NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

BIOLOGY COLLOQUIUM

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Hosted by A/P Ganesh Anand

Towards comprehensive allosteric control of protein activity

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We developed a structure-based statistical mechanical model of allostery (SBSMMA), which allows one to detect causality and to evaluate energy of allosteric signalling as a result of ligand binding and/or mutations. Because of the omnipresence and critical role of global protein dynamics in allosteric mechanisms, we hypothesized reversibility of allosteric communication, according to which allosteric sites can be detected via the perturbation of the functional sites. Validating the "reversibility hypothesis", we also show that, in addition to known allosteric sites, perturbation of functional sites unravels rather extended protein regions that can be used for inducing and tuning allosteric communication and regulation. Defining generic characteristic of the allosteric effect of mutation, the modulation range, we build Allosteric Signaling Maps (ASMs), which can to complement already existing allosteric signaling and to design new elements of regulation. Considering pathological non-synonymous single nucleotide polymorphisms (nsSNPs), we found that some SNPs can work allosterically. We also observed that mutations of a number of residues in the protein may cause modulation comparable to those observed for known pathological SNPs, prompting us to introduce a notion of allosteric polymorphism. The AlloSigMA web-server and AlloMAPS database designed on the basis of SBSMMA will be also briefly discussed.

Igor Berezovsky studied physics in the Moscow Engineering Physics Institute (MSc, 1993) and obtained PhD in biophysics from the Moscow Institute of Physics and Technology (1997). After postdoctoral studies at the Weizmann Institute of Science (1999-2002) and Harvard University (2003-2006), Igor was a Group Leader at the Bergen Center for Computational Science, University of Bergen (Norway) before becoming a Principal Investigator at the Bioinformatics Institute and joining DBS/NUS as an Adjunct Associate Professor in 2014. Dr. Berezovsky is known for the discovery of closed loops as the basic units of protein structure and function, for studies of the evolution of protein function, for works on protein thermostability and molecular mechanisms of adapatation. Dr. Berezovsky's current interests include allosteric modulation of protein activity and biophysics of chromatin and epigenetic regulation.