

QUANTITATIVE AND SYSTEMS BIOLOGY COLLOQUIUM: Mapping from sequence to function in intrinsically disordered regions

<u>Date:</u> 2/23/2024

<u>Time:</u> 12:30 – 1:45 PM

Location: GRAN 135

Alex Holehouse Washington University in St. Louis

About The Speaker:

Alex received a combined bachelor's and master's degree in Biochemistry from the University of Oxford (UK) before completing a second master's degree in Computer Science at Imperial College London (UK). His graduate work (Washington University in St. Louis) focused on applying principles from polymer physics to understand how amino acid chemistry influences the conformational properties of disordered proteins. His subsequent postdoctoral work focused on decoding the molecular grammar of disordered regions that mediate the formation of biomolecular condensates through phase transitions. He started his independent group in the spring of 2020 (do not recommend), where his lab combines simulation, theory, deep learning, and experiments to uncover the general principles that allow intrinsically disordered proteins to play critical functional roles in the absence of a fixed 3D structure.

Abstract:

Intrinsically disordered protein regions (IDRs) are ubiquitous across all life kingdoms and play various essential cellular roles. Unlike folded domains, which are welldescribed by one or a small number of structurally similar states, IDRs exist in a collection of structurally distinct conformers known as an ensemble. While IDRs are 'disordered', they are not 'unstructured' – sequence-specific effects influence intraand inter-molecular interactions that ultimately dictate biological function. Here, we will discuss recent advances that combine chemical physics, informatics, and deep learning to infer biologically important functions directly from sequence. These approaches offer opportunities for understanding IDR evolution, interpretation of disease-associated variants of unknown significance, and rationally designing functional IDRs with specific functional properties.



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