Notes from Webinar 2017-09-19

Mark Alber (UC Riverside) - First Mark introduced the conference.

Mark A: Let's go around the table. What topics/questions are of most interest?

Andy McCulloch (UCSD) - Bridging multiple scales. The three track titles are the major topics of interest. Let's make sure we cover this well, not dilute them. Other ideas he has for discussion are more technical.

Danny Bluestein (Stony Brook) - multiscale mechanotransduction - e.g. initiation of platelet degradation, how mechanotransduction processes could be used to understand cell behavior beyond biochemical pathways. [note: unfortunately Danny had audio issues after this point.]

Darren Tyson (Vanderbilt): How signal transduction pathways control single cell fate in human cancers.

Denise Kirschner (Michigan) - want to focus on the patient aspect of this. What can we provide to clinicians and patients? What they are interested in (or need) might be different to what we're typically interested in or focused on! For example, do they want us to run virtual clinical trials to restrict the possible therapeutic space, or something else?

Gary An (Chicago) - focusing on how pathophysiology and physiology manifests at the clinical level. Interested in methods to use models to capture and understand clinical heterogeneity and the trajectories from physiology to pathophysiology.

Akanksha Bhargava - attending webinar out of interest, getting started in this area.

Jason Haugh (NC State) - directed cell migration in cutaneous wound healing. Signaling, regulation of cytoskeleton, and interaction with microenvironment/matrix. Like Danny, coupling of biochemistry and mechanics - e.g. cell crawling on matrix, interested in molecular-level regulation. Also interested in how to integrate data from microscopy/imaging to inform multi-scale models. - computer vision to extract information, machine learning, use to constrain model, and more.

Jennifer Linderman (Michigan) - want to go across many scales (time and length) - requires coarse graining and fine graining. Need to see more examples of this.

John Rice (?DHS) - how to communicate and translate work, get people who do not understand to get it.

Reinhard Laubenbacher (Jackson Lab) - interests have all been mentioned so far.

Tony Hunt (UCSF) - patients under stress, chronic and acute. To make progress, what requirements would we need to meet to make these models helpful?

Bill Cannon (Pacific Northwest National Lab) - [audio problems]

Dan Beard (Michigan) - How to summarize all this: (1) Methodology; (2) Applications; (3) How to communicate/reproducibility.

Denise K/Mark Alber - yes, let's assign talks along these lines

Start with (3) HOW TO COMMUNICATE WITH CLINICIANS

Mark A - asks for ideas for clinicians to invite (to get their perspective). We could have talks where people talk about their own experience of collaborating with clinicians.

Andrew McC - great idea, will send names of clinicians at UCSD

Denise K: let's ask clinicians who "get" modeling, e.g. Tim Buckman, Marty Glazer (sp?)

Andy McC: agree - clinicians actively involved.

Gary An: What do we want from/expect from clinicians? Questions from a vascular surgeon/cardiologist would be very different from a basic scientist. Very clinical questions, e.g. stent success question - they might have no idea about fluid dynamics. Intellectual curiosity might be more important than theoretical expertise among the clinicians. This is a part of asking: what do we want from the engagement?

John Rice - great to hear about this communication w/clinicians topic. Can we add into the structure a clinician being connected with a modeler? Some sort of registry to communicate and meet with each other.

Bill Cannon - Connection to clinic. Working on methodology: milliseconds to hours, better predictions.

Next discussed (2) SPECIFIC APPLICATIONS

Mark A.: What's the way to approach to arranging these talks? what's the appropriate balance?

Gary An: [puts on clinician hat] interesting to identify clinical contexts that people are looking at - what clinical data is useful or applicable? Some models might be fairly high-res, granular models with basic details.

Feilim: Can we hit all three things - methodology, application, translation/communication with clinician?

Bill Cannon: Trying to bridge all three is difficult. Many people may bridge two.

Mark: Maybe we can provide, in some talks, what worked/what didn't work in terms of connecting with clinicians. Early clinicians have clear targets, and typically it's not methodology. Talking about best practices would be helpful, we just want to coordinate among different talks at the conference.

Denise K: playing devil's advocate... usually at larger MSM meetings, we can't really get into nitty-gritty on multiscale modeling. Often need to stay high level. So, let's focus on multiscale approach to disease, let's communicate about the methods. How can we learn from people who do oncology, cardiovascular, etc? So if we choose one thing... either how we build models, or we do high level clinician reach out... it's in our interest (for a successful conference) to focus, focus, focus.

Mark A: The tracks are not really that separate - models of disease, treatment, patient specificity. Most of the people do all three. Mark mentioned case of patients with blood cancer where modeling the baseline was difficult, because people have diverse treatment history.

Gary An: Can you be more specific about the problem - can't get a cohort of untreated people, so can't make the original model calibration?

Mark A: Right. Overlap is through methodology... how to develop methodology across many applications.

Dan Beard: If we're not careful, it'll be like the annual MSM/IMAG meeting - everyone will just talk about their science. Dan gave an example of a recent invitation to talk at Mathworks. They rejected his abstract because it was a science abstract, not a methods/'how you do what you do' abstract. How about we do that - get everyone to rewrite their 'abstracts' to focus on learning/methodology talks.

Mark A: We could still have some talks on applications.

Andy McC: You don't know, until you try, what the problems and opportunities are until you try translating to the clinic. Would be interested to hear what kind of successes/stories we would get from people about what they encountered when they tried to translate.

Mark A: What about Track 2 - Feilim?
Feilim: describes Track 2 - application of multiscale models to therapeutics, to virtual clinical trials, etc.

Jason H.: Old school PK-PD modeling is still very entrenched. Multiscale modeling has an opportunity to enrich that, and many trainees are going into industry to do just that.

FMG: how about bringing industry people to discuss?

Gary An: Playing devil's advocate: Industry is pretty bad at coming up with drugs that do what we want. One of the reasons they are in difficulty is that drug development is stagnating, there's not enough innovation; absent a coherent strategy for how to do something different, they continue to do what they do. They use 'brute force' on the same old 'proxy models' for the most part. Trying to fix that problem/obstacle is what multiscale modeling is trying to do. If we want to facilitate the expansion of that (that's the therapeutic challenge), it's not about modeling the effect of a drug you already have. It's looking for new levers that could modulate diseases across their disease trajectory. The patient is not the same on day 0 and day 5 after chemo. The intervention that works on day 0 won't necessarily work on day 5. We should focus on this kind of problem...

John Rice (Homeland Security Science & Technology): Regarding the translational issue for multiscale modeling: has anyone tried to capture the landscape of 'to whom' we need to do the translation? Clinicians and Industry (commercial and regulatory). Three target audiences - very different. How do we communicate to the clinician, and how do they communicate to us? How to organize the meeting so that these different groups can feel that they can contribute.

Tony Hunt: from what Gary said: what Modeling & Simulation requirements would one need to have in place to accomplish this? When I show scenarios to clinicians, they ask further scenario questions. Answering those questions adds additional requirements to what we do. Building that

flexibility into the model is important. We need to be in a position to explore the new possibilities that arise when somebody sees our work.

SUMMARY

Grace Peng - Perhaps it's worth starting by asking "what questions we want the tracks to answer?"

Feilim -- let's not do our traditional research talks, but instead focus on how we develop models (methodology) so that the models can be used in a translational way (applications) to impact clinical care or therapeutic development, and how two-way interactions with clinicians enhance this work.

Mark A – we will distribute the notes for corrections/revisions/additions. Let's think about Dan's idea of collecting abstracts, coordinating talks with each other and possible rewriting them in a less traditional way.