Proteins are made of small building blocks (amino acids) that are covalently linked in a specific order/sequence. This specific sequence/arrangement plays a profound role in information processing in biology. For almost half a century now, we have known sequence determines the unique folded structure a protein must take to carry out its biological function (e.g. ability to carry cargo or speeding up important reactions etc). This central notion, however, appears to be at odds with a newly found class of proteins called Intrinsically Disordered Proteins (IDPs). IDPs lack unique folded structure and are constantly shuttling between different conformations. Despite their disordered and highly dynamic nature, in contrast to folded proteins, IDPs have specific conformational features and critical function, the details of which is hidden in their sequence. How do we decipher this code from the sequence? To answer this, we take a theoretical physics approach starting with a coarse-grain analytically tractable Hamiltonian that accounts for electrostatic interaction between amino acids that are also topologically correlated due to chain connectivity (covalent linkage). This formalism -- grounded on tools of classical field theory -- allows us to unmask several elegant mathematical formulae hidden in the sequence that describe conformational features of these disordered proteins. We will discuss how these relations reveal surprises in IDP conformation, yield rules of design and clues to evolution.

Rules of Physical Mathematics Govern Disordered Proteins

Professor Kingshuk Ghosh
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Abstract:
Proteins are made of small building blocks (amino acids) that are covalently linked in a specific order/sequence. This specific sequence/arrangement plays a profound role in information processing in biology. For almost half a century now, we have known sequence determines the unique folded structure a protein must take to carry out its biological function (e.g. ability to carry cargo or speeding up important reactions etc). This central notion, however, appears to be at odds with a newly found class of proteins called Intrinsically Disordered Proteins (IDPs). IDPs lack unique folded structure and are constantly shuttling between different conformations. Despite their disordered and highly dynamic nature, in contrast to folded proteins, IDPs have specific conformational features and critical function, the details of which is hidden in their sequence. How do we decipher this code from the sequence? To answer this, we take a theoretical physics approach starting with a coarse-grain analytically tractable Hamiltonian that accounts for electrostatic interaction between amino acids that are also topologically correlated due to chain connectivity (covalent linkage). This formalism -- grounded on tools of classical field theory -- allows us to unmask several elegant mathematical formulae hidden in the sequence that describe conformational features of these disordered proteins. We will discuss how these relations reveal surprises in IDP conformation, yield rules of design and clues to evolution.

Biography:
Kingshuk Ghosh is a Professor of Physics at the University of Denver. His group works on building theoretical models starting from coarse-grain Hamiltonian to describe several problems in physical biology with particular emphasis in proteins, and genes. Alongside, they also test their models and predictions against computer simulations and experiments, wherever possible. Ghosh received his Masters in Physics in India (IIT Kanpur) and PHD in Physics from the University of Massachusetts, Amherst. His PHD work focused on physics of charged polymers. Subsequently he worked as a Post doctoral scholar at the University of California San Francisco in the department of Pharmaceutical Chemistry. He joined DU as an Assistant Professor in 2008 and became a Professor in 2021. His research is supported by grants from NSF, NIH and Research Corporation for Science Advancement. He received NSF Career award and is a Cottrell Scholar.