NEWSLETTER

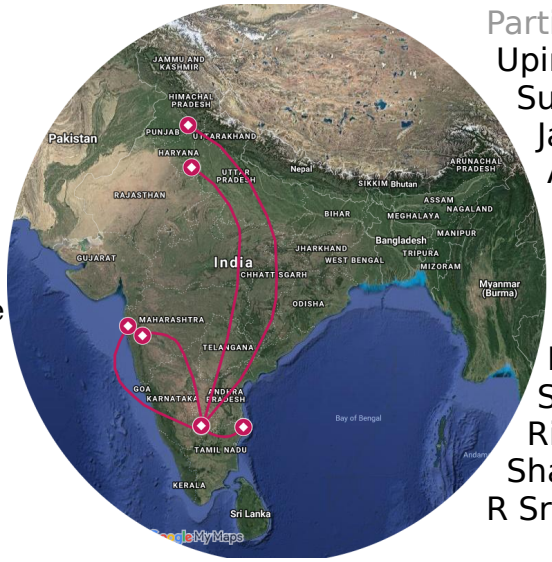
SANKET

Signaling And Neurophysiology Knowledge-resource for Experiments and Theory

Volume 1, Issue 5, Page 1 Date: 17 May 2019

Highlights...

- Consortium name: **SANKET**
- Updates on grants
- Consortium webpage up and running
- Outreach efforts to corporate sector
- "ER may promote reuse of hippocampal synapses."
  - Dr. Suhita Nadkarni



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

General Consortium News

The consortium name "SANKET" has been finalized as it encompasses the theme of the consortium framework.

The 2019 Research Award by SFARI, a Simon's Foundation initiative, will open in the fall of 2019. This award focuses on supporting investigation of key unresolved questions in autism.

Due to the strict eligiblity requirements, we were unable to apply for the Wellcome Trust/ DBT India Alliance "Team Science Grants".

Dr. Vinod Ugale has joined us as a two month summer research fellow. He would work on optimizing a part of the model and beta-testing FindSim interface.

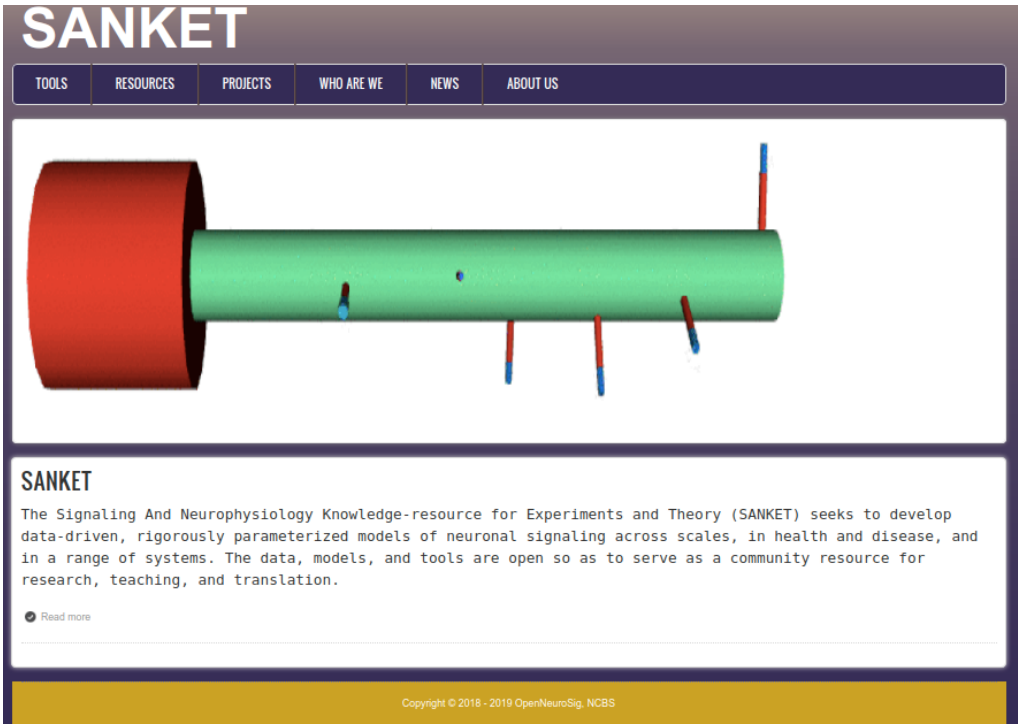
Dr. Suhita is trying to initiate corporate partnership discussions with Persistent Systems, Pune. Persistent Systems build softwares, tools and innovative solutions such as for crowdsourcing in biocuration.

Updates on Websites

The webpage for SANKET is up and running. The link is as given below:

http://sanket.ncbs.res.in/

We have listed out the Principal Investigators and Team Members in the "Who are We" section, the different Tools and Resources that are being used in their respective sections. The different Projects of the Consortium will be highlighted in the "Project" section and also newsletters and updates in the "News" sections.



We have 192 literature-curated experiments added to the FindSim database. These experiments are of different types such as Time Series, Dose Response, Stimuli Barchart and Direct Parameters.

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Work from particitpating labs

The Computational Neurobiology Laboratory at IISER, Pune led by Dr. Suhita Nadkarni is interested in understanding molecular signaling underlying synaptic transmission and plasticity and its implication to brain function. Aberrational sub-cellular signaling resulting in pathological states such as Alzheimer's Disease (AD) are of prime interest to the lab. They investigate causal relationships between modified molecular signaling associated with AD observed in diverse studies, spanning multiple scales from molecules, ion channels, networks to behavior. The changes in alpha rhythm observed in AD serves as a platform to investigate these relationships. They have shown that lower expression of the HCN channel, an observation associated with AD neurons, can adversely affect coherence and amplitude of the alpha rhythms and make it more susceptible to noise.

The hub of synaptic activity takes place in small volumes of synaptic terminals and is coordinated by small number of molecules. This makes it difficult to carry out precise measurements of geometrical arrangement between various molecular components and the dynamics of signal governed by them. One of the approaches has been to devise biophysically-detailed, morphologically realistic computational synaptic models that allow for 'In-Silico' experiments towards testable predictions.

Their recent work on hippocampal presynaptic terminal of Schaffer-Collaterals (SCs) has shown how distinct sources and sinks of Ca2+ differentially modulate short-term plasticity. Small changes in Ca2+ signal is seen to drastically modify the plasticity profile of the synapse, and this may be one of the earliest pathology in AD. Spurred by the curious observation that ER is sparsely distributed in dendritic spines, but over-represented in larger spines that are likely to have undergone activity dependent strengthening, they have investigated the role of Ca2+ release channels on ER in large spines of the SCs. Their reports suggest that the presence of ER modulates NMDAR-dependent plasticity in a graded manner that selectively enhances LTD induction. They propose that, "the ER may locally tune Ca2+-based plasticity, providing a braking mechanism to mitigate runaway strengthening at potentiated synapses. Our study suggests that ER in the spine may promote the re-use of hippocampal synapses with saturated strengths".

Recently, the definition of synapse as a mere junction between an axon and a dendrite has been revisited to include activity dependent participation of the neighboring astrocyte (Tripartite Synapse).

Hippocampal synapses are enveloped in varying degrees, by an astrocytic process. The lab investigated the implication of transmitter release by astrocytes on the plasticity repertoire at a tripartite synapse and have shown that the astrocyte processes close to the junction maintain their own transmitter release activity in close temporal coordination with the presynaptic terminal and aid synchronization of Ca2+ events across several hundred astrocytic processes. Apart from rapid release and uptake of neurotransmitter, crucial brain functions like episodic memory seem to rely on slow modulation of ambient chemicals in the extracellular space. The lab is also developing biophysical models of key signaling pathways mediated by acetylcholine and its modulatory effects on long-term plasticity.

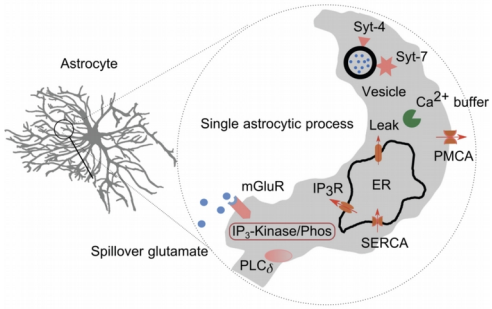

Fig.1. Molecular components in a fine astrocytic process that envelops a synapse and regulates calcium mediated transmitter release (Pillai et al.).

Dr. Suhita believes that propagation of wrong parameters whether in experiments or computational models can seriously misdirect scientific discovery process. She considers scholarly curated models, parameters and experimental protocols as one of the important contributions of the consortium. Also, the availability of the ready-to-use tools and documented computational code for models means that researchers can hit the ground running and spend their time optimally on science.