

Abstract Submitted
for the MAR17 Meeting of
The American Physical Society

Random-phase-approximation theory for sequence-dependent behaviors of intrinsically disordered proteins in liquid-liquid phase separation¹ YI-HSUAN LIN, University of Toronto, JULIE FORMAN-KAY, The Hospital for Sick Children, HUE SUN CHAN, University of Toronto — The amino acid sequences of intrinsically disordered proteins (IDPs) have few hydrophobic but many more polar, charged, and aromatic residues. IDPs do not fold into a unique structure in isolation and can remain disordered while performing key biological functions. Recently, it was discovered that some IDPs can undergo liquid-liquid phase separation in an aqueous milieu. When in the cell, this process underlies membraneless organelles of condensed IDPs that often incorporate other biomolecules such as RNA and DNA. Without a membrane, these organelles can rapidly respond to environmental stimuli and play critical roles in many biological functions. Here, we present a polymer physics approach for this phenomenon by applying the random phase approximation (RPA) theory of polyampholytes to a collection of RNA helicase Ddx4 proteins with a charged and aromatic-enriched IDP region. Our theory predicts that Ddx4 phase behavior is significantly influenced by its specific charged sequence as well as pi-electron interactions associated with aromatic rings, consistent with recent experiments on wildtype and a charge-scrambled mutant of Ddx4. Our theory is applicable to any charged biopolymers and thus provides a general analytical framework for studying biological phase separation.

¹This material is based on the work supported by Canadian Cancer Society Research Institute grant no. 703477 and Canadian Institutes of Health Research grant MOP-84281

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Date submitted: 04 Nov 2016

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