnership to end drug addiction) presented on the development of a conceptual model and design of a preliminary EMA study aimed at informing the development of a tailored JITAI for postpartum risky drinking. Attendees included health scientists working in suicide prevention, smoking cessation, substance use prevention and treatment, treatment adherence, maternal and child health, anger management, and behavioral interventions for adolescents with ADHD, as well as data scientists working on statistical methodologies for data analysis for mobile health applications.

- On September 21, Susan Murphy taught a course, "Digital Health Technologies: Moving Health Care from the Clinic to the Patient" at the virtual ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop. Her part of the course, which focused on micro-randomized trials & reinforcement learning for constructing personalized mobile digital health technologies for behavioral modifications with application to individuals at risk of adverse cardiovascular events, had a wide range of attendees from academia, government agencies, and the health care sector.

- October 13, 2021, Susan Murphy along with scientists in CP1 conducted a workshop at the Addiction Health Services Research Conference on Methods for Adaptive and Personalizing Prevention, Treatment, and Recovery Services for SUD. This workshop is for addiction services scientists who are interested in developing adaptive interventions, particularly in digital health.

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- On October 25-26 Susan Murphy led a 2021 Summer Institute workshop Building Just-in-Time Adaptive Interventions. This is a two-day virtual workshop for 45 behavioral scientists from institutions across the United States. Attendees work in a wide range of fields, including suicide prevention, addiction treatment, HIV prevention, smoking cessation, treatment adherence, and management of chronic conditions. All of the participants are developing digital interventions.

- At UCLA the project activities have partially engaged three Ph.D. students as well as two undergraduate students. The project has furthered their educational training by giving them hands-on experience on various facets of sensor information processing towards biomarker computation on resource-constrained wearable devices, and on quantifying and mitigating privacy risks. Additionally, the research in the project was also incorporated in two graduate courses via special lectures, assignments, and projects, resulting in influencing the training of 50+ students in the ECE and CS Departments.

- In addition to the 35 scholars, the 2021 mHTI also provided an opportunity to 3 graduates in the UCLA School of Education to conduct advanced social network analyses that will inform the growing field of team science.

Major Talks & Presentations

S. Murphy	Numerical Analysis for Data Science Opening Workshop, SAMSI,	Remote	8/27/2020	Intelligent Pooling for Thompson Sampling with Applications to Mobile Health (invited talk)
S. Murphy	Joint Conference of the GMDS & CEN-IBS 2020	REMOTE (Berlin)	09/07/2020	Clinical Trial Designs for Personalizing Digital Interventions (**Keynote**)
S. Murphy	Neyman Statistics Seminar, University of California, Berkeley,	Remote (Berkeley)	10/28/2020	Challenges in Developing Learning Algorithms to Personalize Treatment in Real Time (invited talk)
S. Murphy	4th Annual Mobile & Electronic Health-ARC Symposium	Remote (Boston)	11/12/2020	Data, Personalization, Digital Health! (invited talk)
S. Murphy	Sixth Seattle Symposium in Biostatistics	Remote (Seattle)	11/21/2020	Challenges in Developing Learning Algorithms to Personalize Treatment in Real Time (invited talk)
S. Murphy	Deep Reinforcement Learning Workshop (virtual), NeurIPS 2020		12/11/2020	We used RL…but…did it work?! (invited talk)
S. Murphy	Machine Learning for Mobile Health Workshop (virtual), NeurIPS 2020		12/12/2020	Assessing Personalization in Digital Health (invited talk)
S. Murphy	31st Annual Meeting of the American Academy of Addiction Psychiatry	Virtual workshop	12/13/2020	Trials and Tribulations in Optimizing mHealth Interventions in Addictions (invited talk)
S. Murphy	New York Medical College	Virtual presentation	12/21/2020	Data, Personalization, Digital Health! (invited talk)
S. Murphy	UAB Nutrition Obesity Research Center	Remote (Birmingham)	1/19/2021	Data, Personalization, Digital Health! (invited talk)
S. Murphy	AAAI 2021 Workshop Trustworthy AI for Healthcare	Virtual presentation	2/9/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Webinar, Faculté des sciences médicales et paramédicales, SESSTIM	Remote (Marseille, France)	2/26/2021	Data, Personalization, Digital Health! (invited talk)

S. Murphy	The Obesity Society 2021 Preconference Workshop on Synergistic Rigor in the Intersection of Epidemiology & Obesity	Remote presentation	2/2021	Using Mobile Health Interventions to Support Individual Decision Making (invited talk)
S. Murphy	Workshop on AUI for Public Health, ICLR 2021	Remote presentation	5/7/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Biomedical Data Science Seminar, University of Stanford School of Medicine	Remote (Stanford)	5/20/2021	We used RL but…. Did it work?! (invited talk)
S. Murphy	Frontiers of Causal Inference in Data Science: Perspectives from Leaders in Tech and Academia	Remote presentation	5/28/2021	We used RL but…. Did it work?! (invited talk)
S. Murphy	Distinguished Speaker Virtual Seminar, Department of Statistics, University of Oxford	Remote (Oxford, England)	6/18/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Statistical Learning Methods in Modern AI	Remote conference presentation	6/25/2021	We used RL; but did it work? (invited talk)
S. Murphy	37th Conference on Uncertainty in Artificial Intelligence	Remote conference keynote	7/27/2021	Keynote
S. Murphy	JSM 2021	Invited virtual paper	8/11/2021	Assessing Causal Inference Using Adaptively Collected Data (invited talk)
S. Murphy	Statistical Science Seminar, Duke University	Remote (Durham, NC)	9/3/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	RMME/STAT Colloquium, University of Connecticut	Remote (Storrs, CT)	9/10/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Herbert Wertheim School of Public Health and Human Longevity Science, University of California San Diego	Remote Grand Rounds (San Diego, CA)	9/17/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Department of Statistics, Florida State University	Myles Hollander Distinguished Lecture (virtual)	9/24/2021	We Used a Bandit Algorithm to Personalize But Did It Work? (invited talk)
S. Murphy	Design and Analysis of Experiments 2021 (DAE2021)	Remote conference presentation	10/13/2021	(invited talk) title TBD (see https://sites.google.com/view/dae2021/invited-sessions)
S. Murphy	Department of Statistics, University of Connecticut	Remote (Storrs, CT)	11/10/2021	Makuch Lecture
S. Murphy	Institute for Applied Computational Science, Harvard University	Remote (Boston, MA)	9/24/2021	We Used RL, But Did It Work? (invited talk)
P. Liao	Simons Institute for the Theory of Computing	REmote (Berkeley, CA)	9/24/2021	Batch Policy Learning in Average Reward Markov Decision Process
P. Liao	INFORMS 2020 virtual conference	Remote	11/9/2020	Batch Off-policy Learning in Average Reward Markov Decision Processes

P. Liao	Ubicomp/ISWC 2020 virtual conference	Remote	9/18/2020	Personalized HeartSteps: A Reinforcement Learning Algorithm for Optimizing Physical Activity
P. Liao	Pre-recorded talk, Bernoulli-IMS One World Symposium 2020 (virtual)	Remote	8/2020	Off-Policy Estimation of Long-Term Average Outcomes with Applications to Mobile Health
P. Liao	JSM 2020 virtual conference	Remote	8/3/2020	Off-Policy Estimation of Long-Term Average Outcomes with Applications to Mobile Health
K. Zhang	Statistics Colloquium, Pennsylvania State University	State College, PA (may change to remote)	11/11/201	Statistical Inference with M-Estimators on Adaptively Collected Data
K. Zhang	Virtual presentation, Institute for Operations Research and the Management Sciences (INFORMS) Annual Meeting	Remote	10/2021	Statistical Inference with M-Estimators on Adaptively Collected Data
K. Zhang	Pre-recorded talk, Bernoulli IMS Tenth World Congress in Probability and Statistics	Remote	7/2021	Statistical Inference with M-Estimators on Adaptively Collected Data
K. Zhang	Virtual presentation, Health Data Science Seminar Series, London School of Hygiene and Tropical Medicine	Remote (London, UK)	6/2/2021	Causal Inference for Data Collected with Bandit Algorithms
K. Zhang	Virtual talk, University of Cambridge Medical Research Council Biostatistics Unit	Remote (Cambridge, UK)	4/29/2021	Statistical Inference with M-Estimators on Bandit Data
K. Zhang	Pre-recorded talk, Bernoulli-IMS One World Symposium 2020 (virtual)	Remote	8/2020	Inference for Batched Bandits
M. Menictas	NeurIPS 2020 (virtual), poster and presentation (both with same title)	Remote	12/12/2020	Fast physical activity suggestions: efficient hyperparameter learning in mobile health
SN. Shukla	ML Retrospectives, Surveys & Meta-Analyses (ML-RSA) Workshop at NeurIPS, 2020	Remote	12/11/20	A Survey on Principles, Models and Methods for Learning from Irregularly Sampled Time Series
Santosh Kumar	Discovery, Optimization, and Translation of Temporally-Precise mHealth Interventions	Remote	09/07/2021.	IEEE Digital Health Conference
Santosh Kumar	Synergistic Collaboration Among Computing and Health Researchers	Remote	7/30/2021	
Santosh Kumar	From Sensed Data to Digital Biomarkers – Lessons Learned,	Remote	5/24/2021	NIH Annual mHealth Training Institute
Santosh Kumar	Breakout Session on Real-time Multimodal Data	Remote	5/14/21, 5/28/2021, and 6/11/2021	NSF-NIH Workshop on Establishing the Roadmap for Security, Privacy, and Ethics Research in Health
Santosh Kumar	Experiences in Developing and Deploying ML Models from Wearables	Remote	5/18/2021	NIH Annual mHealth Training Institute

Principal Investigator: Kumar, Santosh

Santosh Kumar	Identifying Location Micro-Patterns Conducive to Smoking from GPS and Activity Traces	Remote	09/29/2020	NIH Workshop on Harnessing Novel Data Sources and Technologies for the Study of Social Determinants of Health (SDOH) in Heart, Lung, Blood, and Sleep (HLBS) Disorders
Ziqi Wang	Virtual Poster Presentation at ACM/IEEE IPSN	Remote (Nashville, TN, USA)	05/2021	Protecting User Data Privacy with Adversarial Perturbations
Mani Srivastava	Joint Keynote, 2nd Intl. Conference on Activity and Behavior Computing (ABC), 9th Intl. Conference on Informatics, Electronics & Vision (ICIEV), and, 4th Intl. Conference on Imaging, Vision & Pattern, 2020.	Remote (Japan)	08/2020	Security and Privacy Challenges in Learning-enabled IoT Systems
Mani Srivastava				The Future of Edge Computing: Towards Intelligent Autonomy in Human Spaces
Mani Srivastava	Invited Talk at Army Science Planning and Strategy Meeting (ASPSM) on Synthetic Environments for AI & ML	Remote	12/2020	Domain Transfer ChallengesBeyond Shifts in Data Distribution: Stochasticity in Time
Mani Srivastava	Invited Panel Talk IEEE 20202 CIC Plenary Panel on Collaborative Intelligence and Killer Applications in Edge Computing	Remote	12/2020	Towards Autonomy in Human Spaces
Mani Srivastava	Invited Talk at the Next Big Research Challenges in Cyper-Physical Systems Workshop	Remote	04/2021	CPS Technology Foundations: Quo Vadis?
James Rehg	Wearable cameras as a source of context for understanding eating behavior,	Virtual	10/22/2020	NSF Workshop on Technology for Automated Capture of Diet, Nutrition, and Eating Behaviors in Context

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?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	Qian T, Klasnja P, Murphy SA. Linear mixed models with endogenous covariates: modeling sequential treatment effects with application to a mobile health study. Statistical science : a review journal of the Institute of Mathematical Statistics. 2020;35(3):375-390. PubMed PMID: 33132496; PubMed Central PMCID: PMC7596885; DOI: 10.1214/19-sts720.
Complete	Li S, Psihogios AM, McKelvey ER, Ahmed A, Rabbi M, Murphy S. Microrandomized trials for promoting engagement in mobile health data collection: Adolescent/young adult oral chemotherapy adherence as an example. Current opinion in systems biology. 2020 June;21:1-8. PubMed PMID: 32832738; PubMed Central PMCID: PMC7437990; DOI: 10.1016/j.coisb.2020.07.002.
Complete	Carpenter SM, Menictas M, Nahum-Shani I, Wetter DW, Murphy SA. Developments in Mobile Health Just-in-Time Adaptive Interventions for Addiction Science. Current addiction reports. 2020 September;7(3):280-290. PubMed PMID: 33747711; PubMed Central PMCID: PMC7968352; DOI: 10.1007/s40429-020-00322-y.
Complete	Bari R, Rahman MM, Saleheen N, Parsons MB, Buder EH, Kumar S. Automated Detection of Stressful Conversations Using Wearable Physiological and Inertial Sensors. Proceedings of the ACM on interactive, mobile, wearable and ubiquitous technologies. 2020 December;4(4). PubMed PMID: 34099995; PubMed Central PMCID: PMC8180313; DOI: 10.1145/3432210.
Complete	Liao P, Klasnja P, Murphy S. Off-Policy Estimation of Long-Term Average Outcomes with Applications to Mobile Health. Journal of the American Statistical Association. 2021;116(533):382-391. PubMed PMID: 33814653; PubMed Central PMCID: PMC8014957; DOI: 10.1080/01621459.2020.1807993.
In Process at NIHMS	Nahum-Shani I, Potter LN, Lam CY, Yap J, Moreno A, Stoffel R, Wu Z, Wan N, Dempsey W, Kumar S, Ertin E, Murphy SA, Rehg JM, Wetter DW. The mobile assistance for regulating smoking (MARS) micro-randomized trial design protocol. Contemporary clinical trials. 2021 July 24:106513. PubMed PMID: 34314855; DOI: 10.1016/j.cct.2021.106513.
In Process at NIHMS	Battalio SL, Conroy DE, Dempsey W, Liao P, Menictas M, Murphy S, Nahum-Shani I, Qian T, Kumar S, Spring B. Sense2Stop: A micro-randomized trial using wearable sensors to optimize a just-in-time-adaptive stress management intervention for smoking relapse prevention. Contemporary clinical trials. 2021 August 8;109:106534. PubMed PMID: 34375749; DOI: 10.1016/j.cct.2021.106534.
In Process at NIHMS	Estimating time-varying causal excursion effect in mobile health with binary outcomes. Biometrika.
In Process at NIHMS	Inference for Batched Bandits. Advances in neural information processing systems.
In Process at NIHMS	A Survey on Principles, Models and Methods for Learning from Irregularly Sampled Time Series: From Discretization to Attention and Invariance. ML-Retrospectives, Surveys & Meta-

	Analyses @ NeurIPS 2020.
In Process at NIHMS	Translating Strategies for Promoting Engagement in Mobile Health: A Proof-of-Concept Micro-Randomized Trial. Health psychology : official journal of the Division of Health Psychology, American Psychological Association.
In Process at NIHMS	IntelligentPooling: practical Thompson sampling for mHealth. Machine learning.
In Process at NIHMS	Power Constrained Bandits. Proceedings of machine learning research.
In Process at NIHMS	mTeeth. Proceedings of the ACM on interactive, mobile, wearable and ubiquitous technologies. DOI: 10.1145/3463494.
In Process at NIHMS	SmokingOpp. Proceedings of the ACM on interactive, mobile, wearable and ubiquitous technologies. DOI: 10.1145/3380987.
In Process at NIHMS	Protecting User Data Privacy with Adversarial Perturbations. IPSN : [proceedings]. IPSN (Conference). DOI: 10.1145/3412382.3458776.

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

Category	Explanation
Software	https://github.com/MD2Korg/
Educational aids or curricula	https://mhti.md2k.org/
Audio or video , Educational aids or curricula	https://www.youtube.com/c/MD2KCenter
Research Material	http://people.seas.harvard.edu/~samurphy/
Research Material	https://mdot.md2k.org
Educational aids or curricula	https://mhealth.md2k.org/

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
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.
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.
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).

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
SKUMAR4	Y	Kumar, Santosh	PHD	PD/PI	0.0	2.3	0.8		Admin-Core-001 (mDOT Administrative Core), Project-001 (mDOT TR&D1 (Discovery) - E…Risk Dynamics), Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA
ATRELLA	N	Trella, Anna Li	BA	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	1.4	0.0	0.0		Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA
BMARLIN	Y	Marlin, Benjamin M.		Co-Investigator	1.0	0.0	0.0		Project-001 (mDOT TR&D1 (Discovery) - E…Risk Dynamics), Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA
ERTIN01	Y	Ertin, Emre	PHD	Co-Investigator	0.0	1.4	0.0		Project-003 (mDOT TR&D3 (Translation): …plementations)		NA
HUIWEI123	N	Wei, Hui	BS,MS,PHD	Graduate Student (research assistant)	1.0	0.0	0.0				NA
HYLAI1	N	Lai, Hsin-Yu		Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	1.0	0.0	0.0		Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA
J.REHG	Y	Rehg, James M.	PHD	Co-Investigator	1.0	0.0	0.0				NA
JEONMJ	N	Jeon, Minjeong		Consultant	1.0	0.0	0.0		Tech-Train-Dissem-001 (mDOT Training and Dissemination)		NA
KARINETUNG	N	Tung, Karine	PHD	Graduate Student (research assistant)	1.0	0.0	0.0		Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA
KELLYZHANG	N	Zhang, Kelly Wang	BA	Graduate Student (research assistant)	1.0	0.0	0.0		Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA

NSUGAVANAM	N	Sugavanam, Nithin	BS,PHD	Graduate Student (research assistant)	1.0	0.0	0.0		Project-003 (mDOT TR&D3 (Translation): …plementations)		NA
PENGLIAO	N	Liao, Peng	BS,PHD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	3.0	0.0	0.0		Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA
SAKTHER	N	Akther, Saymon	MA,BA,PHD	Graduate Student (research assistant)	6.0	0.0	0.0		Project-001 (mDOT TR&D1 (Discovery) - E…Risk Dynamics), Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA
SAMURPHY	Y	MURPHY, SUSAN A	PHD	Co-Investigator	1.5	0.0	0.0		Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA
SATYASHUKLA	N	Shukla, Satya		Graduate Student (research assistant)	3.5	0.0	0.0		Project-001 (mDOT TR&D1 (Discovery) - E…Risk Dynamics)		NA
SBASKAR	N	baskar, siddharth	BS	Graduate Student (research assistant)	1.0	0.0	0.0		Project-003 (mDOT TR&D3 (Translation): …plementations)		NA
SCHTTRJ1	N	Chatterjee, Soujanya	PHD,OTH	Graduate Student (research assistant)	6.0	0.0	0.0		Project-001 (mDOT TR&D1 (Discovery) - E…Risk Dynamics), Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA
SHETTY2	Y	SHETTY, VIVEK	DOTH,DDS	Co-Investigator	1.1	0.0	0.0		Tech-Train-Dissem-001 (mDOT Training and Dissemination)		NA
SHUANGLI3	N	Li, Shuang	PHD,MS,BS	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	2.4	0.0	0.0		Project-002 (mDOT TR&D2 (Optimization):…ment Learning)		NA
SIMIDA	Y	SIM, IDA	MD,PHD	Co-Investigator	0.9	0.0	0.0		Project-003 (mDOT TR&D3 (Translation): …plementations)		NA
SMHSSAIN	N	Hossain, Syed Monowar	PHD,MS	Staff scientist (Doctoral level)	3.6	0.0	0.0		Project-002 (mDOT TR&D2 (Optimization):…ment Learning), Project-003 (mDOT TR&D3 (Translation): …plementations)		NA
SRATHNAM	N	Rathnam,	AB,MS,PHD	Graduate	0.3	0.0	0.0				NA

		Sarah		Student (research assistant)							
SRIVASTAVA2	Y	Srivastava, Mani	PHD,MS,OTH	Co-Investigator	0.0	0.0	0.8		Project-003 (mDOT TR&D3 (Translation): …plementations)		NA
TWHNAT	N	Hnat, Timothy	BS,OTH,PHD	Staff scientist (Doctoral level)	2.0	0.0	0.0		Project-001 (mDOT TR&D1 (Discovery) - E…Risk Dynamics), Project-002 (mDOT TR&D2 (Optimization):…ment Learning), Project-003 (mDOT TR&D3 (Translation): …plementations), Tech-Train-Dissem-001 (mDOT Training and Dissemination)		NA
	N	Saha, Swapnil	MS	Research Assistant	4.0	0.0	0.0		Project-003 (mDOT TR&D3 (Translation): …plementations)		NA
	N	Wang, Brian	BS	Research Asst.	3.0	0.0	0.0		Project-003 (mDOT TR&D3 (Translation): …plementations)		NA
BPAHERN	N	Ahern, Brian		Training Specialist	6.0	0.0	0.0		Tech-Train-Dissem-001 (mDOT Training and Dissemination)		NA
JWBGGERS	N	Biggers, Joseph	MS	Operations Director	2.0	0.0	0.0		Admin-Core-001 (mDOT Administrative Core)		NA
SSAMIEI	N	Samiei, Shahin		Research Coordinator	2.4	0.0	0.0		Admin-Core-001 (mDOT Administrative Core)		NA

Glossary of acronyms:

S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - 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?

Yes

We request for a personnel change on the effort of co-I, Dr. Ida Sim (UCSF) to be reduced from 7.5% to 0% for Years 2 and 3 of the project. Due to taking of a new role she has acquired at UCSF, Dr. Sim has requested to take a hiatus from the project for the next 2 years There will be no overall change in the total budget for the Center, and Dr. Sim's research would temporarily be absorbed within the current team. In addition, Dr. Sim will still be reachable if the mDOT team needs her

advice on some issues. The UCSF budget would be absorbed by the University of Memphis as the Prime Institution on the award for the next two project periods.

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

File Uploaded: All mDOT Supports & Personnel Request.pdf

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

E. OVERALL 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?

All mDOT software is freely available under the BSD 2-Clause license3. By collecting and storing high-frequency raw sensor data, our approach enables external validation of computed biomarkers as well as computation of new biomarkers in the future.

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

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

NOTHING TO REPORT

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?

No

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	DUNS	Congressional District	Address
Primary: UNIVERSITY OF MEMPHIS	055688857	TN-009	UNIVERSITY OF MEMPHIS ADMINISTRATION 315 MEMPHIS, TN 381520001
Georgia Tech Research Corporation	097394084	GA-005	926 Dalney Street NW Atlanta, GA 30318
President and Fellows of Harvard College	082359691	MA-005	1033 Massachusetts Avenue, 5th Floor Cambridge, MA 02138
The Ohio State University	832127323	OH-003	1960 Kenny Road Columbus, OH 43210
The Regents of the University of California	092530369	CA-033	10889 Wilshire Blvd Suite 700, Box 951406 Los Angeles, CA 90095
The Regents of the University of California, San Francisco	094878337	CA-012	3333 California Street, Suite 315 San Francisco, CA 94143
University of Massachusetts Amherst	153926712	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

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

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, mDOT builds on central operations infrastructure developed through 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. mDOT 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.

mDOT 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 mDOT Director, responsible for overseeing all project related activities and will also lead the Administration Core. He will work with an Executive Committee, mDOT Operations Office, and 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 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 on the NIH-funded MD2K National Center of Excellence, the Administration Core will provide the managerial and operational structures through which the mDOT 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 use of mDOT 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 mDOT.

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

Aim 5: Develop quantifiable measures and implement systems to monitor, assess, and evaluate the quality and utility of mDOT 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?

We published articles in peer-reviewed international conferences and journals and book chapters. We disseminated information using our websites and social media. Work was also disseminated directly via the following presentations, several of which are archived at mHealthHUB for broader dissemination.

Professional Conferences & Presentations
*see list in overall dissemination table

Documentation and Manual software website https://github.com/MD2Korg/
Relevant Github repositories contain instructions for each project. The software, mCerebrum and Cerebral Cortex, is freely available from GitHub and can be configured to support high-rate data collection for specific studies via simple changes in configurations. Open-source licensing also allows for others to incorporate new apps for supporting other sensors or new computational models for existing or new biomarkers.
The entirety of the Center's software is designed to be extensible and usable by a variety of researchers, including students and postdocs. Researchers who wish to contribute to the software platform can reach out to the software team and start a discussion to determine how we can best help each other. For external users, we have set up "How-To" pages for software introduction and manuals (https://md2k.org/software/how-to.html) as well as a "Getting Started" page for introductory step-by-step instructions to begin installation and use of the Center software (https://md2k.org/software-how-to/software-smartphone/software-howto-getting-started.html).

mDOT Software adoption https://md2k.org/software-deployments.html
The mDOT software platform is an open-source project (https://github.com/MD2Korg/) with 80 unique repositories for individual components of the various platforms. This platform currently supports 13 independent studies targeting 8 health and workplace targets: Smoking, Eating, Stress, CHF, Oral Health, Cocaine Use, Behavior Change, Workplace Performance. An estimated 2,251 users, 106,806 person-days, and 4.7 trillion data points have been collected from these studies into the

Cerebral Cortex platform.

Software Survey
To evaluate the effectiveness of the Center's activities, anonymous surveys were created and sent to users of mDOT's software tools to gather feedback and satisfaction levels. Responses were collected from researchers of a wide range of mHealth research areas (stress management, oral health, smoking cessation, workplace performance, eating regulation, heart failure care, behavior change, and drug use detection) from locations all over the country who have used the Center's software (mCerebrum smartphone application suite and/or Cerebral Cortex cloud software) between 2016-2020. Of the users surveyed, 100% of respondents have used mCerebrum mobile software; 62% of respondents have used Cerebral Cortex cloud software.
On a rating scale of 1 to 5, the user satisfaction level was determined in various categories for each software application and summarized as follows:
mCerebrum - general software use: average score of 3.4 out of 5, helping to meet research goals: average of 3.7 out of 5, technical support from the Center's team: average of 3.3 out of 5, installation or first use experience: average of 3.0 out of 5.

Cerebral Cortex - general software use: average score of 3.4 out of 5, helping to meet research goals: average of 3.6 out of 5, technical support from the Center's team: average of 3.4 out of 5, installation or first use experience: average of 3.2 out of 5.

Survey recipients provided suggestions for improvements to the software; these include a mCerebrum user experience that is less overwhelming, more stable sensor connections, fixes for mCerebrum software crashes, 24/7 technical support, Cerebral Cortex code documentation, plug-ins that transform data at various intercept points, and an easier installation process. 50% of users continued to use the software for more than one consecutive year, and 54% of survey respondents indicated they are likely to recommend mDOT software to other researchers.

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

Software
Reinforcement Learning: We have already begun the work on our first module, reinforcement learning, through extensive discussions with TR&D2. We created a module and architecture plan that includes a cross-platform (Android, iOS) mobile library which allows developers to input data in a prescribed format to both a cloud-supported decision function and a batch data update function. This module will be published on the respective library repositories for both platforms when complete. It is coupled with a docker-based container stack which allows the cloud environment to receive the mobile data and provide the results of the decision computations. This cloud component will consist of a REST API for handling communications with the mobile modules, a web UI for researchers to define and interact with running reinforcement algorithm deployments, and all necessary support infrastructure such as databases and security layers. In this year, we will complete the preliminary implementations of this in conjunction with CP2. Once complete, we will focus our attention on either TR&D 1 or 3, depending on which one will benefit from our efforts the most given their current project status.
Admin
The Admin Core will continue to provide administrative, managerial, and infrastructure support to enable mDOT to accomplish its Year 2 goals in research, training, and dissemination activities. In addition to continuing its successful strategies for communication and management, mDOT plans to do several activities in Year 2 tied to the Administration Core Aims:

Aim 1 - Administratively Manage The Center
Annual Meeting: mDOT will look to host, hopefully in-person, it's next annual meeting with all Center investigators in attendance. If in-person is not feasible, we will convene an all-virtual meeting as done with the kick-off meeting.
Student Exchange: mDOT will continue to facilitate and enhance scholar exchanges between subsites/CPs/SPs as possible (virtually or in-person).
Website: The Admin Core will look to expand the utility of the mDOT website by providing informative updates about new publications, software resources, and current center progress.
Award: The administration team will again look to receive, process, and execute all grant subcontracts for the Year 2 award and provide assistance to collaborating institutions with their process.

Aim 2 - CP and SP Coordination & Expansion
Appraisal: The mDOT team, in conjunction with the Executive Board and the External Advisory Committee, will finalize CP and SP inclusion and review criteria, paying attention to align new projects to TR&D aims.
Expansion: The mDOT 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 to coordinate relevant CP and SP meetings tailored to the push/pull relationship and research.

Aim 3 - Executive Advisory Committee Engagement
Evaluate: mDOT will look to convene (in-person if feasible) the Executive Advisory Committee for its annual evaluation meeting(s) to review the current progress and future direction of mDOT. The EAC's formal reviews will be included in the Year 2 RPPR.
Integrate: mDOT will look to enhance its engagement with the Executive Advisory Committee throughout Year 2 and include EAC members in relevant meetings and discussions to utilize their expertise and advise with mDOT stakeholders.
Improve: The administration core will review and utilize the feedback given by the EAC during their Year 1 review to improve all facets of the mDOT research agenda and center operations.

Aim 4 - Leveraging Institutional Support for the mDOT Center
Staff: The Admin Operations team will look to retain our current staff and expand as needed and as available in Year 2 while utilizing in-kind positions and resources given by the University of Memphis.
Annual Meeting: The Admin Core will secure University spaces and facilities to host an in-person annual meeting (if able) or enterprise-level video conferencing tools and technology (if virtual) with the goal of bringing together relevant mDOT stakeholders for charting the Center's future research agenda.
Websites, Data, & Servers: The mDOT Software and Admin team will continue to leverage, and modify as needed, the established collaborative infrastructure and computational resources developed through MD2K at the University of Memphis, inclusive of hosting and storage of digital resources and data.
Data Sharing: mDOT 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 2.

Aim 5 - Progress Monitoring & Reporting
Reporting: In year 2, 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 continue to enhance the collaborative culture of mDOT throughout Year 2
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 advancement throughout Year 2 to internal members, institution officials, and external stakeholders.
Improvement: For continuous improvement in the mDOT technologies, its training activities, dissemination channels (e.g., website structure and content), and its administrative procedures, feedback will be regularly sought from mDOT team members, NIH program officers, mDOT affiliates, and the community stakeholders.

Principal Investigator: Kumar, Santosh

B.2 What was accomplished under these goals?

In Year 1, the Administration core undertook a variety of activities (as described below) to fulfill its goals.

B.2.1. Major Activities

Software

An overall software architecture was developed based on multiple rounds of discussion with all TR&D projects. To provide reusable software to the community, we previously developed modularized software that included mCerebrum as a collection of apps for smartphones so that one can pick and choose the suite of apps to meet the data collection needs of a specific research study. This platform included provisions for handling many diverse sensor modalities and real-time signal processing algorithms such as smoking or stress detection. Commercial wearable devices were unable to meet the data demands of our studies and we created the MotionSense platform to get access to wrist-based data. mCerebrum was complemented with a cloud-based big-data companion system called Cerebral Cortex, designed to accept all the data from field participants and further process the information for the purposes of accelerating research in the mHealth domain. For modularity, we made it a containerized cloud-based service. While these software suites were successfully deployed in a wide variety of research studies, they all required heavy involvement from our team.

What we learned over the years is that researchers want a high degree of control in their study and we were always modifying and augmenting the platform to suit their needs. So much so that each study nearly became a custom solution. To better accommodate these requirements, our approach has shifted from a modular, configurable hosted solution, which is not scalable to the 20+ projects involved in mDOT, to one where the team produces reusable modules that embed our research innovations into cross-platform mobile libraries which are coupled with cloud-based containers. This approach will significantly reduce the overhead for anyone wishing to leverage the mDOT software modules in their own mHealth solutions. We see the primary users of these modules falling into two categories: 1) Software developers working with mHealth research groups that will directly support their data collection in research studies and 2) industry groups that are looking for software implementation of cutting edge mHealth technologies being developed by TR&D projects in the mDOT Center. To have a fully working production software system to test each developed software module, we have implemented and deployed a fully functional software system for the MOODS study in collaboration with CP7. As described in more detail in Section B.2.3., it includes computation of the stress biomarker on a commercial smartwatch (Fossil Sport), remote recruitment of participants, deployment of software on both wearable and participants' own smartphones via respective app stores, and collection and analysis of mHealth biomarkers.

Principal Investigator: Kumar, Santosh

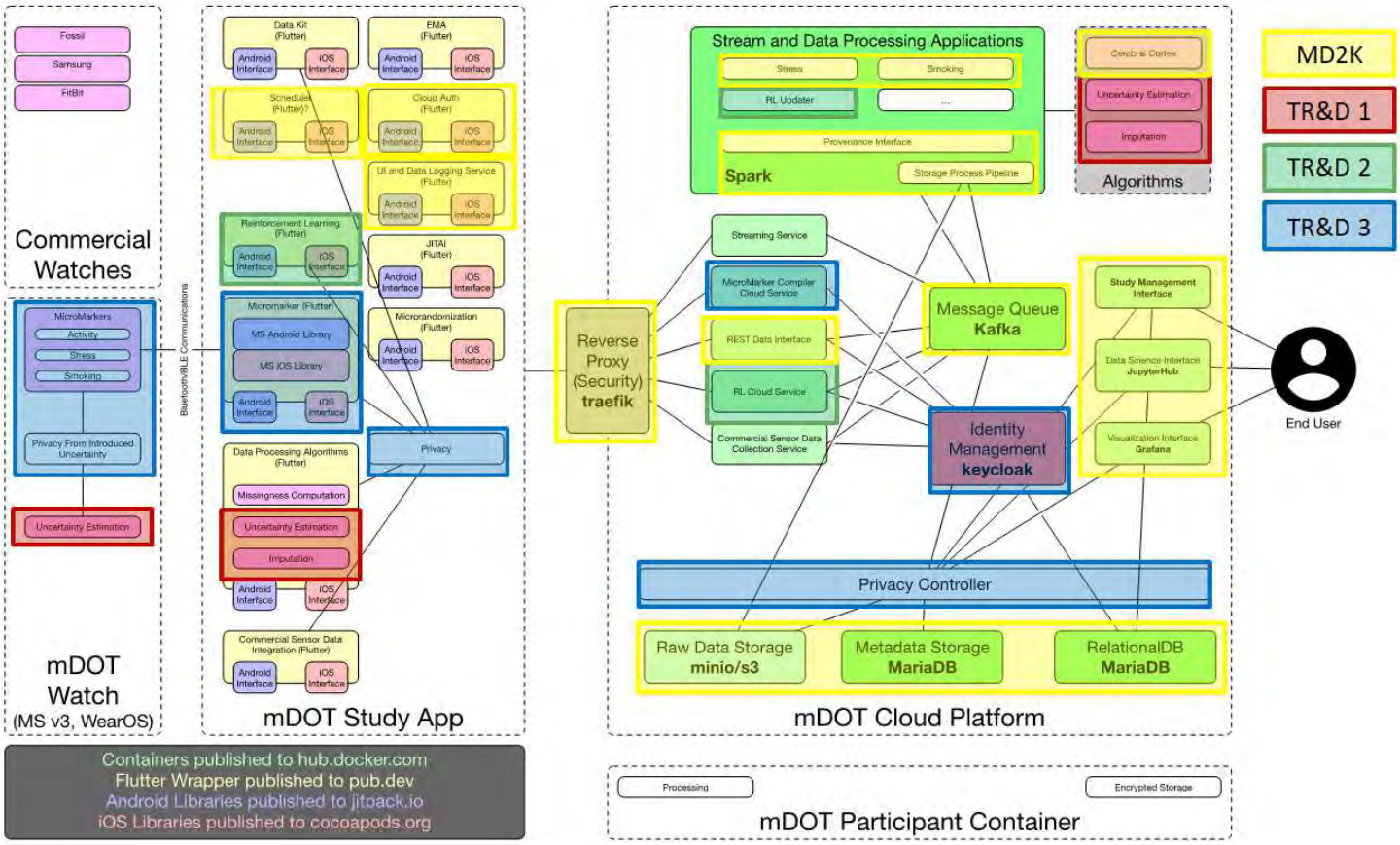

Figure 1 - *Overall mDOT Software Architecture*

Aim 1

Kick-Off Meeting. Through the administrative core, the mDOT Center organized and hosted an all-virtual kick-off meeting event on Monday, September 28, 2020. Participants included all mDOT Team members, students, and various CP and SP leads. The goal of the kick-off meeting was to brainstorm about research, collaboration, training, and outreach as well as set the formal research agenda for the upcoming year.

Establish an organizational structure. The mDOT Center Operations Office, housed in Memphis, Tenn., is the main hub for mDOT 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. The Director of Operations (Joe Biggers) reports to Center Director Kumar and is responsible for supervising all Administration Core staff, developing and implementing policies and practices related to Center record-keeping, activity planning, and monitoring, and acts as liaison to each partner site's designated contact to ensure seamless support for investigators at all sites. The Director of Center Operations established a close working relationship with the TR&D Leads as a means to facilitate the effective day-to-day

operation of all center activities.

Communication & Interaction Strategy. As part of the Center startup, the Administration Core was able to facilitate coordination and interaction among data science and biomedical researchers; enable both targeted and broad-based training and dissemination of methods, tools, and research findings; assess productivity and impact of Center activities; and provide ongoing management, oversight, and planning related to Center funds, resources, and operations for Year 1. This included successfully scheduled all monthly Center calls and assisting with meetings between the TR&Ds, CPs, and SPs as needed.

Launched the mDOT website as the primary hub for information on the Center and its activities. https://mdot.md2k.org/ is the primary domain for the mDOT Center. Its initial design was created in-house through the Administration Core. Its primary purpose is to inform the public about the mDOT Center, the investigators involved in the center, and the collaborative and service projects. As of September 30, 2021, the website recorded **7,523** page views by **2,159** users (source: Google Analytics). Effort on the website is ongoing, with the content being added and updated on a regular basis.

Received, processed, and executed all grant subcontracts and a no-cost extension for Year 1. mDOT is set up with a unique structure in that we have 6 subawards on this project for Year 1, and each sub-site has monthly invoices that are processed at the Administrative Center in Memphis. Establishing the budget, scope of work, and subcontract agreement forms for each subsite and receipt of authorized signatures for all paperwork has been completed. Certifications of investigator efforts towards mDOT work, the negotiation and extension of the NCE for the project period, played into the subcontract processing for Year 1.

Aim 2

Procedures for CP & SP interactions. In Year 1, it was established that the Center Operations Office and staff were responsible for distributing pre-meeting agendas and materials, taking minutes, and disseminating notes from all Center meetings. The administration team was able to successfully schedule all monthly Center calls and set up procedures for CP & SP interactions. The mDOT communications structure provides regular opportunities for both formal and informal communication. Monthly web-based interactions using Zoom video conferencing have been used to discuss research updates, as well as monthly Director meetings between the Center Director (Kumar) and Deputy Director (Rehg) to discuss operational issues.

Scheduling and Collaborative Tools. Each TR&D holds its own separate monthly telecons. In addition, there are various calls involving all the leads of the TR&Ds and their respective CP and SP teams. Quarterly virtual meetings are also held with NIH colleagues to give a running status report of mDOT. The mDOT 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 Google Docs so that all participants can jointly edit these documents in real-time or after the call.

Principal Investigator: Kumar, Santosh

Adapting to 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), were solicited from the team throughout the progression of Year 1 and used to review and revise the communication plan, helping to streamline the procedure and make communication more effective for the entire team.

Maintained appropriate Institutional Review Board approvals for data collection and analysis from CPs. When appropriate, mDOT'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, mDOT works closely with the University of Memphis (UM) Institutional Review Board to facilitate appropriate reviews, such as reliance agreements, across sites performing human subjects research. Additionally, the IRB and the UM 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. mDOT 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. mDOT 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.

Technical Support. The administration team provides ongoing technical support to effect data collection and data analysis for ongoing/current studies by CPs, as well as completed studies from collaborating CPs. mDOT works with current studies to support and troubleshoot questions involving data collection, including technical platform support. Troubleshooting procedures and training documentation are shared with study coordination staff at CP sites to diagnose and intervene on reported issues to improve the quality and yield of collected project data.

An online, limited-access issue-tracking platform (JIRA by Atlassian) constructed and monitored by mDOT personnel facilitates software bug reporting and issue tracking by study coordinators in real-time helps in the building of an issue knowledge base across mDOT projects, allows for delegation of issue support tickets to appropriate mDOT personnel, and establishes progress tracking throughout the issue lifecycle from initiation to resolution. A separate online visualization platform (Grafana) allows for the remote, real-time monitoring of participant data for the purposes of compliance monitoring and data quality diagnoses, and can be accessed by project personnel who have been approved to access those data. mDOT personnel work with study coordinators to interpret and diagnose data collection issues and can use this information to intervene on reported issues and improve data collection outcomes.

Additionally, our knowledge base of data collection procedures and platforms allow for ongoing project and study support after the conclusion of data collection: This information continues to be invaluable to mDOT project collaborators and TR&D investigators to answer data curation questions, articulate project methods throughout the publication process, and supports the consideration and development of future projects.

Established authorized data access procedures of research data from CPs by TR&D investigators. The mDOT project team has also leveraged data access procedures developed and augmented from the MD2K Center of Excellence project

to the present date. Project collaborators who depend on access to raw, transformed, and curated data coordinate with mDOT personnel to ensure those data are readily available to TR&D investigators and collaborating project personnel who have been vetted for appropriate levels of access. Automated tools built by mDOT personnel allow for updated data provision across sites for whom data collection is ongoing, and access control procedures are shared and implemented to ensure data access controls are universally and consistently implemented across mDOT projects.

Aim 3

Selection and ratification of Executive Advisory Committee members. The mDOT Center assembled a high-profile External Advisory Committee (EAB) that includes 5 thought leaders representing Center research expertise in domains such as:

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. Shie Mannor, Professor of Electrical Engineering at Technion – Dr. Mannor is an expert in reinforcement learning, decision making, and control under uncertainty in multi-agent systems. He is advising mDOT's TR&D2 team on dynamic optimization of continuously adapting mHealth interventions based on sensor-derived biomarkers.

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 further ensure a diversity of perspectives and experiences. The EAC provided the high-level guidance, oversight, and review of progress towards research and training goals and the efficacy of Center operating structures and policies for Year 1. 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 initial EAC meetings took place virtually, as each Committee Member was individually presented with an overall view of the mDOT Center and other aspects of research tailored to their interests and expertise. We plan to have the EAC's next meeting be convened as a group with all 5 members in attendance together. EAC members were able to advise the mDOT Team on suitable collaborative interests to pursue and sustainability models for the Center to investigate. The EAC has provided a report to board members concerning the planned implementation of specific guidance received or alternate strategies to be pursued as mDOT heads into Year 2 (found below in this report).

Aim 4

Leveraging Institutional Support. An important aspect of the mDOT administrative team is to acquire institutional support for mDOT in terms of space, staff support, and operational expenses. secure and leverage institutional support that accommodates and sets up the Center for success in achieving the research goals put forth by the investigating team. The University of Memphis has made a significant contribution of space and personnel to ensure the successful operation of the mDOT Center that was originally built out to support the MD2K Center of Excellence. The Center's Administration Core and operations hub is housed within 3,400 square feet of overall, dedicated space in the FedEx Institute of Technology (FIT) at the University of Memphis.

In addition to the personnel requested in the Administration Core budget, the University of Memphis also utilizes non-federal funds to support the salaries and fringe benefits for professional business management, administrative, and marketing and communications support dedicated to Center activities. Only small portions of the salaries of the operations director, software staff, training specialist, and research coordinator are covered by the grant, and the mDOT Center was able to acquire institutional support for their full-time salary to be committed to mDOT. This administrative staff is critical to engaging and supporting a large number of CPs and SPs despite limited funding for them directly from the grant.

The mDOT Center also has access to centrally provided grants accounting, research development, and research compliance staff, along with legal, technology transfer, and human resources support, standard services for sponsored projects.

Aim 5

To have maximum scientific and societal impact, mDOT has developed quantifiable measures and implemented systems to monitor, assess, and evaluate the quality and utility of mDOT products, and continuously improve by systematically securing feedback from collaborators and community stakeholders. Leveraging the successful approach of MD2K, where the center was similarly divided into separate cores, each has its own specific set of metrics. Metrics for measuring administrative tasks include the number of telecons scheduled, number of documents produced, and number of in-person meetings organized (though limited this year due to the pandemic). Administrative efficiency metrics will include satisfaction with administrative support services and processes, collected informally throughout the year and via the annual meeting session. Another important metric tracked by the Administration Core is personnel advancement. Placement of graduate students, tenure & promotion, and important awards received by mDOT personnel, as well as its affiliate members, are also reported in Section G.

mHTI administration

Principal Investigator: Kumar, Santosh

Due to the COVID pandemic, the training activities made a hard pivot to virtual training. The main focus of the training was the development of an all-virtual version of the annual mHealth Training Institute (mHTI). The mDOT Administrative team was instrumental in the setup and backend administration of the virtual event. This entailed deployment of a virtual events platform (vFairs), a comprehensive, online application management system (SmarterSelect), 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, Swag Bag creation, etc.), and providing live, responsive technical support and troubleshooting support. The virtual 2021 mHTI was conducted between May 10 and July 30, 2021 (https://mhti.md2k.org/index.php/program/2021-program).

mDOT Administrative Snapshot

- mDOT has an archive of over 150 videos, with a combined +37,000 views via the Center's YouTube Channel
- We anticipate 3 reusable modules for mobile and cloud to emerge in 2022
- We have had over 7,500 website visits to mDOT.org since launch
- Currently, the mDOT team has over 300 Google Docs used in collaboration
- The mDOT admin team facilitated hosting the all-virtual mHealth Training Institute (mHTI) where mHealth training was offered to 35 scholars with 27 faculty from 20+ institutions in multiple disciplines, conducted in an all-virtual environment over 11 weeks
- The mDOT team evaluated 5 state-of-the-art commercial wearable devices as potential integration platforms within the mDOT ecosystem
- The Admin Core ensured authorized stakeholders (i.e., collaborators) have access/transfer capability to approximately +300 TBs of data to conduct research activities.

B.2.2. Specific Objectives

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

Mobile Open Observation of Daily Stressors (MOODS) Study (CP7)

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.

B.2.4. Key Outcomes & Other Achievements

Mobile Open Observation of Daily Stressors (MOODS) Study (CP7)

Continuing our work from last year, the Memphis site completed the initial implementation of the MOODS Study in conjunction with CP7. Versions of the app were published to both the Google and Apple app stores to facilitate a remote participant population (e.g. makes it easier for them to install and participate). Functional testing was done to ensure that the software and staff processes are operating appropriately and to refine the user experience. This study has been launched and will conclude in the no-cost extension period.

Mobile Platform Enhancements

We have enhanced the capabilities of our mobile software through this project and have included three major features. First, the mobile platform is a cross-platform solution supported on Android and iOS currently. Prior to this enhancement, we were limited to only running on Android due to the need to have low-level system access for many of the sensors. Second, bi-directional communication has been incorporated into both the mobile and cloud capabilities to allow the study apps to be more responsive to the user and provide a more interactive experience that is typical of many commercial apps. This allows us to rapidly gather information from the participants and have the app adjust its visualizations and displays based on cloud-hosted data. Third, the architecture of the mobile platform has changed significantly and is moving from a suite of independent but related apps to a single unified app that uses a modular architecture to add the various capabilities necessary to run studies. We use 3rd party and in-house developed plugins to add functionality to the platform.

We have also successfully used this platform to integrate with a commercially available smartwatch platform to access low-level sensor data.

Principal Investigator: Kumar, Santosh

mDOT Personnel Status & Acknowledgements

INVESTIGATOR	CHANGE IN STATUS/RECOGNITION	DATE
Ben Marlin	Ph.D. student Satya Narayan Shukla completed Ph.D. candidacy requirements.	12/15/2020
Susan Murphy	Anna Trella joined the lab as a Ph.D. student	9/1/2020
Susan Murphy	Sarah Rathnam joined the lab as a Ph.D. student	9/1/2020
Susan Murphy	Eura Shin joined the lab as a Ph.D. student	9/1/2020
Susan Murphy	Xiang Meng joined the lab as a Ph.D. student	9/1/2020
Susan Murphy	Postdoc Maianne Menictas left the lab to take a position as Senior Data Scientist at Grubhub	1/31/2021
Susan Murphy	Postdoc Shuang Li left the lab to take a position as Assistant Professor in the School of Data Science, The Chinese University of Hong Kong (Shenzhen)	5/31/2021
Susan Murphy	Postdoc Peng Liao left the lab to take a position at DRW Holdings, LLC	7/31/2021
Susan Murphy	Hsin-Yu Lai joined the lab as a postdoc	9/1/2021
Susan Murphy	Raaz Dwivedi joined the lab as a postdoc	9/1/2021
Susan Murphy	Zeyang Jia joined the lab as a first-year Ph.D. student	9/1/2021
Emre Ertin	Ph.D. student Siddhart Baskar joined Amazon Project Kuiper group in June 2021 as an RF and DIgital Design Engineer	6/1/2021
Santosh Kumar	Ph.D. student Soujanya Chatterjee joined Facebook AI Research	8/1/2021

Principal Investigator: Kumar, Santosh

mDOT-Related Proposals/Collaborations

LEAD INVESTIGATOR	mDOT COLLABORATORS	SPONSOR	TITLE	DATE OF SUBMISSION	RELEVANCE TO mDOT
Inbal Nahum-Shani, Daniel Almirall	Susan Murphy	NIH	Center for Methodologies for Adapting and Personalizing Prevention, Treatment, and Recovery Services for SUD and HIV (MAPS Center)	10/2020	potential CP; This submission was funded. Start date was 9/1/21
Vijay Subramanian, Marco Pavone, Rahul Jain	Susan Murphy	NSF	AI Institute for Dynamic and Autonomous Systems	12/4/2020	Theory for RL and Multi-agent RL; was not funded.
Deepak Ganesan, Niteesh Choudhry	Benjamin Marlin	NIH	Massachusetts AI and Technology Center for Connected Care in Aging and Alzheimer's Disease	10/1/2020	Development of AI methods for abient and mobile sensor data analysis and decision support with a focus on supporting aging and AD care. P30 mechanism with the potential to fund pilot deployments of mDOT technologies.

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. Shie Mannor**, Professor of Electrical Engineering at Technion – Dr. Mannor is an expert in reinforcement learning, decision making, and control under uncertainty in multi-agent systems. He is advising mDOT's TR&D2 team on dynamic optimization of continuously adapting mHealth interventions based on sensor-derived biomarkers.

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 the high-level guidance, oversight and review of progress towards research and training goals and the efficacy of Center operating structures and policies for Year 1. 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 meetings took place virtually using the Zoom teleconferencing system. Each Committee Member was individually presented an overall view of the mDOT Center and other aspects of research that were tailored to their interests and expertise (schedule below). The EAC's next meeting will be convened as a group with all 5 members in attendance together. 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 heads into Year 2.

- Dr. Jimeng Sun reviewed the mDOT TR&D1 on 8/23/2021
- Dr. David Kennedy reviewed the mDOT Training and Administrative Core on 8/24/2021
- Dr. Veena Misra reviewed the mDOT TR&D3 on 8/26/2021
- Dr. Shie Mannor reviewed the mDOT TR&D2 on 9/2/2021*
- Dr. Jason Hong reviewed the mDOT TR&D3 – Privacy Components on 9/21/2021

**we did not receive Dr. Mannor's formal review back in time for RPPR submission but will make it readily available upon request once received.*

Review of mDOT from Dr. David Kennedy

Project Period 1 (07/15/2020 – 09/30/2021)

1. Overall Center Structure & Direction

1.a. Notable Strengths

- There is a notable need for the proposed mDOT technical developments to support broader, more efficient deployment of "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."
- An extensive team with a proven track record has been assembled for this project.
- There are a plethora of mHealth biomarker opportunities that can take advantage of this center.

1.b. mDOT Response:

Thank you.

1.c. Perceived Weaknesses

- With so many potential application areas and partners, how to make sure you do not get spread too thin, attempting to solve lots of problems, or spread to 'thick' and not successfully demonstrate the power of your approach.
- There are lots of touch-points between this Center and commercial sector. How engaged/engageable is the industrial community? How willing is the commercial side to participate. As there is a potentially large set of sensor hardware providers; are there standards that are being/can be promoted to facilitate or ease the problems you are developing solutions for?

1.d. mDOT Response

- Thank you for your caution about spreading too thin. We adopt the following strategy that we will adapt based on experience. First, each collaboration is assigned a lead investigator from a TR&D. Second, each investigator works closely with a limited number of partners concurrently. Investigators present details of their progress on each collaboration in monthly TR&D meetings. Once a push-pull initiative concludes, they take on additional ones.
- Deeper engagement with industry has been on hold due to the pandemic. We expect to accelerate deeper engagement with the industry and pursue commercialization of our technology via startups.

1.e. Other Comments

- It is not too early to have a high-level 15 year plan in mind, to take you through the 3 P41 cycles that this award can run through.
- Some nice applications are shown (MOODS, Stress, etc.) but sometimes it isn't clear the border between the P41 and projects run by the CP/SPs. Clarifying these distinctions in your presentations will help better define the P41 technology and how it interacts with the real-world outside users.

1.f. mDOT Response

- Thank you for suggesting the articulation of a high-level plan for 15 years. We plan to make this a main brainstorming session together with our advisory board in our first annual meeting.
- Thank you for the suggestion. Broadly speaking, mDOT does not conduct any user studies; it only develops the technology and the resulting tools for deployment and evaluation in user studies conducted by our partner CP's. We will make a more conscious effort to clarify the projects undertaken by the mDOT Center and the CP's.

2. TECHNOLOGY, TRAINING, & DISSEMINATION (TT&D) STRUCTURE & DIRECTION

2.a. Notable Strengths

- Laudable goals: 1) Spread awareness and increase knowledge of mDOT's infrastructure, technologies and approaches; 2) Increase pool of transdisciplinary researchers using mDOT's innovations in their research program
- The mHealth Training Institute seems well established.
- A formal Training and Dissemination evaluation is proposed.

2.b. mDOT Response:

Thank you.

2.c. Perceived Weaknesses

- Training is occurring at least in areas of general knowledge and specific tools. The evaluation of the training may need to be tailored to these different types of training scenarios.

2.d. mDOT Response

Thank you for the suggestion… will be incorporated into future training.

3. TECHNOLOGY, TRAINING, & DISSEMINATION (TT&D) PROGRESS

3.a. Notable Strengths

- mHealth 2021 seems successful and popular with the trainees.

3.b. mDOT Response:

Thank you.

3.c. Perceived Weaknesses

- Be careful of the mDOT versus MD2K mission and branding. Be clear about what is the new material being developed. Training events are good, but is there a 'curriculum' that you'd like the ideal next-generation mDOT-powered research to be skilled in?

3.d. mDOT Response

- mDOT focuses on intervention design, optimization, and delivery. As the mDOT tools develop, the focus of the TTT&D core will shift from the established "biomarker" focus (MD2K) to the mDOT tools
- The focus is on developing team science abilities in addition to core skill sets. Exit surveys poll the mHTI scholars and the curriculum adapts and is updated/optimized to meet evolving needs.

3.e. Other Comments

- Beware of the various skillsets of the various users of your technology. Be prepared to either 'target' specific skill sets (if you can not support them all), or clearly indicate the 'level' that the various training activities are targeted at.
- Continue to actively attend to and monitor diversity and equity efforts.

3.f. mDOT Response

- The curriculum will be adapted to build familiarity/skill sets commensurate with mDOT tools as they are developed and released.
- The planning faculty adjust the screening/review process to ensure geographic, disciplinary, and racial diversity. 75 % of 20212 mHTI scholars were women for 2021 with a large proportion of URMs.

4. TECHNOLOGY, TRAINING, & DISSEMINATION (TT&D) FUTURE DIRECTIONS

4.a. Notable Strengths

- A specific vision for training events is provided.

4.b. mDOT Response:

Thank you.

4.c. Perceived Weaknesses

- More specifics about when the 'hands-on' sessions and bootcamp will be, when, and how many 'industry summits' would be helpful. Do you have target engagement expectations for these different types of events?

4.d. mDOT Response

Due to the fluid COVID pandemic situation, the details of the hand-on sessions are still unclear. Once things stabilize, we will map the particulars onto the available logistical boundary conditions.

4.e. Other Comments

- Make sure not to downplay the 'dissemination' part of the 'technology, training and dissemination' core. Disseminating knowledge is one thing, disseminating the tools (yours and others that are mDOT-empowered) is another.
- Attempt to document tool and resource uptake. No single metric will work for all the types of ways your products get used. Develop a 'basket of indicators' that cover the spectrum of how things are used. Also, when your tech gets used in other products, make sure to track the uptake of that additional product, since that is also a vector of your tech.
- A follow-up evaluation is proposed. Upon what time frame is this follow-up being planned? Knowing what trainees think right after the event is one thing, but 6 month and 1+ year engagement is helpful. What are they

following through with, where do they need additional support? Your various trainees are one of your most valuable assets. Develop them.

4.f. mDOT Response

- mHealthHUB port is the dissemination portal and is being restructured to incorporate google analytics. This will permit documentation of uptake of mDOT tools and serve as the "basket of indicators".
- Follow-up evaluations are planned. We are cautiously optimistic that the prevailing COVID0-induced "response fatigue" will eventually dissipate and we will send out the follow-up surveys as things normalize.

5. SOFTWARE OVERVIEW

5.a. Notable Strengths

- An overall software architecture for the mDOT Center is envisioned.
- The Mobile Open Observation of Daily Stressors (MOODS) program seems to be a good proof of concept project.
- Specific support for the Reinforcement Learning operations are indicated.

5.b. mDOT Response:

Thank you.

5.c. Perceived Weaknesses

- It was not immediately clear what the resultant software products are supposed to be. Clarify what the "mDOT software/product stack" is currently. What are the key deliverable software products? Create a listing of the modules (perhaps name each one) - these are the modules that came out of mDOT and these are the users.

5.d. mDOT Response

Thank you for suggesting a clarification of software deliverables and their end-users. A major change from MD2K to mDOT is the change in both aspects. In MD2K, we provided the entire end-to-end solution from the wearable device with appropriate software installed, working apps for smartphones, and the cloud software to collect, store, and analyze data that our health research collaborators were able to directly use for their data collection and analysis purposes. In mDOT, we are adopting a different approach to be scalable and keep our focus on developing and disseminating novel technology. Therefore, in mDOT, we are developing modules for wearables, smartphones, and the cloud. These modules are to be used by the software developers hired by our collaborating health researchers. In particular, we plan to develop the following.

1. A reinforcement learning module (from TR&D2) for both mobile (Android/iOS) and cloud platforms is being developed and will be the first "product" released through mDOT. The first users will be used by the software and technical team working with CP2 and CP3.

2. A micromarker module that can run directly on a wearable device (from TR&D3) that can efficiently compute multiple mHealth biomarkers in real-time while limiting battery depletion. The first users of this module will be the technical team from CP6.
3. A cloud module that annotates mHealth biomarkers with uncertainty estimates (from TR&D1) and propagates them through the processing chains. The first user of this module will be the technical development teams of CP3 and then CP1 and CP5.

5.e. Other Comments

- 'Build your own' being promoted. How are the results of these efforts being tracked and supported?
- The following comment comes up in the context of the reinforcement learning presentation. But it may be a more general question/comment/problem with my understanding. I get the sensor-subject-behavior loop. But it seems that there is also a "sensorified subject"-'rule optimization'-'health outcome' loop that, while bigger than this center, this Center plays a pivotal role in. Is there an opportunity to position this center also in that bigger picture?
- Amplifier – your technology is potentially being used in other products. You want users to have some of these downstream components that are mDOT-enabled from these other products. Thus you want to be able to track the use of these downstream products as well.

5.f. mDOT Response

This is a very good question and advice to ensure we track the impact of mDOT tools. In addition to tracking the acknowledgment of the mDOT grant in published works, we are looking into analytics tools to incorporate into all mDOT modules to help track usage. We think this can work well in the downstream components.

Thank you for an excellent suggestion to explore the role of mDOT in the bigger picture of connecting the impact of mDOT technology in improving health outcomes, which currently is indirectly via our collaborating projects. We can brainstorm among the team and with our advisory board to develop this vision.

6. ADMINISTRATION PROGRESS

6.a. Notable Strengths

- Center 'activation' tasks (website, contracts, etc.) successfully accomplished.
- Virtual external review performed.
- Managed difficulties of Center initiation in the midst of a challenging public health crisis.
- Negotiated an appropriate no-cost extension to buffer the longer than expected startup time.

6.b. mDOT Response:

Thank you.

6.c. Perceived Weaknesses

- Would be good to be able to express a formal relationship to Stanford's Mobilize Center, to help future evaluators know what the unique contributions are.
- Consider mDOT branding, even though it can leverage past work with the MD2K, make sure that there is also a unique presence.

6.d. mDOT Response

Thank you for this suggestion. We will reach out to the Mobilize Center and explore a synergistic relationship in Year 2.

Great suggestion about mDOT branding. We will begin highlighting the mDOT Center in both our research and training activities to establish this new brand. This will include the mHealthHUB, mHTI, and the software modules that we provide to our partners.

6.e. Other Comments

- Do you use a formal management software of any sort?
- Keep track of your Institutional Support. This is an important leverage point for future funding.

6.f. mDOT Response

We use Jira Issue and Project Tracking for internal software management. We are transitioning to GitHub Issues to keep discussions close to the respective software modules, hosted on GitHub, and to encourage community involvement.

Excellent suggestion about keeping track of institutional support, which is quite substantial. We will quantify it for each year in terms of space, personnel, infrastructure, and meeting support.

7. ADMINISTRATION FUTURE DIRECTIONS

7.a. Notable Strengths

- The future plans include: Annual Meeting; Student Exchange; Website expansion; and Fiscal Award Management.

7.b. mDOT Response

Thank you.

Review of mDOT from Dr. Jimeng Sun

Project Period 1 (07/15/2020 – 09/30/2021)

1. Overall Center Structure & Direction

1.a. Notable Strengths

- The mDOT center focuses on discovering, optimizing, and translating temporally-precise mHealth intervention, which is innovative and coherent with a significant probability of high impact work.
- Their focus on chronic disease management is especially valuable and timely given the skyrocket healthcare cost in the US due to the chronic diseases.
- The team are strong with complementary expertise and have excellent collaboration history.

1.b. mDOT Response:

Thank you for your encouraging words.

1.c. Other Comments

- Given all those exciting collaborative projects (CP), it will be great to show concrete examples of how the mDOT center benefits or interacts with those CP projects. I think this will probably become obvious in later years.

1.d. mDOT Response

Thank you for this suggestion. This being the first time we introduced our center to the advisory board, we spent a significant time in the call on providing the overall vision and the right context for the center and its operation. We are covering some of the concrete aspects of interactions with CPs in the annual report and will be sure to highlight it in our next presentation to the advisory board.

2. TECHNOLOGY RESEARCH AND DEVELOPMENT (TR&D1) Structure & Direction

2.a. Notable Strengths

- The aims (handling noise in mHealth data, risk modeling, and hypothesis generation for intervention design) are realistic and challenging tasks that desperately need more research and innovations.
- The team is strong in both ML, CV, and behavioral modeling.
- All the CPs are very interesting.

2.b. mDOT Response

Thank you for supporting the importance of the problems that the team is focusing on.

2.c. Other Comments

- It will be even great if some concrete examples how TR&D1 interacts with those CPs can be added.

2.d. mDOT Response

Thank you for this suggestion. As noted under 1.d, we are covering some of the concrete aspects of interactions with CPs in the annual report and will be sure to highlight it in our next presentation to the advisory board.

3. TECHNOLOGY RESEARCH AND DEVELOPMENT (TR&D1) Progress

3.a. Notable Strengths

- Great progress in computational methods relates to handling incomplete data using Bayesian Mechanistic Models and Heteroskedastic Temporal VAE by UMass team
- The UoM and GT teams have provided exciting and novel applications on predicting smoking laps and EMA availability, and noncompliance prediction.
- Solid CS methodology publications have been generated even in year 1 of the project, which is impressive.

3.b. mDOT Response

Thank you for your positive assessment of the technical contributions the team has made in Year 1.

3.c. Other Comments

- Some idea using both GAN and PU learning is suggested to UoM team to consider.

3.d. mDOT Response

Thank you for these suggestions. We do plan to build on broader work of the team, which includes GAN-based models for incomplete data [1] as well as models for learning from temporally imprecise data [2]. We will also take into account potential applications of positive-unlabeled learning.

[2] Li, Steven Cheng-Xian, Bo Jiang, and Benjamin Marlin. "MisGAN: Learning from Incomplete Data with Generative Adversarial Networks." *International Conference on Learning Representations*. 2018.

[2] Roy Adams and Benjamin Marlin, “Learning Time Series Segmentation Models from Temporally Imprecise Labels,” in Conference on Uncertainty in Artificial Intelligence, 2018.

4. TECHNOLOGY RESEARCH AND DEVELOPMENT (TR&D1) Future Directions

4.a. Notable Strengths

- The evaluation plan for EMA non-response prediction is thorough and connects with multiple other projects (CP1, 3, and 5 and SP2). This is very exciting, and I'm looking forward to seeing more work on this novel and highly relevant application from TR&D1.

4.b. mDOT Response

Thank you for your encouragement.

4.c. Other Comments

- It will be great to see the future work plan for each aim.

4.d. mDOT Response

As reported in the upcoming RPPR, here are our future work plans tied to the specific aims of TR&D1:

Activity 1.1 - We will complete the development of a diverse set of benchmarks and tasks for learning from incomplete and irregularly sampled time series including both publicly available datasets and data sets from selected CPs. We will conduct an evaluation of the ability of existing methods to accurately propagate uncertainty due to input sparsity using this set of benchmarks. We will then proceed with the development of hierarchical extensions of our modeling approaches applied to both classification and imputation/interpolation tasks. We will also work with our CPs to communicate the results of this work and to support deploying TR&D1 methods within their ongoing modeling work.

Activity 1.2 - We will continue the development of imputation methods for biophysical signals by developing missingness models that reflect real-life patterns of data missingness in mHealth applications. Using these models we will develop a reference task for imputation and test multiple state-of-the-art methods to establish baselines. We will continue our development of a novel transformer-based baseline architecture for imputation.

Activity 1.3 - We will complete our development of continuous-time attention mechanisms for irregularly sampled longitudinal data by establishing the theoretical properties of the deformed kernel exponential family models and obtaining benchmark results on standard datasets.

Activity 2.1 - Towards fulfilling Specific Aim 2, we plan to continue working on developing the mRisk method with CP1 and CP5 to estimate the momentary risk of lapse from mHealth biomarkers time series data. Second, we plan to produce the relevant new mHealth biomarkers that estimate and characterize the lapse risk in the smoking cessation dataset of CP1 and CP5. Third, we plan to implement the new biomarkers emerging from the mRisk model and apply them to the dataset of CP1 and CP5 so they can be used by our collaborating health researchers in pursuing their publication towards the design and development of new mHealth interventions.

Review of mDOT from Dr. Veena Misra

Project Period 1 (07/15/2020 – 09/30/2021)

1. Overall Center Structure & Direction

1.a. Notable Strengths

- Broad vision of addressing chronic diseases with sensing, analysis, and action and stands uniquely among other BTRCs
- Excellent expertise of team in signal processing, wearables, machine learning and interventions
- Director has successfully led previous Centers in mHealth
- Good organization of the TR&Ds
- Bootcamp training program
- The organization chart is well thought out
- Good selection of CP projects that gain from mDOTs expertise

1.b. mDOT Response:

Thank you for your encouraging words.

1.c. Perceived Weaknesses

- Very ambitious research agenda but seems to have been organized well with geographical presence
- Very crowded field and the team must continue to position themselves ahead of the field

1.d. mDOT Response

Thank you for your suggestions and caution.

1.e. Other Comments

- The team clearly understands what drives success and is positioned to achieve those metrics.
- Lot of emphasis on smoking (1 CP and 2 SP). Perhaps this could be an opportunity of industry involvement
- Good process to bring in new CPs.

1.f. mDOT Response

Thank you for suggesting industry involvement in smoking cessation work. We have had some preliminary discussion with GSK as they were looking to use our mHealth biomarker of craving to remind abstinent smokers when to take their nicotine medication. But, the wearable technology (use of ECG) was not ready for regular usage in daily life. This can be revisited once we demonstrate risk score estimation with smartwatches. This work is currently in progress by the TR&D1 team.

2. TECHNOLOGY RESEARCH AND DEVELOPMENT (TR&D3) STRUCTURE & DIRECTION

2.a. Notable Strengths

- Goals of TR&D3 are noteworthy as they are focused on edge device design space and focus in efficient and real time low latency implementation of digital biomarkers.
- Modular and reusable micromarkers can support many different use cases
- They are also developing new sensors and learning architecture while including privacy considerations.
- This TR&D is connected to multiple CPs and SPs
- Focus on both hardware and software

2.b. mDOT Response:

Thank you.

2.c. Perceived Weaknesses

- Can the hardware be easily updated to include new sensors? Will the hardware need to change depending on the goal of a particular CP and SP? Some consideration of this would be good.

2.d. mDOT Response

Thank you for pointing out the need for flexibility. Addition of new sensors in the device does require substantial effort as it includes circuit optimization and battery optimization as you are well aware of yourself as a leader in zero-power sensor design. Fortunately, the sensors we have thus far on our wearables have been multi-purpose. In future iterations, we will look to adapt our design to easily incorporate new sensor modalities so it can help the wearable community experiment easily with them.

3. TECHNOLOGY RESEARCH AND DEVELOPMENT (TR&D3) PROGRESS

3.a. Notable Strengths

- Research progress on TengoSense HF, edge devices and Neural inertial process was commendable
- Compressed sensing and machine learning algorithms
- Student presentations on multichannel PPG data for HR and HRV estimation and inertial navigation were excellent
- The expansion to ballistography will enable additional data analysis opportunities for the team

3.b. mDOT Response:

Thank you.

4. TECHNOLOGY RESEARCH AND DEVELOPMENT (TR&D3) FUTURE DIRECTIONS

4.a. Notable Strengths

- Future directions seem to be aligned mostly with the CP and SPs

4.b. mDOT Response:

Thank you.

4.c. Perceived Weaknesses

- Some lack of what the big picture of TR&D 3 future plans might be.
- More technology and ML road mapping might be useful as it will provide a clear research pathway for this team. While being customer driven in CP and SP, a mDOT timeline of its new directions in this and other TR&D would be useful for future opportunities.

4.d. mDOT Response

Thank you for a very useful suggestion. The technology in this field is moving rapidly, both in academia and in industry. We plan to brainstorm with the team and our advisory board (in our annual meeting) to chart out a clearer roadmap for the big picture in terms of direction, given where the field is right now and where we expect it to be in the near future, looking at major centers recently funded and device announcements from the industry.

Review of mDOT from Dr. Jason Hong

Project Period 1 (07/15/2020 – 09/30/2021)

1. Overall Center Structure & Direction

1.a. Notable Strengths

- Overall, the work by the Center looks extremely promising, in terms of the team, the projects, and the angle of attack. Below are my comments about privacy and security, as well as other thoughts about mobile health in general.

1.b. mDOT Response:

Thank you.

2. TECHNOLOGY RESEARCH AND DEVELOPMENT (TR&D3) Privacy & Security

2.a. Suggestions and Considerations

- Suggest having a common threat model to help analyze potential privacy and security risks for all of the mobile health apps, as a complement to having some projects focused specifically on privacy and security. Even though each app is different, having a common threat model can help different teams have common ground and lead to common solutions for increasingly common scenarios, while also reducing the burden of each team to come up with a threat model. In particular, I would suggest for the threat model to at least include (a) a data leak scenario where all of the sensed data is made public, (b) an intimate partner violence scenario where a controlling partner is trying to use the sensed data to monitor a partner, and (c) an incidental privacy scenario, where people who are not directly using the mobile sensing device might be inadvertently sensed (though it might be the case for the mobile sensing devices that this scenario is infeasible, in which case it can be dropped).

2.b. mDOT Response

Thank you for this very nice suggestion. In fact, a plausible threat model has been a challenge that we are starting to work on. It will be great if you can brainstorm with you (in our annual meeting or earlier if possible) to develop a threat model that captures the various scenarios that you have so carefully articulated here.

2.c. Suggestions and Considerations

- Suggest establishing basic security minimums and best practices for each mobile health app, and where possible, common standards so that code and best practices can be shared. The goal here is to protect against basic kinds of attacks and accidents, while also imposing little burden on research teams so that they can still focus on the main research. The basic security minimums might focus on the device (e.g. data minimization in sensing and transfer off device, encryption of stored data), network (e.g. using TLS for all network traffic), cloud storage (e.g. all databases have password protection), and data access (e.g. all accesses logged, IP addresses that can read access the database are restricted, etc)

2.d. mDOT Response

Thank you for emphasizing these important issues in storing and managing access to mHealth data. We currently have the following processes in place.

1. All MD2K servers use disk-level encryption for all data stores. Data is also part of a RAID6/raidz2 at a minimum so that no single disk contains a whole data file.
2. TLS is used for all communications between mobile and cloud and for researchers using the cloud to see data
3. New versions of our mobile and wearable apps use app-specific storage of data which minimizes the risk of others being able to read the information.
4. All data is stored on mobile and wearable without user credentials. User IDs are only added when uploading to the cloud.
5. All user IDs are randomly generated and a third-party is used to link identifiers (e.g. email) to these IDs. The dataset will not have a direct link back to an individual.
6. DB passwords are standard practices and we have done this since the beginning.
7. DB access is limited to the compute cluster and firewalled off from the rest of the network and internet

2.e. Suggestions and Considerations

- Similarly, suggest having basic privacy minimums and best practices for each mobile health app. This part is trickier since there are fewer clear best practices for privacy. For now, it might be best to have a simple interface for describing what data is sensed and how it is used, along with who to contact for questions. A physical card might also serve the same purpose.

2.f. mDOT Response

We have been improving on this issue, including simplifying our language in the informed consent document that spells out each data source being collected as well as privacy risks emerging from them. We also describe in detail how these risks are managed and which risks the data collecting users should be aware of prior to enrolling in studies. We have also been describing these issues as a FAQ on the website with a link in the app. We will continue to improve this process so all data contributors have a better understanding of the risks involved, which continue to evolve rapidly as new AI models get developed to infer new privacy-sensitive information from wearable data.

2.g. Suggestions and Considerations

- Consider having some common questions asking participants and other stakeholders (doctors, nurses, caregivers, etc) about privacy when evaluating deployed systems. These might include asking about what data they think is being sensed, how sensitive that data is, who they think can see their data, etc. A few short questions can help assess people's mental models, which arguably is more useful than just informed consent. A more challenging issue here is a way to measure how many people have declined participating and using the mobile health system due to privacy concerns (or other reasons). Only measuring people who have already chosen to use the system will lead to survivorship bias.

2.h. mDOT Response

Thank you for this wonderful suggestion. Although we had conducted such a study in the past to understand the willingness to participate due to privacy and change in privacy concerns after seeing their own data, keeping a record of the number of participants who decline to participate after reading the informed consent will be useful. We will incorporate this in future studies that use mDOT apps. Surveying the stakeholder on their understanding of privacy risks is also a very useful suggestion. We will plan to introduce this in the near future.

2.i. Suggestions and Considerations

- Consider relatively simple practices that might be established to share best practices amongst the mDOT teams. For example, assuming that there are big meetings with all team members, there might be a short session where different teams are grouped in pairs or triples to share how they are managing privacy and security. This could be a lightweight way of sharing knowledge, best practices, and code, as well as improve cohesion across teams.

2.j. mDOT Response

Thank you for this suggestion. We can plan for this structure when discussing directions for privacy research in our first annual meeting.

2.k. Suggestions and Considerations

- With respect to the research on privacy and security, the work presented was high quality. I have two suggestions. The first is to see if the tools / methods can be applied to any of the projects directly, with those other projects acting as customers. This is to make sure that the use cases being addressed make sense, to uncover any issues in deployment, and to help take the research to the next level. The second is, for new projects on privacy and security, to consider processes for uncovering potential privacy problems faster and earlier with customers. That is, look for fast and easy ways to find and validate use cases for privacy solutions much earlier in the research process.

2.l. mDOT Response

Thank you for this wonderful suggestion. We can incorporate this for our next privacy research project so we know about the gaps in the privacy practice in the mHealth space, especially when sharing or using mHealth biomarkers for intervention development, optimization, and deployment.

3. Miscellaneous Comments

3.a. Miscellaneous Comment

- One design consideration for health interventions is that sometimes it is not the person themselves that needs the intervention, but other people in their proximity. For example, to eat healthier, it might be better to have an intervention for the person who regularly shops for food for a household (assuming they are not the same person).

3.b. mDOT Response

Very insightful comment to target intervention to decision makers. One external project to whom we provided mDOT technology for stress intervention, targets caregivers directly. We will brainstorm with our other collaborating health researchers to see if they can target decision makers in their next project on mHealth intervention.

3.c. MIscellaneous Comments

- Another design consideration is that a growing number of AI systems for healthcare have been demonstrated to exhibit bias against minorities, largely due to systemic issues in the data being used to train those algorithms. While there is no clear best practices yet, it is important for the team to be cognizant of those issues and consider ways to help ensure that participants are diverse and representative of intended population of target users.

3.d. mDOT Response

Thank you for raising this issue. Fortunately, many of our collaborating projects are collecting data from ethical and racial minorities and those with a lower socio-economic status as they are disproportionately affected by several chronic health and adverse behavioral issues (e.g., addictive behaviors).

3.e. MIscellaneous Comments

- A final design consideration is making sure that the mobile health systems can fit well into the complex ecosystem of healthcare in the United States. For example, a mobile health system that tries to improve some kind of efficiency might result in lost jobs, which might lead to rejection by practitioners. Alternatively, a mobile health system that collects a lot of data might increase the workload and burden of practitioners and subject them to lawsuits for missing sensed data that could have been prevented. Cost is also an important driver for hospitals and insurance companies, though focusing too much on cost might also lead people to inadvertently make patient outcomes secondary. The main design recommendation here is to get lots of feedback throughout the entire design process from multiple stakeholders (doctors, nurses, patients, caregivers, insurance), to help improve the odds of adoption of technologies developed by mDOT, rather than at the end of the design process.

3.f. mDOT Response

Thank you for sharing this insight that can help ensure a high societal impact of mDOT technology. We work directly with our collaborating health researchers, who then interface with the translational research community, who then work directly with practitioners and decision makers. Informally, we have regular dialogues with several clinicians who reach out to express an interest in mDOT technology and enquire about its availability for their use. We inform them that there is a process in place for the mDOT technology to transition into practice, rather than directly from the mDOT Center. Additionally, we can begin to survey some of these end use stakeholders early in the process to assess how likely the mHealth technology being developed by mDOT will be of interest and and an enabler for them.

Principal Investigator: Kumar, Santosh

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

Managing and Mentoring - The software, mCerebrum and Cerebral Cortex, 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 PivitolTracker for handling bug report and project planning.

Archive - 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 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 Google Drive and PivotalTracker which allow for easy access to information in a usable and consumable manner.

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 webinars.
https://mhealth.md2k.org/

Publication Reviews - mDOT investigators have published or have submitted and under review 21 papers related to mDOT research. The papers have been readily available for team review to facilitate broader discussion.

Webinars - We have an archive of over 150 webinars and over 110 hours of training video content. Students and staff are encouraged to attend live, and webinars are posted to the MD2K YouTube channel and links are featured on the mHealthHUB. https://www.youtube.com/c/MD2KCenter

Student Mentoring - Each mDOT-affiliated graduate student has a faculty advisor to guide them in their studies and is available for discussions about coursework and research.

mHealth Training Institute - All the presentations by the mHTI faculty are archived on mHealthHUB.
https://mhealth.md2k.org/mhealth-training-institute

mDOT Website -
https://mdot.md2k.org

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

Webinars -
https://www.youtube.com/c/MD2KCenter

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 (see table below of recent talks and presentations).

- On December 13, 2020, we conducted a workshop at the 31st Annual Meeting of the American Association of Addiction Psychiatry entitled, "Trials and Tribulations in Optimizing mHealth Interventions in Addictions." This workshop provided training in MRT design and three addiction health scientists presented their MRTs.

- On December 16 and 18, 2020, we conducted virtual brainstorming sessions for health scientists who have conducted an MRT (first session) or are designing an MRT (second session). The first session was with scientists who conducted an MRT with the Drink Less app in the U.K. and the second session was with a health scientist developing dialectical behavior therapy for individuals in distress. Attendees included health scientists working on MRTs including exercise for cancer patients (Harvard Dana Farber Cancer Institute), smoking (Johns Hopkins, National Institute on Minority Health and Health Disparities, the University of Texas at Austin), physical activity (UC Berkeley), suicide prevention (Harvard Psychology), cancer prevention (Harvard Mass General), addiction (Univ of New Mexico, McLean Hospital), immunosuppressant medication adherence among adolescents and young adults (Johns Hopkins), mental health (Northwestern Univ., Brigham and Women's Hospital), ADHD (George Washington Univ. School of Medicine), postpartum risky drinking (Partnership to End Addiction), stress management (UCSF Department of Psychiatry and Behavioral Sciences), engagement (University Michigan) as well as data scientists from Harvard, Univ. Michigan, UC Irvine, Apple, and the University of Wisconsin. It was very exciting!

- On January 6,7,8, 2021 we ran a workshop at the Winter School AI4Health (Paris, virtual); this 6-hour workshop targets data scientists (CS, Eng, Stat) who are interested in machine learning for designing interventions in mobile health.

- In June 2021 we ran two virtual brainstorming sessions. The first session was with behavioral scientists who are designing an MRT for suicide prevention (M. Nock, Harvard Univ). In the second S. Dauber (Partnership to end drug addiction) presented on the development of a conceptual model and design of a preliminary EMA study aimed at informing the development of a tailored JITAI for postpartum risky drinking. Attendees included health scientists working in suicide prevention, smoking cessation, substance use prevention and treatment, treatment adherence, maternal and child health, anger management, and behavioral interventions for adolescents with ADHD, as well as data scientists working on statistical methodologies for data analysis for mobile health applications.

- On September 21, Susan Murphy taught a course, "Digital Health Technologies: Moving Health Care from the Clinic to the Patient" at the virtual ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop. Her part of the course, which focused on micro-randomized trials & reinforcement learning for constructing personalized mobile digital health technologies for behavioral modifications with application to individuals at risk of adverse cardiovascular events, had a wide range of attendees from academia, government agencies, and the health care sector.

- October 13, 2021, Susan Murphy along with scientists in CP1 conducted a workshop at the Addiction Health Services Research Conference on Methods for Adaptive and Personalizing Prevention, Treatment, and Recovery Services for SUD. This workshop is for addiction services scientists who are interested in developing adaptive interventions, particularly in digital health.

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- On October 25-26 Susan Murphy led a 2021 Summer Institute workshop Building Just-in-Time Adaptive Interventions. This is a two-day virtual workshop for 45 behavioral scientists from institutions across the United States. Attendees work in a wide range of fields, including suicide prevention, addiction treatment, HIV prevention, smoking cessation, treatment adherence, and management of chronic conditions. All of the participants are developing digital interventions.

- At UCLA the project activities have partially engaged three Ph.D. students as well as two undergraduate students. The project has furthered their educational training by giving them hands-on experience on various facets of sensor information processing towards biomarker computation on resource-constrained wearable devices, and on quantifying and mitigating privacy risks. Additionally, the research in the project was also incorporated in two graduate courses via special lectures, assignments, and projects, resulting in influencing the training of 50+ students in the ECE and CS Departments.

- In addition to the 35 scholars, the 2021 mHTI also provided an opportunity to 3 graduates in the UCLA School of Education to conduct advanced social network analyses that will inform the growing field of team science.

Major Talks & Presentations

S. Murphy	Numerical Analysis for Data Science Opening Workshop, SAMSI,	Remote	8/27/2020	Intelligent Pooling for Thompson Sampling with Applications to Mobile Health (invited talk)
S. Murphy	Joint Conference of the GMDS & CEN-IBS 2020	REMOTE (Berlin)	09/07/2020	Clinical Trial Designs for Personalizing Digital Interventions (**Keynote**)
S. Murphy	Neyman Statistics Seminar, University of California, Berkeley,	Remote (Berkeley)	10/28/2020	Challenges in Developing Learning Algorithms to Personalize Treatment in Real Time (invited talk)
S. Murphy	4th Annual Mobile & Electronic Health-ARC Symposium	Remote (Boston)	11/12/2020	Data, Personalization, Digital Health! (invited talk)
S. Murphy	Sixth Seattle Symposium in Biostatistics	Remote (Seattle)	11/21/2020	Challenges in Developing Learning Algorithms to Personalize Treatment in Real Time (invited talk)
S. Murphy	Deep Reinforcement Learning Workshop (virtual), NeurIPS 2020		12/11/2020	We used RL…but…did it work?! (invited talk)
S. Murphy	Machine Learning for Mobile Health Workshop (virtual), NeurIPS 2020		12/12/2020	Assessing Personalization in Digital Health (invited talk)
S. Murphy	31st Annual Meeting of the American Academy of Addiction Psychiatry	Virtual workshop	12/13/2020	Trials and Tribulations in Optimizing mHealth Interventions in Addictions (invited talk)
S. Murphy	New York Medical College	Virtual presentation	12/21/2020	Data, Personalization, Digital Health! (invited talk)
S. Murphy	UAB Nutrition Obesity Research Center	Remote (Birmingham)	1/19/2021	Data, Personalization, Digital Health! (invited talk)
S. Murphy	AAAI 2021 Workshop Trustworthy AI for Healthcare	Virtual presentation	2/9/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Webinar, Faculté des sciences médicales et paramédicales, SESSTIM	Remote (Marseille, France)	2/26/2021	Data, Personalization, Digital Health! (invited talk)

S. Murphy	The Obesity Society 2021 Preconference Workshop on Synergistic Rigor in the Intersection of Epidemiology & Obesity	Remote presentation	2/2021	Using Mobile Health Interventions to Support Individual Decision Making (invited talk)
S. Murphy	Workshop on AUI for Public Health, ICLR 2021	Remote presentation	5/7/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Biomedical Data Science Seminar, University of Stanford School of Medicine	Remote (Stanford)	5/20/2021	We used RL but…. Did it work?! (invited talk)
S. Murphy	Frontiers of Causal Inference in Data Science: Perspectives from Leaders in Tech and Academia	Remote presentation	5/28/2021	We used RL but…. Did it work?! (invited talk)
S. Murphy	Distinguished Speaker Virtual Seminar, Department of Statistics, University of Oxford	Remote (Oxford, England)	6/18/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Statistical Learning Methods in Modern AI	Remote conference presentation	6/25/2021	We used RL; but did it work? (invited talk)
S. Murphy	37th Conference on Uncertainty in Artificial Intelligence	Remote conference keynote	7/27/2021	Keynote
S. Murphy	JSM 2021	Invited virtual paper	8/11/2021	Assessing Causal Inference Using Adaptively Collected Data (invited talk)
S. Murphy	Statistical Science Seminar, Duke University	Remote (Durham, NC)	9/3/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	RMME/STAT Colloquium, University of Connecticut	Remote (Storrs, CT)	9/10/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Herbert Wertheim School of Public Health and Human Longevity Science, University of California San Diego	Remote Grand Rounds (San Diego, CA)	9/17/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Department of Statistics, Florida State University	Myles Hollander Distinguished Lecture (virtual)	9/24/2021	We Used a Bandit Algorithm to Personalize But Did It Work? (invited talk)
S. Murphy	Design and Analysis of Experiments 2021 (DAE2021)	Remote conference presentation	10/13/2021	(invited talk) title TBD (see https://sites.google.com/view/dae2021/invited-sessions)
S. Murphy	Department of Statistics, University of Connecticut	Remote (Storrs, CT)	11/10/2021	Makuch Lecture
S. Murphy	Institute for Applied Computational Science, Harvard University	Remote (Boston, MA)	9/24/2021	We Used RL, But Did It Work? (invited talk)
P. Liao	Simons Institute for the Theory of Computing	REmote (Berkeley, CA)	9/24/2021	Batch Policy Learning in Average Reward Markov Decision Process
P. Liao	INFORMS 2020 virtual conference	Remote	11/9/2020	Batch Off-policy Learning in Average Reward Markov Decision Processes

P. Liao	Ubicomp/ISWC 2020 virtual conference	Remote	9/18/2020	Personalized HeartSteps: A Reinforcement Learning Algorithm for Optimizing Physical Activity
P. Liao	Pre-recorded talk, Bernoulli-IMS One World Symposium 2020 (virtual)	Remote	8/2020	Off-Policy Estimation of Long-Term Average Outcomes with Applications to Mobile Health
P. Liao	JSM 2020 virtual conference	Remote	8/3/2020	Off-Policy Estimation of Long-Term Average Outcomes with Applications to Mobile Health
K. Zhang	Statistics Colloquium, Pennsylvania State University	State College, PA (may change to remote)	11/11/201	Statistical Inference with M-Estimators on Adaptively Collected Data
K. Zhang	Virtual presentation, Institute for Operations Research and the Management Sciences (INFORMS) Annual Meeting	Remote	10/2021	Statistical Inference with M-Estimators on Adaptively Collected Data
K. Zhang	Pre-recorded talk, Bernoulli IMS Tenth World Congress in Probability and Statistics	Remote	7/2021	Statistical Inference with M-Estimators on Adaptively Collected Data
K. Zhang	Virtual presentation, Health Data Science Seminar Series, London School of Hygiene and Tropical Medicine	Remote (London, UK)	6/2/2021	Causal Inference for Data Collected with Bandit Algorithms
K. Zhang	Virtual talk, University of Cambridge Medical Research Council Biostatistics Unit	Remote (Cambridge, UK)	4/29/2021	Statistical Inference with M-Estimators on Bandit Data
K. Zhang	Pre-recorded talk, Bernoulli-IMS One World Symposium 2020 (virtual)	Remote	8/2020	Inference for Batched Bandits
M. Menictas	NeurIPS 2020 (virtual), poster and presentation (both with same title)	Remote	12/12/2020	Fast physical activity suggestions: efficient hyperparameter learning in mobile health
SN. Shukla	ML Retrospectives, Surveys & Meta-Analyses (ML-RSA) Workshop at NeurIPS, 2020	Remote	12/11/20	A Survey on Principles, Models and Methods for Learning from Irregularly Sampled Time Series
Santosh Kumar	Discovery, Optimization, and Translation of Temporally-Precise mHealth Interventions	Remote	09/07/2021.	IEEE Digital Health Conference
Santosh Kumar	Synergistic Collaboration Among Computing and Health Researchers	Remote	7/30/2021	
Santosh Kumar	From Sensed Data to Digital Biomarkers – Lessons Learned,	Remote	5/24/2021	NIH Annual mHealth Training Institute
Santosh Kumar	Breakout Session on Real-time Multimodal Data	Remote	5/14/21, 5/28/2021, and 6/11/2021	NSF-NIH Workshop on Establishing the Roadmap for Security, Privacy, and Ethics Research in Health
Santosh Kumar	Experiences in Developing and Deploying ML Models from Wearables	Remote	5/18/2021	NIH Annual mHealth Training Institute

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Santosh Kumar	Identifying Location Micro-Patterns Conducive to Smoking from GPS and Activity Traces	Remote	09/29/2020	NIH Workshop on Harnessing Novel Data Sources and Technologies for the Study of Social Determinants of Health (SDOH) in Heart, Lung, Blood, and Sleep (HLBS) Disorders
Ziqi Wang	Virtual Poster Presentation at ACM/IEEE IPSN	Remote (Nashville, TN, USA)	05/2021	Protecting User Data Privacy with Adversarial Perturbations
Mani Srivastava	Joint Keynote, 2nd Intl. Conference on Activity and Behavior Computing (ABC), 9th Intl. Conference on Informatics, Electronics & Vision (ICIEV), and, 4th Intl. Conference on Imaging, Vision & Pattern, 2020.	Remote (Japan)	08/2020	Security and Privacy Challenges in Learning-enabled IoT Systems
Mani Srivastava				The Future of Edge Computing: Towards Intelligent Autonomy in Human Spaces
Mani Srivastava	Invited Talk at Army Science Planning and Strategy Meeting (ASPSM) on Synthetic Environments for AI & ML	Remote	12/2020	Domain Transfer ChallengesBeyond Shifts in Data Distribution: Stochasticity in Time
Mani Srivastava	Invited Panel Talk IEEE 20202 CIC Plenary Panel on Collaborative Intelligence and Killer Applications in Edge Computing	Remote	12/2020	Towards Autonomy in Human Spaces
Mani Srivastava	Invited Talk at the Next Big Research Challenges in Cyper-Physical Systems Workshop	Remote	04/2021	CPS Technology Foundations: Quo Vadis?
James Rehg	Wearable cameras as a source of context for understanding eating behavior,	Virtual	10/22/2020	NSF Workshop on Technology for Automated Capture of Diet, Nutrition, and Eating Behaviors in Context

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

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?

Activity 1.1 - Modeling uncertainty in irregularly sampled and incomplete multivariate time series - Our initial work on the multi-time attention model was presented at the Learning with Missing Values Workshop at the International Conference on Machine Learning in summer 2020. A full version of the paper is currently under review at the International Conference on Learning Representations. A preliminary version of our survey paper on learning from irregularly sampled and incomplete time series data was presented at the ML-Retrospectives, Surveys & Meta-Analyses Workshop held in conjunction with NeurIPS 2020. A journal submission is pending and a preprint is currently available on arxiv (https://arxiv.org/abs/2012.00168v2). Publication for the mRisk work is currently under preparation and expected to be completed in Year 2.

Presentations and Workshops
S. Kumar, "Discovery, Optimization, and Translation of Temporally-Precise mHealth Interventions," Panel on "The future of Digital Health: Vision and Challenges" at IEEE Digital Health Conference, 09/07/2021.
S. Kumar, "Synergistic Collaboration Among Computing and Health Researchers," NIH Annual mHealth Training Institute, UCLA, 7/30/2021.
S. Kumar, "From Sensed Data to Digital Biomarkers – Lessons Learned," NIH Annual mHealth Training Institute, UCLA, 5/24/2021.
S. Kumar, "Breakout Session on Real-time Multimodal Data", NSF-NIH Workshop on Establishing the Roadmap for Security, Privacy, and Ethics Research in Health, 5/14/21, 5/28/2021, and 6/11/2021.
S. Kumar, "Experiences in Developing and Deploying ML Models from Wearables," Cyber Physical Health Systems Panel in IEEE CPS-IoT Week, 5/18/2021.
S. Kumar, "Identifying Location Micro-Patterns Conducive to Smoking from GPS and Activity Traces," NIH Workshop on Harnessing Novel Data Sources and Technologies for the Study of Social Determinants of Health (SDOH) in Heart, Lung, Blood, and Sleep (HLBS) Disorders, 09/29/2020.
S. Shukla. Multi-Time Attention Networks for Irregularly Sampled Time Series. International Conference on Learning Representations, 2021.
S. Shukla. A Survey on Principles, Models and Methods for Learning from Irregularly Sampled Time Series. ML Retrospectives, Surveys & Meta-Analyses (ML-RSA) Workshop at NeurIPS, 2020.
J. M. Rehg, "Wearable cameras as a source of context for understanding eating behavior," NSF Workshop on Technology for Automated Capture of Diet, Nutrition, and Eating Behaviors in Context, Virtual Meeting, 10/22/20.

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

Activity 1.1 - We will complete the development of a diverse set of benchmarks and tasks for learning from incomplete and irregularly sampled time series including both publicly available datasets and data sets from selected CPs. We will conduct an evaluation of the ability of existing methods to accurately propagate uncertainty due to input sparsity using this set of benchmarks. We will then proceed with the development of hierarchical extensions of our modeling approaches applied to both classification and imputation/interpolation tasks. We will also work with our CPs to communicate the results of this work

and to support deploying TR&D1 methods within their ongoing modeling work.

Activity 1.2 - We will continue the development of imputation methods for biophysical signals by developing missingness models that reflect real-life patterns of data missingness in mHealth applications. Using these models we will develop a reference task for imputation and test multiple state-of-the-art methods to establish baselines. We will continue our development of a novel transformer-based baseline architecture for imputation.

Activity 1.3 - We will complete our development of continuous-time attention mechanisms for irregularly sampled longitudinal data by establishing the theoretical properties of the deformed kernel exponential family models and obtaining benchmark results on standard datasets.

Activity 2.1 - Towards fulfilling Specific Aim 2, we plan to continue working on developing the mRisk method with CP1 and CP5 to estimate the momentary risk of lapse from mHealth biomarkers time series data. Second, we plan to produce the relevant new mHealth biomarkers that estimate and characterize the lapse risk in the smoking cessation dataset of CP1 and CP5. Third, we plan to implement the new biomarkers emerging from the mRisk model and apply them to the dataset of CP1 and CP5 so they can be used by our collaborating health researchers in pursuing their publication towards the design and development of new mHealth interventions.

Principal Investigator: Kumar, Santosh

B.2 What was accomplished under these goals?

In Year 1, the TR&D1 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: *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 have focused on the fundamental problem of developing deep learning models for sparse, irregularly sampled, and incomplete time series data. We developed a novel approach for this problem that we refer to as *Multi-Time Attention Networks.* This model family generalizes past approaches to modeling irregularly sampled and incomplete time series data by enabling the learning of temporal similarity functions both within and across different dimensions of a time series using a novel attention-based layer that can operate directly over incomplete and irregularly sampled time series. Using this model class as a building block, we are exploring both its ability to reflect input uncertainty due to significant missing data and are developing modeling extensions to accommodate the hierarchical classification/imputation setting. In conjunction with this work, we have also completed an extensive survey of recent work on the problem of learning from irregularly sampled and incomplete time series data.

Activity 1.2: *Imputing Quasiperiodic Biophysical Signals* - In additional work, we have explored a deep learning approach to the imputation of biophysical signals which exhibit a quasi-periodic signal structure in the form of “beats” resulting from the physiology of the cardiovascular and cardiopulmonary systems. A broad range of wearable sensor modalities, including ECG, PPG, SCG, and so forth, exhibit such a beat structure, and missingness in these signals is a common challenge for mHealth researchers. We are developing an attention-based deep learning architecture that can learn to leverage the quasi-periodic signal structure to perform accurate imputation in the face of substantial amounts of missingness, such as the absence of multiple beats.

Activity 1.3 *Kernel Deformed Exponential Families for Sparse Continuous Attention* - Recent work is providing an additional approach to developing continuous-time attention models which provide a flexible means to address irregularly sampled longitudinal data via attention densities. We are building on a recent formulation of continuous-time attention that has been shown to generalize the popular transformer architecture for learning discrete attention representations. Our work generalizes the standard approach, which is based on unimodal attention densities to encompass multimodal attention densities based on exponential and deformed exponential family distributions.

Activity 2.1: *mRisk: Sensing the Imminent Risk of Impulsive Behavior Using Mobile Sensors* - Our goal in Aim 2 is to derive uncertainty-aware composite risk scores to identify timing triggers for delivering temporally-precise interventions. In recent years, several research works have developed machine learning models to passively and continuously detect dynamically varying states or risk factors of impulsive behaviors (such as impulsive buying, suicide attempts, overeating, binge-drinking, and smoking lapse). These factors can be internal to an individual (e.g., stress, craving, and self-efficacy) or exposure to risky environments (e.g., geo-exposures and social interactions). However, just the detection of such risk factors in isolation may not serve the purpose for the development of mHealth technologies for delivering just-in-time adaptive interventions (JITAI). According to prior work, JITAI-based intervention design aims to provide timely support to an individual by adapting to both the changing internal and environmental/contextual stimuli of that individual. Hence, we have explored the interaction of the varying internal and external risk factors/stimuli for developing a computational model to predict the imminent risk (in the form of a composite risk score) of impulsive behavior. Estimation of the continuous risk state may be critical for delivering temporally-precise interventions and treatment adaptations in

cessation programs. For data analysis, we plan to work with CP1 (Novel Use of mHealth Data to Identify States of Vulnerability and Receptivity to JITAIs). Furthermore, once the model is developed, we aim to coordinate with CP5 (Affective Science and Smoking Cessation: Real-time Real-world Assessment) for its incorporation into the study.

Activity 2.2 *Prediction of EMA Nonresponse Using Transformers* - The collection of self-reported data from participants via EMA is a key tool that is used in mHealth studies to identify the timing and occurrence of outcomes such as relapse to smoking and obtain information about mood and behavioral states such as craving which are difficult to measure from passive sensing. A major challenge in EMA data collection is non-response when participants fail to provide EMA items in response to a prompt. We have developed a transformer-based deep learning architecture for predicting nonresponse given a history of past EMA responses in conjunction with demographic and contextual data. Our novel approach outperforms classical machine learning methods on this task.

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 sensor and EMA data to support the development of novel interventions for smoking cessation. TR&D1 investigator Kumar collaborated with CP1 and CP5 on the challenges of smoking lapse prediction which directly influenced the mRisk work under Aim 2 Activity 2.1 and led to a joint publication. TR&D1 investigator Rehg also worked closely with the CPs on the nonresponse prediction problem in EMA data which led to Activity 2.2. Additional work on biophysical signal imputation and continuous-time attention models in Activities 1.2 and 1.3 is a direct result of a dialog with CP1 and CP5, based on concerns about dealing with missing sensor data when building models for risk prediction. These works will be further integrated with CP activities once the technology has been developed.

- **CP3 (Klasnja):** CP3 began enrolling participants in its version of the HeartSteps V2 study in July 2020 and currently has 18 completed participants and an additional 58 participants currently enrolled and active. TR&D1 investigator Marlin completed an IRB reliance agreement to obtain access to CP3 data and via his dual role as multiple project director on CP3 has gained a strong understanding of the challenges with missingness and irregularly sampling in CP3 data that will help to inform the development work being conducted under Aim 1 Activity 1.1. The missing data imputation and time series interpolation methods developed under Activity 1.1 will be deployed for evaluation in CP3. The missing data handling and modeling tools that are being developed under CP3 are also being shared back with the mDOT team.

- **CP4 (Rivera):** The CP4 team is specifically interested in differential equation-based models where missing data also causes problems for parameter identification methods. Members of the TR&D1 team have been working to gain more familiarity with this class of models. Members of CP3, CP4, and TR&D1 are jointly considering approaches for integrating single-level imputation methods and parameter identification for differential equation models.

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.

Principal Investigator: Kumar, Santosh

B.2.3. Significant Results

Activity 1.1 - *Modeling uncertainty in irregularly sampled and incomplete multivariate time series* - Our initial work on the multi-time attention model was presented at the Learning with Missing Values Workshop at the International Conference on Machine Learning in summer 2020 and the full version of the paper was presented at the International Conference on Learning Representations in Spring 2021. This approach was able to match or exceed the predictive performance of current state-of-the-art methods for time series classification with missing data as well as time series imputation/interpolation while achieving one to two orders of magnitude speedups in training time. Our survey of the recent literature in this space included 40 papers and introduced a new organizing principle for methods based on modeling primitives for dealing with irregular sampling and incompleteness. Across this related work, we identified the lack of focus on characterizing uncertainty as a major limitation of current approaches.

Activity 2.1 - *mRisk: Sensing the Imminent Risk of Impulsive Behavior Using Mobile Sensors* - The mRisk method has been developed and evaluated on a dataset of 92 participants (newly abstinent smokers) obtained from CP1 and CP5. The evaluation approach addressed several key parameters including classifier selection, window size, and impact of within-person and between-person variability. We obtained promising results of intervention hit rate of 0.71 and false positive rate of 0.066 using a 60 min window length. In addition, we obtained promising results in generating explanations for model outputs based on the SHAP algorithm. These results are now being prepared for journal submission.

B.2.4. Key Outcomes & Other Achievements

- Personnel achievements (graduation, job placement, etc.)
    - Soujanya Chatterjee, Ph.D. - Joined Amazon as an Applied Scientist
    - Satya Narayan Shukla, PhD. - Joined Facebook AI Research
- Development of software components
    - Released new data streams of smoking spots and smoking opportunity contexts. New Python software modules were implemented in Cerebral Cortex V3 and applied to the data collected by CP1 and CP5. These newly computed datastreams were provided to collaborating investigators from CP1 and CP5 for use in their publications.
    - Our reference implementation of multi-time attention networks was released on GitHub: https://github.com/reml-lab/mTAN
    - Developed a common GitHub infrastructure for the release of TR&D1 software components and initiated a process for organizing datasets for TR&D1 to support push-pull interactions with our CPs.

Principal Investigator: Kumar, Santosh

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

At UMass Amherst, two students received training in the development of machine learning methods for incomplete and irregularly sampled data. Both students had the opportunity to participate in telecons with CP3 and CP4 investigators as well as on TR&D1 telecons. One student completed their Ph.D. degree during this reporting period. This student also gained experience presenting their research at workshops as well as major international conferences. This training, in part, helped one student secure a full-time position with Facebook AI Research upon graduation with a Ph.D.

At Georgia Tech, two students received training in the development of machine learning and data analysis methods for mHealth data types including EMA and ECG signals, and the utility of these methods to behavioral science researchers. These students also gained knowledge of the challenges and opportunities in using ML technology to address smoking cessation. These students participated in weekly conference calls with the CP1 and CP5 teams as part of our collaboration activities.

At the University of Memphis, the students participated in the telecons with TR&D1 investigators and students to enhance their learning of machine learning methods for risk estimation. They also regularly participated with domain science collaborators of CP1 and CP5 and engaged in push-pull interaction by making presentations to seek their feedback, providing processed data and consultations to help them document and interpret the processed data. This push-pull interaction helped them learn interdisciplinary collaboration skills. These experiences and training, in part, helped one student secure a full-time position of applied scientist at Amazon.

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
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.

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?

With regards to the adoption of new practices, the brainstorming sessions listed under B.4 have now begun to have an impact on many health scientists conducting MRTs. Also, we are increasing discussion of personalization (via RL) as part of the MRT--this bodes well for the future.

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

Principal Investigator: Kumar, Santosh

B.2 What was accomplished under these goals?

In Year 1, the TR&D2 undertook a variety of activities (as described below) to fulfill its goals.

B.2. Major Activities (include push-pull activities with CPs)

Activity 1

Inference from an MRT employing an RL algorithm (Aims 1, 2). The use of RL algorithms results in "adaptively sampled" data. Standard inferential methods can lead to undercoverage in the case of confidence intervals or bias in the case of estimation. In Zhang et al. we developed the first method for inference in these settings. Further, we developed a statistical inferential weighting method that permits the most common approaches to inference (Zhang et al., 2021). This work will be used to inform how to design RL algorithms that both allow within user personalization as well as facilitate experiment learning (facilitate the building of scientific knowledge via after experiment data analyses). We also completed work on methods for analyzing adaptive sampled data when there is no sharing of data among users (see CP3 below). We developed a simple approach to ensure sufficient after-study statistical power to test hypotheses when there is no sharing of data among users; this paper will soon appear.

With regards to Aim 2, we developed an efficient computational approach to hyperparameter tuning when the RL algorithm uses a mixed-effects model with data from multiple users to personalize intervention delivery for a particular user. This paper was presented at the NeurIPS 2020 workshop on Machine Learning for Mobile Health.

Activity 2

To limit user burden, RL algorithms in mHealth use a budget to constrain the number of times an intervention is triggered. To ensure a uniform spread of the intervention prompt throughout the day, RL algorithms need an estimate of the remaining number of times the state of the user is expected to satisfy the criteria for prompting an intervention. Under this activity, we are developing a method for conditional forecasting of user state estimated from sensors. In particular, we are using the stress assessment produced by wrist-worn PPG sensors in the context of smoking cessation from CP1. The goal is to develop a forecasting method that can provide an estimate of the remaining stress events expected on the day when the user will be wearing sensors and producing pulse-plethysmography data of acceptable quality. The event to condition the forecast is the quit event. When a smoker quits smoking, their stress profile changes in the post-quit days when compared with the pre-quit days. The stress profile is also expected to change when a user engages in a stress intervention (of their own volition or in response to a prompt generated by an RL algorithm). We plan to test the utility of the forecasting method by evaluating how accurately it is able to estimate the dynamic change in the craving state by analyzing deviations in the stress state when compared with the forecast based on pre-quit data for the given location and time context. We are in the process of curating the data by producing the stress inferences from wrist-worn PPG sensor data with appropriate screening, cleaning, and application of a suitable stress model.

Summary of Push Pull Activities with CPs:

- **CP1 (Nahum-Shani):** We completed a paper on the results of an MRT (the SARA MRT in addiction); this paper is in the press for *Health Psychology*. Further, we collaborated on a paper describing the design of a second MRT study in smoking cessation. We are currently engaged in an additional paper with CP1. This paper is written for quantitative psychologists and concerns how to design MRTs as well as how to structure primary data analyses.

Principal Investigator: Kumar, Santosh

The paper received a very positive review from the journal *Psychological Methods* and has been revised and resubmitted. We are also engaged with CP1 for Activity 2 on developing a conditional forecasting model.

- **CP2 (Shetty):** In collaboration with this CP we are developing an RL algorithm that will pool accruing data over clusters of individuals in order to speed up learning of a personalized oral health digital intervention. We expect that the trial deploying our RL algorithm will go into the field in late spring, 2022. We are working with the mDOT Software team and Chief Architect Tim Hnat to ensure that mDOT developed APIs can be tested and used by this CP.

- **CP3 (Klasnja):** Much of TR&D2's work is currently in collaboration with this CP. In collaboration with CP3, we wrote a paper on methods for analyzing binary longitudinal outcomes from an MRT (here the outcome was whether the user monitored their weight each day) and a second paper on approaches for pooling data across individuals in after-study analyses in mobile health. Both of these papers were selected by the editors of the respective journals for discussion. We completed and presented a workshop paper on flexible modeling strategies for MRT data as well. Further, we are engaged in writing multiple papers with CP3. The first paper (Aim 2) concerns how to analyze mhealth data collected via a reinforcement learning (RL) algorithm (e.g. HeartSteps) to ascertain if there is evidence of real-time personalization of treatments to users (here personalized delivery of activity suggestions to the user). The second paper (Aim 1) is a case study paper, based on one of the HeartSteps MRTs, that will illustrate and provide best practices for analyzing data from an MRT that includes interventions targeted at moments of risk (here times at which the user is sedentary). Further with regards to Aims 1 and 3, Murphy and Klasnja along with other scientists are meeting weekly to think through the potential causal pathways that can be used by a manager RL algorithm to accommodate delayed effects and to enhance collaboration between multiple intervention components.

Murphy, Klasnja, and Hnat have held a series of meetings as the CP3 is providing guidance for our mDOT APIs for use on the smart device as well as on the cloud to conduct JITAIs targeted at moments of opportunity or moments of risk and for conducting scientist-interpretable reinforcement learning.

Principal Investigator: Kumar, Santosh

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

On December 13, 2020, we conducted a workshop at the 31st Annual Meeting of the American Association of Addiction Psychiatry entitled, "Trials and Tribulations in Optimizing mHealth Interventions in Addictions." This workshop provided training in MRT design and three addiction health scientists presented their MRTs.

On December 16 and 18, 2020, we conducted virtual brainstorming sessions for health scientists who have conducted an MRT (first session) or are designing an MRT (second session). The first session was with scientists who conducted an MRT with the Drink Less app in the U.K. and the second session was with a health scientist developing dialectical behavior therapy for individuals in distress. Attendees included health scientists working on MRTs including exercise for cancer patients (Harvard Dana Farber Cancer Institute), smoking (Johns Hopkins, National Institute on Minority Health and Health Disparities, the University of Texas at Austin), physical activity (UC Berkeley), suicide prevention (Harvard Psychology), cancer prevention (Harvard Mass General), addiction (Univ of New Mexico, McLean Hospital), immunosuppressant medication adherence among adolescents and young adults (Johns Hopkins), mental health (Northwestern Univ., Brigham and Women's Hospital), ADHD (George Washington Univ. School of Medicine), postpartum risky drinking (Partnership to End Addiction), stress management (UCSF Department of Psychiatry and Behavioral Sciences), engagement (University Michigan) as well as data scientists from Harvard, Univ. Michigan, UC Irvine, Apple, and the University of Wisconsin. It was very exciting!

On January 6,7,8, 2021 we ran a workshop at the Winter School AI4Health (Paris, virtual); this 6-hour workshop targets data scientists (CS, Eng, Stat) who are interested in machine learning for designing interventions in mobile health.

In June 2021 we ran two virtual brainstorming sessions. The first session was with behavioral scientists who are designing an MRT for suicide prevention (M. Nock, Harvard Univ). In the second S. Dauber (Partnership to end drug addiction) presented on the development of a conceptual model and design of a preliminary EMA study aimed at informing the development of a tailored JITAI for postpartum risky drinking. Attendees included health scientists working in suicide prevention, smoking cessation, substance use prevention and treatment, treatment adherence, maternal and child health, anger management, and behavioral interventions for adolescents with ADHD, as well as data scientists working on statistical methodologies for data analysis for mobile health applications.

On September 21, Susan Murphy taught a course, "Digital Health Technologies: Moving Health Care from the Clinic to the Patient" at the virtual ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop. Her part of the course, which focused on micro-randomized trials & reinforcement learning for constructing personalized mobile digital health technologies for behavioral modifications with application to individuals at risk of adverse cardiovascular events, had a wide range of attendees from academia, government agencies, and the health care sector.

October 13, 2021, Susan Murphy along with scientists in CP1 conducted a workshop at the Addiction Health Services Research Conference on Methods for Adaptive and Personalizing Prevention, Treatment, and Recovery Services for SUD. This workshop is for addiction services scientists who are interested in developing adaptive interventions, particularly in digital health.

On October 25-26 Susan Murphy led a 2021 Summer Institute workshop Building Just-in-Time Adaptive Interventions. This is a two-day virtual workshop for 45 behavioral scientists from institutions across the United States. Attendees work in a wide range of fields, including suicide prevention, addiction treatment, HIV prevention, smoking cessation, treatment adherence, and management of chronic conditions. All of the participants are developing digital interventions.

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?

Results are disseminated via publications across the scientific fields as well as via workshops as described above. For example, we wrote a paper to discuss how MRTs can be used to promote engagement in data collection for a computational biology audience. We also wrote a paper for addiction research scientists on Just-in-Time Adaptive Interventions in mobile health.

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&D3 (Translation): Translation of Temporally Precise mHealth via Efficient and Embeddable Privacy-aware Biomarker Implementations
Component Project Lead Information: Ertin, Emre

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, 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 present 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 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?

File Uploaded : mDOT TR&D3 B.4. 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.

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

In Year 2, we will follow the following research thrusts:
Deriving micro-markers for the new modality of ballistography signals to support cardiac health features in collaboration with CP6.
Deriving micro-markers for motion signal processing that can support various inference tasks of Metabolic rate estimation, Physical Activity Assessment, Gesture Recognition (e.g. Brushing, Smoking gestures), Activity Recognition.
Developing methods for fusing micro markers from multiple modalities to support higher layer inferences such as stress, craving, physical performance, fatigue.
Developing new algorithms for edge computation of markers of BioRF sensing arrays for assessing tissue liquid content with applications in monitoring lymphedema and pulmonary edema.
Build upon our WristPrint work to characterize reidentification risk from sharing of data collected by other widely used modalities of sensors on smartwatches (e.g., PPG, gyroscope). We plan to investigate both when raw sensor data are shared and when sensor data are transformed via emerging mitigation methods, such as sharing the time series of micromarkers and mHealth biomarkers. We also plan to formalize an overarching threat model that captures several emerging scenarios of privacy or identity leaks, several of which were summarized by our advisory board member, Dr. Jason Hong.

Principal Investigator: Kumar, Santosh

B.2 What was accomplished under these goals?

In Year 1, 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: ***Deriving micromarker abstractions for PPG signals for heart rate and heart rate variability assessment using task-specific autoencoders*****:** PPG sensors embedded into commercial and research-grade wristbands provide data on pulsatile blood flow at the wrist enabling heart rate and heart rate variability assessment. Each band typically has multiple LED and photodiode pairs to maximize coverage of the skin surface and signal to noise. This multiple-channel of data needs to be fused to derive a tachogram signal relating to beat-to-beat intervals in the PPG signal. Classical methods consider the task of sensor fusion, signal compression, heartbeat detection, and tachogram estimation -smoothing as separate tasks. Our goal in Aim 1 is to develop hierarchical computing methods to support scalable, low-latency, power-efficient computation of biomarker computations. We use a multichannel autoencoder structure paired with a tachogram estimation based on convolutional neural networks as an end-to-end trainable algorithm using a task-specific error metric that penalizes deviations from the actual tachogram signal derived from an ECG sensor during training. Then we use the latent codes learned in the autoencoder framework as the micromarker representations of the heart rate signal that are tailored for tachogram estimation. In future work, we will assess the utility of these micromarkers in a stress inference task.

Activity 1.2: ***Development of the next generation of MotionSense HRV platform as a reference implementation of micromarker abstractions for PPG and IMU signals:*** TR&D3 specific objectives include development of reference designs and associated software development kits to put techniques to develop and disseminate micromarker based biomarker implementations with built-in controls to explore privacy-utility tradeoff. The new learning techniques we explore under Aim 1 and 2 require embedding of the ML architectures such as deep nets, autoencoders at the edge devices. Towards this end, we have developed a dual-core version of our wristband and rewrote the software stack from the ground up to support common machine learning abstractions often encountered in bio/micro marker implementations. This concrete implementation based on current industry standards will allow us to explore power, latency, data rate tradeoffs in real-time biomarker computations.

Activity 1.3 ***Development of biomarkers for RF sensing of internal tissues:*** We seek to recover the characteristic properties, including permittivity, conductivity, and thickness, of the target tissues illuminated by an BioRF sensor. Following a Bayesian setting, we derive a comprehensive and adaptive MCMC sampling mechanism that achieves enhanced sampling efficiency compared to conventional sampling schemes. We provide marginal posterior density estimations of the unknowns and calculate credibility intervals along with the point estimations for all the tissues under investigation. We also derive theoretical lower bounds to quantify the best possible estimator performance in terms of the mean squared error. This techniques will allow us to assess liquid content in various tissues and can be used in applications such as monitoring lung water in congestive health failure patients.

Activity 1.4: Development of computational mechanisms for sharing clinical time-series data to assure privacy while retaining utility: The aim of this activity is to enable the optimization of privacy-utility tradeoffs in biomarker computations via cross-layer mechanism design. It seeks to do so by creating computational mechanisms and a general biomarker privacy framework to enable participant control over the privacy-utility trade-offs during study design, data collection, and sharing of collected mHealth data for third-party research when data cross trust domains. During the reporting period, we used the opportunity offered by the NeurIPS 2020 hide-and-seek privacy challenge which focused on clinical time series data to develop methods for protecting time series data against membership inference attacks

while maintaining utility on a variety of inferences. The basic problem is to share in a privacy-preserving manner the longitudinal time series data for a subpopulation (study participants) in a manner that the recipient cannot deanonymize them (i.e. link back to specific members of the overall population) while maintaining high utility on a variety of task performed using the privacy-preserving synthetic data that was shared. For utility purposes, we focused specifically on two tasks: missing feature prediction and 1-step-ahead prediction. We developed several novel methods for privacy-preserving synthetic time series data generation. One approach is *Adversarial Noise Generation* where we add noise to the data in an adversarial manner. A trained feature extraction neural network will generate a feature embedding for each data entry. A small perturbation in the raw data entry may cause its embedding to change drastically because of the discontinuity of the function approximated by the neural network. The added noise is trained to "drag" the feature embedding of the current data entry towards that of a data entry from a different user so that their identity can be confused. A second approach we developed is *Genetic Noise Adder* where we apply the genetic algorithm to find synthetic data that meets the utility threshold and has maximal noise in the perturbation - an approach that is inspired by our prior work on adversarial perturbation. A third approach that we implemented is *Binning and Swapping* where we introduce noise to the data by grouping the data points in each feature dimension based on their cumulative distribution, and randomly switch the data points that fall into the same bin. Of these approaches, the first one performed the best and was ranked 2nd out of 36 participants in the hider category of the competition. We are preparing a paper based on this work and meanwhile have released our code in open-source form at https://github.com/nesl/hide-and-seek-challenge.

Activity 1.5: Characterizing user re-identification risks from wrist-worn accelerometry data : The aim of this activity is to characterize the privacy risks arising from sensor data in wrist-worn devices, particularly motion data. Public release of such data is growing as they enable and accelerate research in developing new algorithms to passively track daily activities, resulting in improved health and wellness utilities of smartwatches and activity trackers. But, when combined with sensitive attribute inference attack and linkage at- tack via re-identification of the same user in multiple datasets, undisclosed sensitive attributes can be revealed to unintended orga- nizations with potentially adverse consequences for unsuspecting data contributing users. To guide both users and data collecting researchers, we characterize the re-identification risks inherent in motion sensor data collected from wrist-worn devices in users' natural environment. For this purpose, we use an open-set formulation, train a deep learning architecture with a new loss function, and apply our model to a new data set consisting of 10 weeks of daily sensor wearing by 353 users. We find that re-identification risk increases with an increase in the activity intensity and the risk is 96% for an average user when sharing a full day of sensor data. THis research was conducted as a collaboration between Memphis, UCLA, and IBM Research, and a paper based on this activity was accepted at the prestigious ACM CCS '21 conference which is one of the top conferences focused on security and privacy in computing.

Activity 1.6: Hardware-aware efficient neural network models for on-device movement tracking and motion activity classification: In this activity we have developed TinyOdom, an optimization and synthesis framework for implementing robust and real-time neural network models for making inferences with IMU data on extremely resource constrained wearable sensors, particularly for purposes such as 3D movement tracking that is a building block for many biomarkers. The framework directly communicates with target hardware to optimize latency, flash and SRAM while trying to find a neural network that can provide the highest odometric resolution possible within the device constraints. The framework yields accurate yet lightweight neural inertial localization models robust to sensory and ambient dynamics. To provide 3D tracking robust to ambient dynamics, we bring in significant improvements to the 2D neural-inertial sequence learning formulation. First, we developed a velocity-centric position tracker robust to heading rate singularity, which is present in displacement-heading centric formulation. Secondly, we guide neural network learning through physics metadata, which signifies transportation modes and valid translational motion steps. Thirdly, we incorporate

magnetometer readings to provide an additional anchor apart from gravity robust to gravity, orientation and inertial pollution. Lastly, we expand 2D sequence learning to 3D using barometric alpha-beta filters to provide altitude estimation. For hardware-in-the-loop optimization of network architecture, we use Bayesian optimization with latency, SRAM, flash and accuracy being optimized jointly. We use a Gaussian Process as the surrogate function and Thomson sampling with upper-confidence bound as the acquisition function. For the network backbone, we use a lightweight temporal CNN design space, which can perform time-series machine-learning without the computational and training disadvantages of RNN, LSTM or GRU. We are currently in the process of submitting a paper based on this work as well as releasing the framework in open-source form.

Summary of Push-Pull Activities with CPs:

- **CP1 (Nahum-Shani):** The Mobile-Assistance for Regulating Smoking (MARS) project drafted the protocol for the study, where MotionSense sensors will be used to assess the smoking state and HRV as a measure of self-regulatory capacity. We used the study protocol to inform micromarker abstractions required to support the study objectives while minimizing latency and data rates to mobile devices.

- **CP2 (Shetty):** CP2 and mDOT researchers developed algorithms for detecting and characterizing brushing behavior assessment from wrist-worn inertial sensors. They were reported in two UbiComp papers. TR&D3 used this work as a starting point for learning micromarker abstraction for fine-grain motion data using learning-based tracking algorithms developed.

- **CP6 (Inan):** We have had several meetings with Dr. Inan discussing the role of Micromarkers in assessing cardiac state using signals from Ballistocardiography and seismocardiography. Dr. Inan gave a research talk to the TR&D3 reviewing his previous work and key results. We worked with CP6 to determine the time scale and features of these signal modalities and identified key features in the BCG and SSG signals for micromarker implementation. With Dr. Inan's group, we are also exploring the implementation of accelerometer arrays for cardiac monitoring which will be an alternative modality to investigate under Aim2.

- **CP7 (Ives):** In conjunction with the mProv group, the Mobile Open Observation of Daily Stressors (MOODS) project aims to answer several key questions regarding stress and stressors (precipitants of stress) in the computational, clinical, and data science domains. TR&D3 worked with the mProv investigators to develop metadata proposals to annotate the representation of stress biomarkers and the processing steps involved, including the computation of data quality. The metadata developed will ensure that the openly available, labeled dataset produced from this study will be an unprecedented community resource that we anticipate will advance the research community for years to come. This project has also undertaken the task of implementing the stress biomarker machine learning model on a commercial smartwatch platform (Fossil Sport Watch) with triggered sensing and computation to achieve energy efficiency. This project is under software and logistical development with the expectation to launch in Q2, 2021.

B.2.2. Specific Objectives

TR&D3 will provide the research community with 1) mDOT 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 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

OSU

- Variational Autoencoders for learning micromarkers of heart rate and heart rate variability
- MCMC methods for computing RF-based biomarkers of cardiovascular health
- Tensorflow Lite ready firmware/hardware stack on MotionSense HRV platform

UCLA

- TinyOdom software framework for hardware-aware efficient neural network models for on-device movement tracking and motion activity classification
- Adversarial perturbation based approach for preventing membership inference from shared sensor trace databases while maintaining utility for model training

Memphis + UCLA

- WristPrint software framework for characterizing user re-identification risks from wrist-worn accelerometry data

B.2.4. Key Outcomes & Other Achievements

- TR&D3 has designed a new dual-core version of MotionSense HRV that will allow collaborating researchers to run their trained ML algorithms on the wristband at the second core, while the first core implements sensor access, Bluetooth communication, and storage functions compatible with mDOT and M2DK infrastructure.
- TR&D3 rewrote the firmware from grounds upon open-source zephyr OS to enable mDOT institutions and collaborating projects to modify and contribute to the codebase. The new firmware supports seamlessly integrating the Tensor flow lite framework into the devices
- The software team is working with the TR&D3 team to begin identifying how to interface with new hardware and how to define micromarker abstractions at the mobile and cloud levels.
- TR&D3 has developed WristPrint, a deep learning model based on a novel boosting approach, that enables quantification of risks from linkage attacks across databases of sensor traces
- TR&D3 has developed TinyOdom, a software framework that allows the implementation of accuracy-latency-memory optimized deep learning models for motion sensor processing on wearable devices.

Principal Investigator: Kumar, Santosh

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

At UCLA the project activities have partially engaged three Ph.D. students as well as two undergraduate students. The project has furthered their educational training by giving them hands-on experience on various facets of sensor information processing towards biomarker computation on resource-constrained wearable devices, and on quantifying and mitigating privacy risks. Additionally, the research in the project was also incorporated in two graduate courses via special lectures, assignments, and projects, resulting in influencing the training of 50+ students in the ECE and CS Departments.

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
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.
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).

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 Training and Dissemination
Component Project Lead Information: SHETTY, VIVEK

B. COMPONENT ACCOMPLISHMENTS

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

The main goals of the mDOT's Technology Training and Dissemination (TT&D) Core are two-fold: (a) improve the general understanding and uptake of the mDOT technologies and methods by the mHealth research communities; (b) develop a perpetuating cadre of transdisciplinary researchers conversant with the mDOT technologies and able to effectively apply them in their own research programs. The TT&D core will accomplish its goals through 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 mDOT 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 mDOT, and to both promote and enable a broader use of the mDOT 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?

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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 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.

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

Write up and publish the analysis of the mHTI to advance Team Science
Organize and conduct the 2022 mHTI
Reorganize the mHealthHUB portal
Resume the online webinars by mDOT (currently on hold due to Zoom fatigue!)

Principal Investigator: Kumar, Santosh

B.2 What was accomplished under these goals?

In Year 1, the Training & Dissemination core undertook a variety of activities (as described below) to fulfill its goals.

B.2.1. Major Activities

Aim 1: [Training]. Due to the COVID pandemic, the training activities made a hard pivot to virtual training. The main focus of the training was the development and conduct of a virtual version of the annual mHealth Training Institute (mHTI). This entailed deployment of a virtual events platform (vFairs) and a comprehensive, online application management system (SmarterSelect). From a pool of 280 applicants, 35 were chosen as scholars for the 2021 mHTI (https://mhti.md2k.org/index.php/scholars/2021-scholars). A corresponding group of faculty, comprising both academics and NIH Program Officers (https://mhti.md2k.org/index.php/faculty/2021-faculty), was also recruited. The virtual 2021 mHTI was conducted between May 10 and July 30, 2021 (https://mhti.md2k.org/index.php/program/2021-program).

Aim 2: [Dissemination] To allow the didactic content of the 2021 mHTI to be broadly accessible, 13 webinars were recorded and curated on the mHTI's website (https://mhti.md2k.org/index.php/gallery/2021-1/2021-lectures) as well as our mHealthHUB platform (https://mhealth.md2k.org/training/webinars.html)

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 2021 mHTI. The process evaluation questions investigate aspects of the design and implementation of the mHTI, 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.

Principal Investigator: Kumar, Santosh

B.2.3. Significant Results

1. Sociodemographics

Table. Background Characteristics of mHTI Scholars

	N	%
Race/Ethnicity (participants could select multiple)	28	100
White/Caucasian	19	67.86
Asian	6	21.43
Hispanic/Latino/Latina	1	3.57
Black/African American	2	7.14
Gender	27	100
Female	21	77.78
Male	6	22.22
Region	28	100
Northeast	3	10.71
Midwest	7	25
Southeast	5	17.86
West	7	25
Southwest	3	10.71
International (not from the U.S.)	3	10.71
Institution Type	28	100
University	25	89.29
Hospital or Clinic	3	10.71
Discipline	27	100
CS/Engineering/Data Science	6	22.22
Medicine/Nursing	6	22.22
Psychology	7	25.93
Public Health/Others	8	29.63

2. Key summaries of evaluation:
    a. The majority of the participants responded that the 2021 virtual mHTI was “extremely worthwhile” [mean score = 6.31 (out of 7) with SD of 1.07 (N=26)].

    b. Most of the participants had extremely positive views of the 2021 virtual 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.

    The mean of each question above was larger than 4.0 (out of 5.0, extremely positive).

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.

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.

Principal Investigator: Kumar, Santosh

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

In addition to the 35 scholars, the 2021b mHTI also provided an opportunity to 3 graduates in the UCLA School of Education to conduct advanced social network analyses that will inform the growing field of team science.

Principal Investigator: Kumar, Santosh

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

Managing and Mentoring - The software, mCerebrum and Cerebral Cortex, 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 PivitolTracker for handling bug report and project planning.

Archive - 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 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 Google Drive and PivotalTracker which allow for easy access to information in a usable and consumable manner.

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 webinars.
https://mhealth.md2k.org/

Publication Reviews - mDOT investigators have published or have submitted and under review 21 papers related to mDOT research. The papers have been readily available for team review to facilitate broader discussion.

Webinars - We have an archive of over 150 webinars and over 110 hours of training video content. Students and staff are encouraged to attend live, and webinars are posted to the MD2K YouTube channel and links are featured on the mHealthHUB. https://www.youtube.com/c/MD2KCenter

Student Mentoring - Each mDOT-affiliated graduate student has a faculty advisor to guide them in their studies and is available for discussions about coursework and research.

mHealth Training Institute - All the presentations by the mHTI faculty are archived on mHealthHUB.
https://mhealth.md2k.org/mhealth-training-institute

mDOT Website -
https://mdot.md2k.org

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

Webinars -
https://www.youtube.com/c/MD2KCenter

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 (see table below of recent talks and presentations).

- On December 13, 2020, we conducted a workshop at the 31st Annual Meeting of the American Association of Addiction Psychiatry entitled, "Trials and Tribulations in Optimizing mHealth Interventions in Addictions." This workshop provided training in MRT design and three addiction health scientists presented their MRTs.

- On December 16 and 18, 2020, we conducted virtual brainstorming sessions for health scientists who have conducted an MRT (first session) or are designing an MRT (second session). The first session was with scientists who conducted an MRT with the Drink Less app in the U.K. and the second session was with a health scientist developing dialectical behavior therapy for individuals in distress. Attendees included health scientists working on MRTs including exercise for cancer patients (Harvard Dana Farber Cancer Institute), smoking (Johns Hopkins, National Institute on Minority Health and Health Disparities, the University of Texas at Austin), physical activity (UC Berkeley), suicide prevention (Harvard Psychology), cancer prevention (Harvard Mass General), addiction (Univ of New Mexico, McLean Hospital), immunosuppressant medication adherence among adolescents and young adults (Johns Hopkins), mental health (Northwestern Univ., Brigham and Women's Hospital), ADHD (George Washington Univ. School of Medicine), postpartum risky drinking (Partnership to End Addiction), stress management (UCSF Department of Psychiatry and Behavioral Sciences), engagement (University Michigan) as well as data scientists from Harvard, Univ. Michigan, UC Irvine, Apple, and the University of Wisconsin. It was very exciting!

- On January 6,7,8, 2021 we ran a workshop at the Winter School AI4Health (Paris, virtual); this 6-hour workshop targets data scientists (CS, Eng, Stat) who are interested in machine learning for designing interventions in mobile health.

- In June 2021 we ran two virtual brainstorming sessions. The first session was with behavioral scientists who are designing an MRT for suicide prevention (M. Nock, Harvard Univ). In the second S. Dauber (Partnership to end drug addiction) presented on the development of a conceptual model and design of a preliminary EMA study aimed at informing the development of a tailored JITAI for postpartum risky drinking. Attendees included health scientists working in suicide prevention, smoking cessation, substance use prevention and treatment, treatment adherence, maternal and child health, anger management, and behavioral interventions for adolescents with ADHD, as well as data scientists working on statistical methodologies for data analysis for mobile health applications.

- On September 21, Susan Murphy taught a course, "Digital Health Technologies: Moving Health Care from the Clinic to the Patient" at the virtual ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop. Her part of the course, which focused on micro-randomized trials & reinforcement learning for constructing personalized mobile digital health technologies for behavioral modifications with application to individuals at risk of adverse cardiovascular events, had a wide range of attendees from academia, government agencies, and the health care sector.

- October 13, 2021, Susan Murphy along with scientists in CP1 conducted a workshop at the Addiction Health Services Research Conference on Methods for Adaptive and Personalizing Prevention, Treatment, and Recovery Services for SUD. This workshop is for addiction services scientists who are interested in developing adaptive interventions, particularly in digital health.

Principal Investigator: Kumar, Santosh

- On October 25-26 Susan Murphy led a 2021 Summer Institute workshop Building Just-in-Time Adaptive Interventions. This is a two-day virtual workshop for 45 behavioral scientists from institutions across the United States. Attendees work in a wide range of fields, including suicide prevention, addiction treatment, HIV prevention, smoking cessation, treatment adherence, and management of chronic conditions. All of the participants are developing digital interventions.

- At UCLA the project activities have partially engaged three Ph.D. students as well as two undergraduate students. The project has furthered their educational training by giving them hands-on experience on various facets of sensor information processing towards biomarker computation on resource-constrained wearable devices, and on quantifying and mitigating privacy risks. Additionally, the research in the project was also incorporated in two graduate courses via special lectures, assignments, and projects, resulting in influencing the training of 50+ students in the ECE and CS Departments.

- In addition to the 35 scholars, the 2021 mHTI also provided an opportunity to 3 graduates in the UCLA School of Education to conduct advanced social network analyses that will inform the growing field of team science.

Major Talks & Presentations

S. Murphy	Numerical Analysis for Data Science Opening Workshop, SAMSI,	Remote	8/27/2020	Intelligent Pooling for Thompson Sampling with Applications to Mobile Health (invited talk)
S. Murphy	Joint Conference of the GMDS & CEN-IBS 2020	REMOTE (Berlin)	09/07/2020	Clinical Trial Designs for Personalizing Digital Interventions (**Keynote**)
S. Murphy	Neyman Statistics Seminar, University of California, Berkeley,	Remote (Berkeley)	10/28/2020	Challenges in Developing Learning Algorithms to Personalize Treatment in Real Time (invited talk)
S. Murphy	4th Annual Mobile & Electronic Health-ARC Symposium	Remote (Boston)	11/12/2020	Data, Personalization, Digital Health! (invited talk)
S. Murphy	Sixth Seattle Symposium in Biostatistics	Remote (Seattle)	11/21/2020	Challenges in Developing Learning Algorithms to Personalize Treatment in Real Time (invited talk)
S. Murphy	Deep Reinforcement Learning Workshop (virtual), NeurIPS 2020		12/11/2020	We used RL…but…did it work?! (invited talk)
S. Murphy	Machine Learning for Mobile Health Workshop (virtual), NeurIPS 2020		12/12/2020	Assessing Personalization in Digital Health (invited talk)
S. Murphy	31st Annual Meeting of the American Academy of Addiction Psychiatry	Virtual workshop	12/13/2020	Trials and Tribulations in Optimizing mHealth Interventions in Addictions (invited talk)
S. Murphy	New York Medical College	Virtual presentation	12/21/2020	Data, Personalization, Digital Health! (invited talk)
S. Murphy	UAB Nutrition Obesity Research Center	Remote (Birmingham)	1/19/2021	Data, Personalization, Digital Health! (invited talk)
S. Murphy	AAAI 2021 Workshop Trustworthy AI for Healthcare	Virtual presentation	2/9/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Webinar, Faculté des sciences médicales et paramédicales, SESSTIM	Remote (Marseille, France)	2/26/2021	Data, Personalization, Digital Health! (invited talk)

Principal Investigator: Kumar, Santosh

S. Murphy	The Obesity Society 2021 Preconference Workshop on Synergistic Rigor in the Intersection of Epidemiology & Obesity	Remote presentation	2/2021	Using Mobile Health Interventions to Support Individual Decision Making (invited talk)
S. Murphy	Workshop on AUI for Public Health, ICLR 2021	Remote presentation	5/7/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Biomedical Data Science Seminar, University of Stanford School of Medicine	Remote (Stanford)	5/20/2021	We used RL but…. Did it work?! (invited talk)
S. Murphy	Frontiers of Causal Inference in Data Science: Perspectives from Leaders in Tech and Academia	Remote presentation	5/28/2021	We used RL but…. Did it work?! (invited talk)
S. Murphy	Distinguished Speaker Virtual Seminar, Department of Statistics, University of Oxford	Remote (Oxford, England)	6/18/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Statistical Learning Methods in Modern AI	Remote conference presentation	6/25/2021	We used RL; but did it work? (invited talk)
S. Murphy	37th Conference on Uncertainty in Artificial Intelligence	Remote conference keynote	7/27/2021	Keynote
S. Murphy	JSM 2021	Invited virtual paper	8/11/2021	Assessing Causal Inference Using Adaptively Collected Data (invited talk)
S. Murphy	Statistical Science Seminar, Duke University	Remote (Durham, NC)	9/3/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	RMME/STAT Colloquium, University of Connecticut	Remote (Storrs, CT)	9/10/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Herbert Wertheim School of Public Health and Human Longevity Science, University of California San Diego	Remote Grand Rounds (San Diego, CA)	9/17/2021	Assessing Personalization in Digital Health (invited talk)
S. Murphy	Department of Statistics, Florida State University	Myles Hollander Distinguished Lecture (virtual)	9/24/2021	We Used a Bandit Algorithm to Personalize But Did It Work? (invited talk)
S. Murphy	Design and Analysis of Experiments 2021 (DAE2021)	Remote conference presentation	10/13/2021	(invited talk) title TBD (see https://sites.google.com/view/dae2021/invited-sessions)
S. Murphy	Department of Statistics, University of Connecticut	Remote (Storrs, CT)	11/10/2021	Makuch Lecture
S. Murphy	Institute for Applied Computational Science, Harvard University	Remote (Boston, MA)	9/24/2021	We Used RL, But Did It Work? (invited talk)
P. Liao	Simons Institute for the Theory of Computing	REmote (Berkeley, CA)	9/24/2021	Batch Policy Learning in Average Reward Markov Decision Process
P. Liao	INFORMS 2020 virtual conference	Remote	11/9/2020	Batch Off-policy Learning in Average Reward Markov Decision Processes

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P. Liao	Ubicomp/ISWC 2020 virtual conference	Remote	9/18/2020	Personalized HeartSteps: A Reinforcement Learning Algorithm for Optimizing Physical Activity
P. Liao	Pre-recorded talk, Bernoulli-IMS One World Symposium 2020 (virtual)	Remote	8/2020	Off-Policy Estimation of Long-Term Average Outcomes with Applications to Mobile Health
P. Liao	JSM 2020 virtual conference	Remote	8/3/2020	Off-Policy Estimation of Long-Term Average Outcomes with Applications to Mobile Health
K. Zhang	Statistics Colloquium, Pennsylvania State University	State College, PA (may change to remote)	11/11/201	Statistical Inference with M-Estimators on Adaptively Collected Data
K. Zhang	Virtual presentation, Institute for Operations Research and the Management Sciences (INFORMS) Annual Meeting	Remote	10/2021	Statistical Inference with M-Estimators on Adaptively Collected Data
K. Zhang	Pre-recorded talk, Bernoulli IMS Tenth World Congress in Probability and Statistics	Remote	7/2021	Statistical Inference with M-Estimators on Adaptively Collected Data
K. Zhang	Virtual presentation, Health Data Science Seminar Series, London School of Hygiene and Tropical Medicine	Remote (London, UK)	6/2/2021	Causal Inference for Data Collected with Bandit Algorithms
K. Zhang	Virtual talk, University of Cambridge Medical Research Council Biostatistics Unit	Remote (Cambridge, UK)	4/29/2021	Statistical Inference with M-Estimators on Bandit Data
K. Zhang	Pre-recorded talk, Bernoulli-IMS One World Symposium 2020 (virtual)	Remote	8/2020	Inference for Batched Bandits
M. Menictas	NeurIPS 2020 (virtual), poster and presentation (both with same title)	Remote	12/12/2020	Fast physical activity suggestions: efficient hyperparameter learning in mobile health
SN. Shukla	ML Retrospectives, Surveys & Meta-Analyses (ML-RSA) Workshop at NeurIPS, 2020	Remote	12/11/20	A Survey on Principles, Models and Methods for Learning from Irregularly Sampled Time Series
Santosh Kumar	Discovery, Optimization, and Translation of Temporally-Precise mHealth Interventions	Remote	09/07/2021.	IEEE Digital Health Conference
Santosh Kumar	Synergistic Collaboration Among Computing and Health Researchers	Remote	7/30/2021	
Santosh Kumar	From Sensed Data to Digital Biomarkers – Lessons Learned,	Remote	5/24/2021	NIH Annual mHealth Training Institute
Santosh Kumar	Breakout Session on Real-time Multimodal Data	Remote	5/14/21, 5/28/2021, and 6/11/2021	NSF-NIH Workshop on Establishing the Roadmap for Security, Privacy, and Ethics Research in Health
Santosh Kumar	Experiences in Developing and Deploying ML Models from Wearables	Remote	5/18/2021	NIH Annual mHealth Training Institute

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Santosh Kumar	Identifying Location Micro-Patterns Conducive to Smoking from GPS and Activity Traces	Remote	09/29/2020	NIH Workshop on Harnessing Novel Data Sources and Technologies for the Study of Social Determinants of Health (SDOH) in Heart, Lung, Blood, and Sleep (HLBS) Disorders
Ziqi Wang	Virtual Poster Presentation at ACM/IEEE IPSN	Remote (Nashville, TN, USA)	05/2021	Protecting User Data Privacy with Adversarial Perturbations
Mani Srivastava	Joint Keynote, 2nd Intl. Conference on Activity and Behavior Computing (ABC), 9th Intl. Conference on Informatics, Electronics & Vision (ICIEV), and, 4th Intl. Conference on Imaging, Vision & Pattern, 2020.	Remote (Japan)	08/2020	Security and Privacy Challenges in Learning-enabled IoT Systems
Mani Srivastava				The Future of Edge Computing: Towards Intelligent Autonomy in Human Spaces
Mani Srivastava	Invited Talk at Army Science Planning and Strategy Meeting (ASPSM) on Synthetic Environments for AI & ML	Remote	12/2020	Domain Transfer ChallengesBeyond Shifts in Data Distribution: Stochasticity in Time
Mani Srivastava	Invited Panel Talk IEEE 20202 CIC Plenary Panel on Collaborative Intelligence and Killer Applications in Edge Computing	Remote	12/2020	Towards Autonomy in Human Spaces
Mani Srivastava	Invited Talk at the Next Big Research Challenges in Cyper-Physical Systems Workshop	Remote	04/2021	CPS Technology Foundations: Quo Vadis?
James Rehg	Wearable cameras as a source of context for understanding eating behavior,	Virtual	10/22/2020	NSF Workshop on Technology for Automated Capture of Diet, Nutrition, and Eating Behaviors in Context

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