Eric Hekler, PhD University of California, San Diego Using Control Systems Engineering To Optimize Adaptive Mobile Health Interventions June 4, 2019

Methods: Mind the Gap Presentation Questions from the Audience

1. What type of experience, skills, or career path do you recommend for someone interested in control systems engineering for medical/health applications?

Starting with career paths, at present, doing this type of work is inherently interdisciplinary. This means that individuals with domain expertise (e.g., behavioral scientists, physicianscientists, etc.) and individuals with technical experience (e.g., engineers, software developers) could each have a successful career pathway that aligns, but each is a bit different.

For the domain expertise track, developing experience in understanding the complexity of your problem domain is essential. This includes understanding the dynamics (i.e., change with respect to time) of your problem, how context influences it, and understanding individual differences, along with strong understanding on how to measure phenomena with appropriate fidelity to the concept. In addition, gaining insights on how modeling efforts work is essential. This does not necessarily mean that you need to be able to run modeling efforts yourself, or even fully code a controller, but you do need to understand how it works. The basic rule we use in our discussions is the "Are we assuming magic" test?

In brief, I do not feel comfortable using a method, or working through it, until I can talk through what it is doing and how its working produces an effect without ever resorting to "magic." For example, I have heard many people describing an effort such as "I'm going to use 'machine learning'" to determine the right time to provide support to someone. When I probe further on how machine learning would do this, the response comes down to something that sounds a lot like "It will do its magic and I'll get what I want." It is not magic; it is math. Someone who works on this type of effort needs to be comfortable understanding how to think mathematically and how to use that way of thinking to then unpack the basic steps a modeling effort is using to take data and produce the results it is producing.

For those more technically oriented, the career pathway, experience, and skills will differ. The mathematics of control systems engineering requires knowledge of differential equations and Laplace transforms; proficiency in system identification and predictive control will require background in digital signals and systems, statistics, and optimization. Introductory courses in control engineering are taught in nearly every engineering discipline. The work done by our group (see the references included in the presentation) describes a wide variety of problems in behavioral medicine that have been expressed with control engineering formulations; these should be helpful to anyone wishing to embark on this approach.

On one final note, some of my postdocs are getting much more comfortable with this work—including learning the basics in terms of modeling efforts, such as setting up mathematical models as simulation environments, in R. I mention this to highlight that, as with many things, career pathways will evolve, and eventually there may be more of a combined pathway for this type of work.

2. I have a question about absence of an objective daily measure analogous to "actual steps." We have self-reported proxy measures of the behavior, and infrequent objective measurement (e.g., every 6–-12 months). Is it possible to apply these methods?

You can use self-report; you do not need passively measured per say. The key caveat is your capacity to have people willing to fill out the measures over time. Advances in EMA, such as Stephen Intille and Genevieve Dunton's work on microEMA (both for using wristworn tracking and using more event-based triggering to reduce overall sampling), set up a valuable space for engaging in this type of work. Related to this, a follow-up question is the timescale of your measurement—if you can measure something more frequently, that is advantageous as it allows you to get more samples about the dynamics more quickly. Technically, it's possible to use slow timescales (e.g., weekly measurement). It will just take you more time with that person to really start to model the dynamics. These points are discussed in detail in our *Journal of Medical Internet Research (JMIR)* paper and, in particular, the section that highlights problems that are well-aligned with control systems engineering.

3. Do you incorporate any machine learning or deep learning in designing models?

In brief, yes, we do pay attention to advances in modeling approaches that grow out of computer science traditions, such as machine learning and deep learning. And we often seek to take advantage of whichever methods are most well-aligned to our problem (and also most parsimonious). We are exploring this in a U01 grant with MPIs of Donna Spruijt-Metz, Ben Marlin, and Pedja Klasnja. Within this group, we are exploring both machine learning-based, Bayesian neural network-based (i.e., the methodological grounding of deep learning), and dynamical modeling (i.e., the approach used in system ID/control systems engineering) approaches for understanding behavioral data. For us, the most important thing to do is to think through the history of a method and, by extension, the implications on its utility and definition of success from data.

For example, supervised and unsupervised machine learning are very valuable for identifying clusters within vector spaces, and the field has a great history of doing thoughtful and effective feature extraction from data. We are taking advantage of these tools for our current modeling efforts on our National Library of Medicine R01 focused on advancing multi-timescale controllers for just-in-time adaptive interventions. The issue we have noticed is that, often, those who have limited knowledge about the subtleties of data modeling efforts often ask for or assume the concept, term, or buzzword getting the most press (e.g., AI right now) is "the answer" to their problems. I do not mean to claim that the person who asked this question is falling into that trap but I wanted to raise this issue.

Returning to the earlier point, if you are interested in getting more acquainted with different modeling approaches, it is essential to start with a clear focus and understanding on the implied success of the methods to ensure what the modeling produces is actually aligned with the real-world requirements. I have a paper that is in press at *BMC Medicine* arguing for a small data commentary. In the last section of that paper, I provide a basic visual to further unpack this point.

4. Have you done any interventions with medications and behavioral support combined?

We have yet to implement experimentally an intervention that combines pharmacological and behavioral support components. However, Daniel and his students have developed models based on secondary analysis of data to illustrate how a control engineering approach would work for problems of this nature.

One reference is an intervention for treating fibromyalgia using low-dose naltrexone, published in *TBM:* Deshpande, S., D.E. Rivera, J.W. Younger, and N. N. Nandola, "A control systems engineering approach for adaptive behavioral interventions: illustration with a fibromyalgia intervention," *Translational Behavioral Medicine*, Vol 4, No. 3, pp. 275-289, 2014. An illustration for smoking cessation is presented in: Timms, K.P., D.E. Rivera, L.M. Collins, and M.E. Piper, "A dynamical systems approach to understand self-regulation in smoking cessation behavior change," *Nicotine and Tobacco Research*, Special Issue on New Methods for Advancing Research on Tobacco Dependence Using Ecological Momentary Assessments, 16 (Suppl 2): S159-S168, 2014.

Both problems are discussed in our chapter in the edited volume: Rivera, D.E., C.A. Martin, K.P. Timms, S. Deshpande, N. Nandola, and E.B. Hekler, "Control systems engineering for optimizing behavioral *mHealth* interventions," in Mobile Health: Sensors, Analytic Methods, and Applications, (J. Regh, S. Murphy, and S. Kumar, eds.), 455-493, 2017).

5. In order to do this, you need almost continuous monitoring of each of the subjects on multiple variables (and possibly even his/her environment); or do you use some form of sampling approach for that?

Not exactly. You do need to be able to measure one variable at sufficient frequency to model dynamics. Just like a boat monitoring a compass: if you have that, you can build a controller. It just would not be model-based. If you can gather more data than that one variable, you can potentially start using that additional information in model-based controllers. We go into some depth about these subtleties in the two core papers referenced in the talk, particularly the *JMIR* paper.

6. Is relevance for COT equally applicable to stopping an addictive behavior versus adopting a voluntary behavior?

This is an interesting and open question. From the perspective of the controller, they are equivalent... just different desired setpoints. From the perspective of the behavioral phenomenon, of course there are important differences and those differences could impact the tool. In particular, if a behavior occurs infrequently, then that will make the modeling and controller development efforts more difficult, simply because there is less data about variation available. That said, the more prior knowledge you have about dynamics (which is arguably the case for some key cessation targets, like smoking, because of the rich history of EMA work), the more it allows you to establish things that are "known" in the model—thus requiring less individualized learning (e.g., key locations are actions that are high-risk areas for a person to smoke). As you picked up, our focus has been on maintenance though. I think a deeper focus on cessation behaviors might reveal hidden assumptions that I might be unaware of.