NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Elston, Timothy

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-4601-2117

Position Title: Professor of Pharmacology

Organization and Location: University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Los Alamos National Laboratory, Los Alamos, NM, United States	Postdoctoral Fellow	08/1993	07/1996	Biophyiscs
Georgia Institute of Technology , Atlanta, GA, USA	DOCTOR OF PHILOSOPHY	09/1988	12/1993	Physics
Georgia Institute of Technology , Atlanta , GA, USA	BACHELOR OF SCIENCE	09/1985	06/1988	Physics

Appointments and Positions

2008 - present	Professor of Pharmacology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States
2018 - present	Co-Director, Computational Medicine Program, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States
2005 - 2019	Director, Curriculum in Bioinformatics and Computational Biology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States
2005 - 2008	Associate Professor of Pharmacology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States
2002 - 2005	Associate Professor of Mathematics, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States
2001 - 2002	Director, Biomathematics Graduate Program, North Carolina State University, Raleigh , North Carolina, United States
1998 - 2002	Assistant Professor of Statistics, North Carolina State University, Raleigh , North Carolina, United States
1997 - 1998	Assistant Professor of Physics, DePaul University, Chicago, Illinois, United States
1996 - 1997	Visiting Scholar, University of California at Berkeley, Berkeley, California, United States
1994 - 1997	Postdoctoral Fellow, The Center for Nonlinear Science, Los Alamos National Laboratory, Los Alamos, New Mexico, United States

Products

Products Closely Related to the Proposed Project

1. Guan K, Curtis ER, Lew DJ, Elston TC. Particle-based simulations reveal two positive feedback loops allow relocation and stabilization of the polarity site during yeast mating. PLoS Comput Biol. 2023 Oct;19(10):e1011523. PubMed Central PMCID: PMC10569529.
2. Crocker AW, Petrucco CA, Guan K, Wirshing ACE, Ekena JL, Lew DJ, Elston TC, Gladfelter AS. Negative feedback equalizes polarity sites in a multi-budding yeast. Curr Biol. 2025 Jul 7;35(13):3022-3034.e4. PubMed Central PMCID: PMC12237600.
3. Herron JC, Hu S, Liu B, Watanabe T, Hahn KM, Elston TC. Spatial models of pattern formation during phagocytosis. PLoS Comput Biol. 2022 Oct;18(10):e1010092. PubMed Central PMCID: PMC9560619.
4. Herron JC, Hu S, Watanabe T, Nogueira AT, Liu B, Kern ME, Aaron J, Taylor A, Pablo M, Chew TL, Elston TC, Hahn KM. Actin nano-architecture of phagocytic podosomes. Nat Commun. 2022 Jul 27;13(1):4363. PubMed Central PMCID: PMC9329332.

5. Liu B, Stone OJ, Pablo M, Herron JC, Nogueira AT, Dagliyan O, Grimm JB, Lavis LD, Elston TC, Hahn KM. Biosensors based on peptide exposure show single molecule conformations in live cells. Cell. 2021 Oct 28;184(22):5670-5685.e23. PubMed Central PMCID: PMC8556369.

Other Significant Products Highlighting Contributions to Science

1. Howell AS, Jin M, Wu CF, Zyla TR, Elston TC, Lew DJ. Negative feedback enhances robustness in the yeast polarity establishment circuit. Cell. 2012 Apr 13;149(2):322-33. PubMed Central PMCID: PMC3680131.
2. Elston T, Wang H, Oster G. Energy transduction in ATP synthase. Nature. 1998 Jan 29;391(6666):510-3. PubMed PMID: 9461222.
3. Guido NJ, Wang X, Adalsteinsson D, McMillen D, Hasty J, Cantor CR, Elston TC, Collins JJ. A bottom-up approach to gene regulation. Nature. 2006 Feb 16;439(7078):856-60. PubMed PMID: 16482159.
4. Kepler TB, Elston TC. Stochasticity in transcriptional regulation: origins, consequences, and mathematical representations. Biophys J. 2001 Dec;81(6):3116-36. PubMed Central PMCID: PMC1301773.
5. Behar M, Dohlman HG, Elston TC. Kinetic insulation as an effective mechanism for achieving pathway specificity in intracellular signaling networks. Proc Natl Acad Sci U S A. 2007 Oct 9;104(41):16146-51. PubMed Central PMCID: PMC2042176.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

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NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Elston, Timothy

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-4601-2117

Position Title: Professor of Pharmacology

Organization and Location: University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States

Personal Statement

Research.

I received my graduate training in physics with an emphasis on statistical physics and nonlinear dynamics. As a postdoctoral researcher, I became interested in applying tools from these fields to problems in biophysics and cell biology. Currently, my lab integrates computational approaches, including mathematical modeling and quantitative image analysis, with experimental investigations to understand complex cellular behavior. We are particularly interested in understanding network motifs that regulate the spatiotemporal dynamics of cell signaling pathways. We also develop novel computational techniques for quantitative analyses of live-cell images, single molecule studies and simulating spatiotemporal models of signaling systems. Current projects in the lab focus on phagocytosis, cell migration, polarity establishment and gradient sensing. My lab also is involved in multiple collaborative projects to investigate signaling pathways in various physiological contexts and their dysregulation in human disease.

Training and Mentorship.

I am fully committed to serving as a co-mentor for Dr. Pengning Xu during his K99/R00 Pathway to Independence Award. Pengning and I will have weekly one-on-one meetings, and he will attend my lab meetings. I have always had a strong commitment to graduate student and postdoctoral training. I have completed the Mentor Training for Biomedical Researchers course run by the UNC Office of Graduate Education. I have mentored 18 graduate students and 14 postdoctoral researchers; all of whom have gone on to successful careers using the skills they acquired at UNC-CH. My philosophy is to provide guidance tailored to the specific needs and career goals of the trainee and to encourage the development of scientific independence. Dr. Klaus Hahn and I have collaborated for over 15 years. During that time, we have a proven track record for providing interdisciplinary training to postdoctoral fellows and graduate students. Our former trainees hold faculty position at research universities and research positions in pharmaceutical and biotech companies. Before moving to UNC-CH, I served as the Director of the Graduate Program in Biomathematics at North Carolina State University. From 2005-2019, I served as Director of the Curriculum in Bioinformatics and Computational Biology.

Service.

Throughout my career I have made significant contributions to the research community both within and outside the University of North Carolina at Chapel Hill. At UNC-CH, I am currently the Co-Director of the Computational Medicine Program and serve as Chair of the Research Computing Advisory Committee and the Appointments, Tenure and Promotion Committee for Full Professors for the School of Medicine. I was Director of the Curriculum in Bioinformatics and Computational Biology from 2005-2019. Outside of the university, I have served as a standing member of the NIH Modeling and Analysis of Biological Systems (MABS) Study Section and have served on multiple NSF review panels. From 2011-2021 I was on the Board of Reviewing Editors for Science Magazine.

Honors

2018	Jeffrey Houpt Distinguished Investigator, University of North Carolina at Chapel Hill

Contributions to Science

1. **Polarity establishment and gradient sensing**. A current interest of my lab is to understand the mechanisms used by cells to polarize and detect gradient chemical gradients. In collaboration with Dr. Amy Gladfelter, we combined mathematical modeling with experimental analysis to understand the mechanisms that allow multiple polarity sites to form in multi-budding yeast (Crocker et al, 2025). In collaboration with Dr. Daniel Lew, using a similar multidisciplinary approach we demonstrated how ratiometric sensing improves yeast's ability to detect gradients and how negative feedback in the polarity signaling pathway of yeast ensures robust polarization in the presence of fluctuations in protein abundance (Howell et al, 2012). Finally, we have used particle-based simulations to determine the role of feedback regulation in polarity establishment (Guan et al, 2023).

2. **Signal transduction**. My lab develops models of intracellular signaling pathways to understand how cells are able to sense and respond to their environment. Using both theoretical and computational techniques we have determined how molecular switches determine the response properties of signaling pathways, how kinetic insulation can be used as mechanism for pathway specificity (Behar et al, 2007) and demonstrated how dose-to-duration encoding can be used to transmit information. Our investigations also use model-driven experimental design to identify feedback loops in signaling pathways and distinguish competing models.

3. **Image analysis and single molecule methods**. My lab develops computational methods for performing quantitative image analysis at the single cell and single molecule level. This work is primarily carried out in collaboration with Dr. Klaus Hahn (Liu et al, 2021, Herron et al, Herron et al, 2022). At the single cell level, we developed open source MATLAB applications that allow simultaneous, automated tracking and analysis of dynamic changes in cell shape. We have also used deep learning to enable structured illumination microscopy using low light levels and enhanced imaging speed. Currently, we are interested in developing computational approaches for the analysis of single molecule biosensors.

4. **Noise in gene regulation**. After starting my independent academic career, I became interested in the origins and consequences of noise in gene expression and signaling pathways. Together with Dr. Tom Kepler, we developed some of the initial theories into how molecular level noise can qualitatively change the dynamical behavior of simple gene networks (Kepler and Elston, 2001). In collaboration with Dr. Jim Collins, my lab developed predictive stochastic models for gene expression that were then validated using engineered gene networks in E. coli (Guido et al, 2006). Recently, we developed a stochastic model for gene regulation by the Human Papillomavirus early promoter and used the model to understand how a combination of positive and negative feedback regulation generates stochastic bursts of gene expression.

5. **Motor proteins**. As a postdoctoral fellow working with Dr. George Oster, I became interested in the mechanisms used by motor proteins to convert chemical energy into directed motion. My work during this time focused on energy transduction in the rotary motors ATP synthase (Elston et al, 1998) and the bacterial flagellar motor. These studies demonstrated how linear proton fluxes could be converted into rotary motion. More recently, I have worked on force generation by the motor protein dynein. This work developed the first computational model for two-headed dynein that couples conformational changes of the motor's subunits to the biochemical steps involved in ATP hydrolysis. I have also developed fast and efficient numerical methods for simulating stochastic models of motor proteins.

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