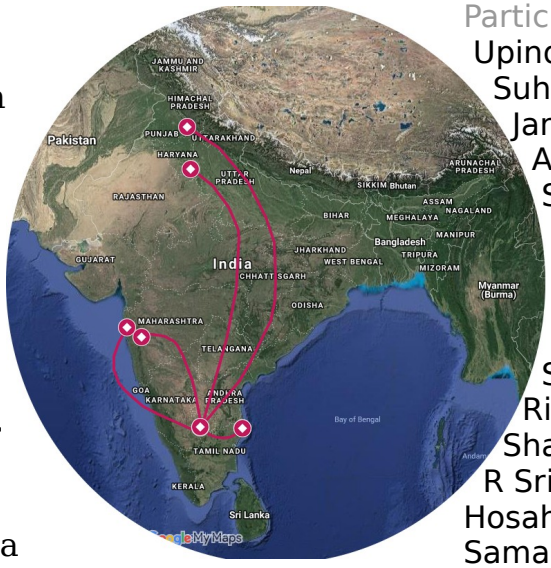
SANKET NEWSLETTER

Signaling And Neurophysiology Knowledge-resource for Experiments and Theory

Volume 1, Issue 9, Page 1 Date: 19 August 2019

Highlights...

- 2nd meeting with NSG team
- GsoC-2019
- Updates on FindSim
- Project discriptions on the SANKET portal
- "Signaling pathways under -lying memory and plasticity"
  - Prof. Upinder Singh Bhalla



Participating labs:
Upinder Bhalla, NCBS
Suhita Nadkarni, IISER Pune
James Chellaiah, JNCASR
Aditi Bhattacharya, InStem
Sayak Mukherjee, IBAB
Rohit Manchanda, IITB
Sourav Bannerjee, NBRC
Raghu Padinjat, NCBS
Deepak Nair, IISc
Srinivasa Chakravarthy, IITM
Rishikesh Narayanan, IISc
Shailesh Appukuttan, CNRS
R Srivatsan, IBAB
Hosahalli Subramanya, IBAB
Samarjit Bhattacharya, IISER Mohali

General Consortium News

➢ Another meeting was held with the NSG team on 6th August 2019. The NSG team has suggested that we use their REST API to run the FindSim experiment. We will need to get an "Umbrella" type account. Umbrella is a special use case in which multiple users can submit their jobs to NSG via one NSG account.

➢ The Google Summer of Code (GSoC) 2019 project is coming to an end. Chen has developed REST APIs for both running experiments and model optimization. Both of these APIs are planned to be set up on the NCBS local server to run small experiments in-house. The project code and documentation can be found on GitHub (https://github.com/surbhit21/GSoC-2019)

Updates on Websites

Nisha and Surbhit have collectively curated 217 experiments on biochemical signaling.

Content moderation workflow has been set-up on the FindSim web interface. Now logged-in users can maintain their own private list of experiments. Any new experiment that they create/upload will show up in their private list by default. The interface also has a public database list. The content moderation workflow allows users to push their experiments to the public list. This process requires users to submit their experiments for review by admin. Admin can then review the experiment and accept/reject the submission. The workflow design also has a feature to send an email to the admin when there is a submission.

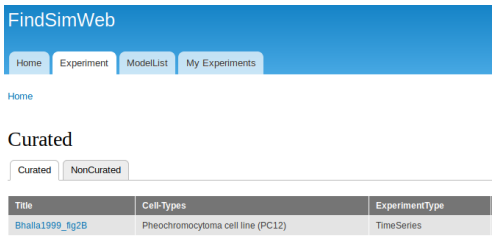


Figure 1: View of the public list under the menu item "Experiments".

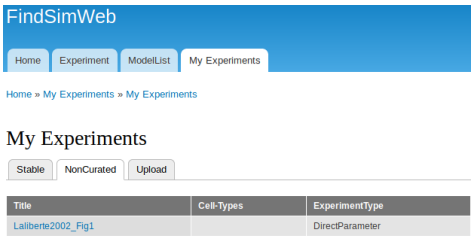


Figure 2: View of the private list under the menu item "My Experiments"

The projects page on the SANKET portal is updated. Description of on-going project of the consortium are uploaded on the portal along with the list of participating labs. There are currently three projects:

- *AUTism SIMulation (AutSim)*
- *Presynaptic processes*
- *Synaptic plasticity*

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Work from particitpating labs

I have been interested in the signaling pathways underlying memory and neuronal computation for over 20 years. We have taken the approach of developing quite detailed multiscale models to look at these functions, ideally with close reference to experimental observations. Since this effort has frequently required novel techniques, we have also invested heavily in tool development. This includes,

- simulators
  - GENESIS
  - MOOSE
- databases
  - DOQCS
- graphical interfaces
  - XODUS/GENESIS
  - Kinetikit
  - MOOGLI
  - MooseGUI

and many other tools. Over the years, our modeling work has examined many aspects of synaptic function. We have looked at induction of synaptic plasticity, memory storage, synaptic computation, the role of stochasticity, the role of trafficking, activity driven protein synthesis, and activity-driven transcriptional control. Several other projects including multiscale activity feedback and sequence selectivity have looked at larger scales of neural computation. A major item we have not been able to address is presynaptic signaling.

While we have gained many insights from these studies, there has been a lingering concern that we and other researchers in the area perceive, which is that the model development and parameterization process is very hand-crafted. While it is of course valuable to bring individual intuition and higher-level scientific understanding to model development, this can also lead to model bias and exclusion of key datasets. A closely related problem is that manual model development doesn't scale well. It is interesting that few published neuronal signaling models have over a hundred reactants - far fewer than the known players in the synapse.

We perceive the SANKET project as a way to transcend these barriers. On the computational side, it integrates many of the extant tools with a principled pipeline to develop models at scale. It most importantly has a structured way to incorporate experimental data. On the experimental side, it brings in a systematic and targeted large-scale data harvesting for the purposes of model parameterization. More broadly, these experimental datasets will explicitly and systematically define the extremely complex neuronal processes of our interest. For the SANKET consortium, even this vital model-experiment synergy is just the start of the journey. The most powerful attribute of good models is that they let you explore the system far beyond what one can do experimentally. We envision many such spin-offs from SANKET. Our particular interests are in Autism signaling, and in synaptic plasticity. We look forward to an exciting and sustained basic and applied biomedical science from the SANKET consortium.