# Yi-Hsuan Lin, PhD

## **EDUCATION**

Ph.D., Physics 2015

The Ohio State University, Ohio, USA

Thesis: The interplay between single-stranded binding proteins on RNA secondary structure

Supervisor: Ralf Bundschuh

B.Sc., Physics

University of Illinois at Urbana-Champaign, Illinois, USA

High Distinction in Physics

(National Taiwan University, Taiwan, 2005-2007, transferred)

#### RESEARCH SUMMARY\_

Theoretical and computational physics, chemistry, and biology. Focusing on polymer physics theories, protein molecular mechanisms, biopolymer phase separation, and RNA-protein interaction. 11 invited talks, 15 papers, 806 citations, h-index = 11 (Jun 2021)

## ACADEMIC POSITIONS

Jul 2015 – Jul 2021

Department of Biochemistry, University of Toronto

Molecular Medicine, Hospital for Sick Children, Toronto, ON, Canada

- Developing statistical physics theories for the "sequence specificity" in biological liquid-liquid phase separation
- · Collaborating with experimentalists and computational biologists to test the above-mentioned physics theory
- Develop Monte Carlo simulation programs from scratch for modelling protein assemblies
- Published 13 peer-reviewed papers in theoretical/computational physics, chemistry, and biology
- Supervised and mentored over 4 junior scientists (graduate students and trainees)

Project: Theories for sequence-dependent phase behaviors of biomolecular condensates

Supervisors: Hue Sun Chan & Julie D. Forman-Kay

#### **Graduate Research Associate**

Aug 2012 - May 2015

Department of Physics, The Ohio State University

- · Developed statistical physics theory for RNA secondary structure and RNA-protein binding systems
- Developed Monte Carlo simulation programs for investigating RNA membrane translocation
- Developed solvable Markov system describing DNA-repair process
- Established theoretical framework for online RNA-protein binding predictor RBPBind
- Published 2 first-author papers in theoretical physics and bioinformatics

Project: Biophysics of interactions between proteins and nucleic acids

Supervisor: Ralf Bundschuh

#### **Graduate Research Associate**

Aug 2011 - May 2012

Department of Physics, The Ohio State University

• Applied the Noziéres-Schmitt-Rink method to calculate the critical temperature in BEC-BCS crossover

Project: BEC-BCS crossover in cold-atomic systems

Supervisor: Tin-Lun Ho

#### **PUBLICATIONS**

- 15. Wessén J, Pal T, Das S, **Lin Y-H**, and Chan HS (2021) A simple explicit-solvent model of polyampholyte phase behaviors and its ramifications for dielectric effects in biomolecular condensates. *J Phys Chem B* **125** 4337–4358 (selected supplementary cover)
- Das S, Lin Y-H, Vernon RM, Forman-Kay JD, and Chan HS (2020) Comparative roles of charge, π, and hydrophobic interactions in sequence-dependent phase separation of intrinsically disordered proteins. *Proc Natl Acad* Sci USA 117 28795–28805
- 13. Amin AN\*, **Lin Y-H**\*, Das S, and Chan HS (2020) Analytical theory for sequence-specific binary fuzzy complexes of charged intrinsically disordered proteins. *J Phys Chem B* **124** 6709–6720 (\*equal contribution; selected supplementary cover)
- 12. **Lin Y-H**, Brady JP, Chan HS, and Ghosh K (2020) A unified analytical theory of heteropolymers for sequence-specific phase behaviors of polyelectrolytes and polyampholytes. *J Chem Phys* **152** 045102
- 11. Cinar H, Oliva R, **Lin Y-H**, Chen X, Zhang M, Chan HS, and Winter RHA (2020) Pressure sensitivity of SynGAP/PSD-95 condensates as a model for postsynaptic densities and its biophysical and neurological ramifications. *Chem Eur J* **26** 11024–11031 (cover feature)
- Das S, Amin AN, Lin Y-H, and Chan HS (2018) Coarse-grained residue-based models of disordered protein condensates: utility and limitations of simple charge pattern parameters. Phys Chem Chem Phys 20 28558–28574
- 9. **Lin Y-H**, Forman-Kay JD, and Chan HS (2018) Theories for sequence-dependent phase behaviors of biomolecular condensates. *Biochemistry* **57** 2499–2508
- 8. Das S, Eisen A, **Lin Y-H**, and Chan HS (2018) A lattice model of charge-pattern-dependent polyampholyte phase separation. *J Phys Chem B* **122** 5418–5431
- 7. **Lin Y-H**, Brady JP, Forman-Kay JD, and Chan HS (2017) Charge pattern matching as a "fuzzy" mode of molecular recognition for the functional phase separations of intrinsically disordered proteins. *New J Phys* **19** 115003
- Brady JP, Farber PJ, Sekhar A, Lin Y-H, Huang R, Bah A, Nott TJ, Chan HS, Baldwin AJ, Forman-Kay JD, and Kay LE (2017) Structural and hydrodynamic properties of an intrinsically disordered region of a germ-cell specific protein upon phase separation. *Proc Natl Acad Sci USA* 114 E8194–E8203
- 5. **Lin Y-H** and Chan HS (2017) Phase separation and single-chain compactness of charged disordered proteins are strongly correlated. *Biophys J* **112** 2043–2046
- Lin Y-H, Song J,Forman-Kay JD, and Chan HS (2017) Random-phase-approximation theory for sequence-dependent, biologically functional liquid-liquid phase separation of intrinsically disordered proteins. J Mol Lia 228 176–193
- 3. Lin Y-H, Forman-Kay JD, and Chan HS (2016) Sequence-specific polyampholyte phase separation in membraneless organelles. *Phys Rev Lett* **117** 178101
- 2. **Lin Y-H** and Bundschuh R (2015) RNA structure generates natural cooperativity between single-stranded RNA binding proteins targeting 5' and 3'UTRs. *Nucleic Acids Res* **43** 1160–1169
- 1. **Lin Y-H** and Bundschuh R (2013) Interplay between single-stranded binding proteins on RNA secondary structure. *Phys Rev E* **88** 052707

# **Working Papers**

- Lin Y-H, Wu H, Zhang M, and Chan HS (2021) Chemical theory for exploring the correlation between heteromultimeric protein complex formation and liquid-liquid phase separation (in preparation)
- Lin Y-H, Wessén J, Pal T, Das S, and Chan HS (2021) Numerical techniques for applications of analytical theories to sequence-dependent phase separations of intrinsically disordered proteins (submitted)
- Gaither J, **Lin Y-H**, and Bundschuh R (2016) RBPBind: Quantitative prediction of Protein-RNA Interactions. Preprint: arXiv:1611.01245

## HONORS AND AWARDS

| Postdoctoral Award, Intrinsically Disordered Protein Subgroup, Biophysical Society (USA)      | 2019 |
|---|------|
| Connell Award for Postdoctoral Fellow, Department of Biochemistry, University of Toronto      | 2018 |
| Dean's List, College of Liberal Arts and Sciences, University of Illinois at Urbana-Champaign | 2007 |
| Presidential Award, Department of Physics, National Taiwan University                         | 2007 |
| Gold Medal, The 36 <sup>th</sup> International Physics Olympiad                               | 2005 |

# **Scholarships and Travel Awards**

| <b>Travel Award</b> , Biophysical Society 63 <sup>rd</sup> Annual Meeting (USA) | 2019      |
|---|-----------|
| Scholarship for Study Abroad, Graduate Study, Taiwan Ministry of Education      | 2009-2013 |
| Scholarship for Study Abroad, Undergraduate Study, Taiwan Ministry of Education | 2007-2009 |

#### PROFESSIONAL SERVICE

- Poster judge for divisional student poster competition for the Division of Physics in Medicine and Biology at the Canadian Association of Physicists Congress 2021
- Co-chair of "Using Polymer Sequence to Control Material Properties" session at the American Physical Society March Meeting 2019 (with Dr. Lisa Hall at The Ohio State University)

## INDUSTRIAL EXPERIENCE

#### Molecular Modelling Lead

Jan 2021 – present

HTuO Biosciences, Vancouver, BC, Canada

- · Establishing the physics principles of a new molecular dynamics force field for pharmaceutical applications
- · Developing a molecular dynamics simulation software with the above-mentioned new force field embedded
- · Incorporating machine learning to parametrize force fields and optimize their simulation performance
- · Implementing mathematical physics to validate stability of various simulation methods

Data Scientist Jun 2020 – Oct 2020

Sustainability. Exchange, Toronto, ON, Canada

• Applied supervised machine learning algorithms and Bayesian statistics to build models for time series forecasting of environmental, social and corporate governance (ESG) financial data.

Science Advisor Nov 2019 – Dec 2019

StemCellerant, Remotely

 Providing consultation on biotech application and business development of new stem cell differentiation technology and systems biology.

#### MENTORING EXPERIENCE

#### Department of Biochemistry, University of Toronto

Designed research projects, provided instructions on math, physics, and computational methods, and manuscript writing

Alan Amin, Research Undergraduate Student

Sep 2017 - Jun 2019

Project: Cluster-expansion theory for sequence-specific IDP-IDP interactions

Adam Eisen, Research Undergraduate Student

Jun 2016 - Aug 2016

Project: Monte Carlo simulation of lattice models for polyampholytes

#### Molecular Medicine, The Hospital for Sick Children

Provided instructions on thesis writing and defense preparation

Shuo-Chin Yen, Masters Student

Jul 2018 - Sep 2018

Thesis: Characterization of the dependence of Src:ND2 binding on phosphorylation and intramolecular Src interactions

## TEACHING EXPERIENCE

#### Lecturer, Center for Study Oversee Inc.

2020

Taught undergraduate level online courses in biology and physics, designing homework and exams and grading standards, and providing recitation sessions upon request

 $\begin{array}{c} \text{Introduction to Physics } (\sim \! 10 \text{ students}) & \text{Summer 2020} \\ \text{Introduction to Biology } (\sim \! 10 \text{ students}) & \text{Summer 2020} \end{array}$ 

#### Teaching Associate, Department of Physics, The Ohio State University

2009 - 2011

Taught regular homework review sessions and recitations before exams, provided office hours for students' needs of extra learning helps, and graded homework

| Physics 836, Electromagnetic Field Theory III (Graduate Level, $\sim$ 70 students ) | Spring 2011 |
|---|-------------|
| Physics 835, Electromagnetic Field Theory II (Graduate Level, ~70 students)         | Winter 2011 |
| Physics 834, Electromagnetic Field Theory I (Graduate Level, $\sim$ 70 students)    | Autumn 2010 |
| Physics 730, Methods of Theoretical Physics ( $\sim$ 20 students)                   | Spring 2010 |
| Physics 664, Theoretical Mechanics (~40 students)                                   | Spring 2010 |
| Physics 622, Statistical Physics II ( $\sim$ 40 students)                           | Winter 2010 |
| Physics 656, Fields and Waves II (~40 students)                                     | Winter 2010 |
| Physics 621, Statistical Physics I (~40 students)                                   | Autumn 2009 |

#### **PRESENTATIONS**

#### **Invited Seminars and Colloquia**

- 11. Introduction to machine learning and its application in biophysics and computational biology, Division of Physics in Medicine and Biology (DPMB) 101 Lecture, Canadian Association of Physicists Congress, Online, **Jun 7, 2021**
- 10. Polymer field theory for sequence-specific intracellular phase separation of biological heteropolymers, Department of Physics, University of Manitoba, Winnipeg, MB, Canada, **Nov 25, 2020**
- 9. Polymer theory for the sequence-specific phase separation behaviors of charged intrinsically disordered proteins, Intrinsically Disordered Protein Subgroup Postdoctoral Award Talk, Biophysical Society 63<sup>rd</sup> Annual Meeting, Baltimore, MD, USA, **Mar 2, 2019**
- 8. Theories and simulations for sequence-specific behaviors of intrinsically disordered proteins in liquid-liquid phase separation, Institute of Chemistry, Chinese Academy of Sciences, Beijing, China PRC, Oct 16, 2018
- 7. Theories and simulations for sequence-specific behaviors of intrinsically disordered proteins in liquid-liquid phase separation, Center for Quantitative Biology, Peking University, Beijing, China PRC, Oct 15, 2018
- 6. Theories and simulations for liquid-liquid phase separation in biology, Institute of Biophysics, Central China Normal University, Wuhan, China PRC, Oct 12, 2018
- Sequence-specific theory for intrinsically disordered proteins in liquid-liquid phase separation (Connell Award for Postdoctoral Fellow), Department of Biochemistry Retreat of University of Toronto, Geneva Park, Orillia, ON, Canada, Oct 2, 2018
- 4. Sequence-specific behaviors of charged intrinsically disordered proteins in liquid-liquid phase separation, Protein Folding Consortium, University of California, Berkeley, CA, USA, Jun 3, 2017
- 3. The interplay between single-stranded binding proteins on RNA secondary structures, Molecular Structure and Function, The Hospital for Sick Children, Toronto, ON, Canada, Mar 12, 2015
- 2. The interplay between single-stranded binding proteins on RNA secondary structures, Center for Theoretical Biophysics, Rice University, Houston, TX, USA, Oct 27, 2014
- 1. The interplay between single-stranded binding proteins on RNA secondary structures, National Center for Theoretical Sciences, National Cheng Kung University, Tainan, Taiwan ROC, Jun 9, 2014

#### **Contributed Talks**

- 7. Random phase approximation and renormalized Gaussian chain for charged hetero-biopolymers and their sequence-specific phase behavior, Canadian Association of Physicists Congress, Burnaby, BC, Canada, **Jun 4, 2019**
- 6. Cluster-expansion theory for sequence-specific "fuzzy" interaction between pairs of intrinsically disordered proteins, American Physical Society March Meeting, Boston, MA, USA, Mar 8, 2019
- 5. Sequence-specific random-phase-approximation theory for polyampholytic intrinsically disordered proteins in liquid-liquid phase separation, Canadian Association of Physicists Congress, Halifax, NS, Canada, **Jun 14, 2018**
- 4. Sequence-specific polymer theory for charged intrinsically disordered proteins in liquid-liquid phase separation, Chemical Biophysics Symposium at University of Toronto, Toronto, ON, Canada, May 4, 2018
- 3. Random-phase-approximation theory for sequence-dependent behaviors of intrinsically disordered proteins in liquid-liquid phase separation, American Physical Society March Meeting, New Orleans, LA, USA, Mar 15, 2017
- 2. Loop cost in RNA secondary structures and the long-range cooperativity between RNA-binding proteins, American Physical Society March Meeting, Denver, CO, USA, Mar 5, 2014
- 1. The interplay between single-stranded binding proteins on RNA secondary structures, American Physical Society March Meeting, Baltimore, MD, USA, Mar 22, 2013

#### **Poster Presentations**

| 10. | Biophysical Society of Canada $5^{ m th}$ Annual Meeting, Mississauga, ON, Canada    | May 28-31, 2019 |
|-----|--|-----------------|
| 9.  | Biophysical Society 63 <sup>rd</sup> Annual Meeting, Baltimore, MD, USA              | Mar 2-6, 2019   |
| 8.  | Gordon Research Conference – Polymer Physics, South Hadley, MA, USA                  | Jul 21-27, 2018 |
| 7.  | Protein Folding Consortium, Ann Arbor, MI, USA                                       | Jun 8-10, 2018  |
| 6.  | Gordon Research Conference – Protein, Holderness, NH, USA                            | Jun 18-23, 2017 |
| 5.  | Biophysical Society of Canada $3^{\mathrm{rd}}$ Annual Meeting, Montréal, QC, Canada | May 24–26, 2017 |
| 4.  | Protein Folding Consortium, St. Louis, MO, USA                                       | Jun 9-12, 2016  |
| 3.  | Rustbelt RNA Meeting, Pittsburgh, PA, USA  | Oct 17–18, 2014 |
| 2.  | Soft Matter Science Summer School, Mittelwihr, France                                | Jul 6-11, 2014  |
| 1.  | Rustbelt RNA Meeting, Cleveland, OH, USA   | Oct 18–19, 2013 |

#### SKILLS

- Math/Stat: Numerical Analysis, Bayesian Statistics, Multivariate Linear/Nonlinear Optimization, Linear Algebra, Multivariable Calculus, Stochastic Calculus, Partial Differential Equation, Complex Analysis
- Modelings: Theoretical Physics, Molecular Biophysics, Bioinformatics, Monte Carlo Simulation, Molecular Dynamics Simulation, Data-Driven Statistical Modeling, Machine Learning, Deep Learning, Data Visualization, Principal Component Analysis, Time Series Forecasting
- Programming: Python, Matlab/Octave, C/C++, Mathematica, Julia, SQL
- Tools: Numpy, Scipy, Pandas, Matplotlib, Scikit-Learn, PyMC, SQLite, MPI, PyCharm, Git

# **CERTIFICATES**

Financial Engineering and Risk Management I & II (Coursera.org/Columbia Univ) Introduction to Deep Learning with Honors (Coursera.org/HSE Univ) Bayesian Methods for Machine Learning with Honors (Coursera.org/HSE Univ) Practical Reinforcement Learning with Honors (Coursera.org/HSE Univ)