PHYSICAL CHEMISTRY COLLOQUIUM

Machine learning algorithms reveal the mechanisms encoded in the massive data from computational biophysics simulations of molecular machines that enable a cell's life processes.

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205 Gore Hall

The talk will present results of the lab's combined approach of experimental and computational investigation of structure and function that are obtained by students and postdocs. They usually select a project centered on a cell process or molecular machine and take it as far as possible in their investigation to enrich our knowledge and our understanding about the machines and their molecular mechanisms. The aim of the specific findings is to learn how to keep the machines working, and repair or support them when they are damaged by disease causing changes (e.g., mutations and molecular poisons). The mechanistic elements discovered in each study feed into the lab's parallel eKort to understand dysfunction in disease and develop designs for repair and modulation in the context of computational biophysics that is iteratively tested, verified, and refined by specific experimental collaborations.

A. Cellphysiologicalprocessesofinterest.

1. Thecell'sinteractionwithitsenvironment(CellcommunicationandSignaling)

• To maintain tissue integrity and function (e.g., the beating heart)

• To conduct information (e.g., brain neurons)

2. Uptakenutrientsandexpeltoxicsubstances(Transport)

3. Distributecellcomponentsto/fromthemembraneandamongitsinternal organelles (Intracellular traKic)

4. Maintaintheappropriatemembranebarrierthatwillpreserveitsintegritybutenable the activities (Lipid flipping/scrambling)

B. Thecorrespondingmolecularmachinesstudied.

1. Receptors(e.g.,Gproteincoupledreceptors-GPCRs)

2. Transporters(e.g.,theneurotransmittertransportersfordopamine(DAT),serotonin (SERT))

3. IntracellularCholesterolDistributors(e.g.,theSTARD4intracellularsterol transporter)

4. TheTMEM16familyofchannelsandlipidscramblases(e.g.,TMEM16F)

With a detailed mechanistic description of one or more of these classes of molecular machines the emphasis of the presentation will be on the acquisition of the massive simulation data and new methods of trajectory analysis developed in the lab to discover and quantify the structural and dynamic details of the mechanisms.

Our work on the other processes and molecular machines mentioned above will be open for discussion during the visit.

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