Biographical Sketch

Name: John J. Tyson	Title: University Distinguished Professor
Email: tyson@vt.edu	Department: Biological Sciences

Education/Training:

Institution/Location	Degree/Postdoc	Year(s)	Field of Study
Wheaton College, Illinois	B.S.	1969	Chemistry
University of Chicago	Ph.D.	1973	Chemical Physics
Max Planck Inst Biophys Chem	Postdoc	1974	Biophysical Chemistry
Univ Innsbruck	Postdoc	1976-77	Biochemistry & Cell Biology

Personal Statement:

My expertise is building deterministic and stochastic models of the molecular control systems that underlie various aspects of cell physiology, including the cell cycle control system in yeast, drug sensitivity and resistance in breast cancer cells, circadian rhythms, cell differentiation in the immune system, stem cell dynamics in the shoot apical meristem of plants, and the growth, division and differentiation of alphaproteobacteria. My group builds comprehensive, accurate, predictive models of these control systems and uses these models to understand the observations and data collected by our experimental colleagues. Deterministic models are formulated in terms of nonlinear differential equations describing the temporal dynamics of the reaction network, and, when appropriate, including spatial transport and diffusion of molecules. Stochastic models are formulated in terms of elementary chemical reactions and transport processes, simulated by Gillespie's stochastic simulation algorithm, or, for more complex networks, by chemical Langevin equations.

Selected Publications:

B. Novak & J.J. Tyson, "Numerical analysis of a comprehensive model of M-phase control in *Xenopus* oocyte extracts and intact embryos," J. Cell Sci. 106:1153-1168 (1993). http://www.ncbi.nlm.nih.gov/pubmed/8126097

J.J. Tyson, K. Chen & B. Novak, "Network dynamics and cell physiology," *Nature Rev. Mol. Cell Biol.* 2:908-916 (2001). http://www.ncbi.nlm.nih.gov/pubmed/11733770

W. Sha, J. Moore, K. Chen, A.D. Lassaletta, C-S. Yi, J.J. Tyson & J.C. Sible, "Hysteresis drives cell-cycle transitions in *Xenopus laevis* egg extracts," *Proc. Natn. Acad. Sci. USA* **100**:975-980 (2003). http://www.ncbi.nlm.nih.gov/pubmed/12509509

J.J. Tyson, K.C. Chen & B. Novak, "Sniffers, buzzers, toggles and blinkers: dynamics of regulatory and signaling pathways in the cell," *Curr. Opin. Cell Biol.* **15**:221-231 (2003). http://www.ncbi.nlm.nih.gov/pubmed/12648679

K.C. Chen, L. Calzone, A. Csikasz-Nagy, F.R. Cross, B. Novak & J.J. Tyson, "Integrative analysis of cell cycle control in budding yeast," *Mol. Biol. Cell* **15**:3841-3862 (2004). http://www.ncbi.nlm.nih.gov/pubmed/15169868

B. Novak, J.J. Tyson, B. Gyorffy & A. Csikasz-Nagy, "Irreversible cell-cycle transitions are due to systems-level feedback," *Nat. Cell Biol.* **9**:724-728 (2007). http://www.ncbi.nlm.nih.gov/pubmed/17603504

C.I. Hong, E.D. Conrad, B. Novak & J.J. Tyson, "A proposal for robust temperature compensation of circadian rhythms." *Proc. Natl. Acad. Sci. U.S.A.* **104**:1195-1200 (2007). http://www.ncbi.nlm.nih.gov/pubmed/17229851

J.J. Tyson, W.T. Baumann, C. Chen, A. Verdugo, I. Tavassoly, Y. Wang, L.M. Weiner & R. Clarke, "Dynamic modeling of oestrogen signaling and cell fate in breast cancer cells," *Nat. Rev. Cancer* **11**:523-32 (2011). http://www.ncbi.nlm.nih.gov/pubmed/21677677

T. Hong, J. Xing, L. Li & J.J. Tyson, "A mathematical model for the reciprocal differentiation of T helper 17 cells and induced regulatory T cells," *PLoS Comput. Biol.* 7:e1002122 (2011). http://www.ncbi.nlm.nih.gov/pubmed/21829337

K. Subramanian, M.R. Paul & J.J. Tyson, "Potential role of a bistable histidine kinase switches in the asymmetric division cycle of *Caulobacter crescentus*," *PLoS Comput. Biol.* **9**:e1003221 (2013). http://www.ncbi.nlm.nih.gov/pubmed/24068904

C. Chen, W.T. Baumann, J. Xing, L. Lu, R. Clarke & J.J. Tyson, "Mathematical models of the transitions between endocrine therapy responsive and resistant states in breast cancer," *J. Roy. Soc. Interface* **11**:20140206 (2014). http://www.ncbi.nlm.nih.gov/pubmed/24806707

I. Tavassoly, A.N. Shajahan, J.J. Tyson, R. Clarke & W.T. Baumann, "Dynamic modeling of the interaction between autophagy and apoptosis in mammalian cells," *CPT: Pharmacometrics & Systems Pharmacology* **4**:263-272 (2015). http://www.ncbi.nlm.nih.gov/pubmed/26225250

D. Battogtokh & J.J. Tyson, "A bistable switch mechanism for stem cell domain nucleation in the shoot apical meristem," *Front. Plant Sci.* **7**:674 (2016). http://www.ncbi.nlm.nih.gov/pubmed/27242874

F. Li, K. Subramanian, M. Chen, J.J. Tyson & Y. Cao, "A stochastic spatiotemporal model of a response-regulator network in the *Caulobacter crescentus* cell cycle," *Phys. Biol.* **13**:035007 (2016). http://www.ncbi.nlm.nih.gov/pubmed/27345750

T. Laomettachit, K.C. Chen, W.T. Baumann & J.J. Tyson, "A Model of yeast cell-cycle regulation based on a standard component modeling strategy for protein regulatory networks" *PLoS ONE* **11**:e0153738 (2016). http://www.ncbi.nlm.nih.gov/pubmed/27187804

Current and/or Recently Completed Research Grants: (as applicable)

NIH-GMS	R01-GM078989	PI: John Tyson	June 2006 – April 2020
Title: Stochastic Models of Cell Cycle Regulation in Eukaryotes			
The goals of this long-running project are to build accurate stochastic models of cell cycle regulation in budding yeast cells and to test these models experimentally. The current renewal of this project focuses on robustness of cell cycle checkpoints in the face of molecular noise, in wild-type yeast cells and in mutant strains that are compromised in checkpoint function.			
NSF-CIS	CCF-1526666	PI: Yang Cao	July 2015 – June 2018
Title: Algorithmic Foundations of Hybrid Stochastic Modeling and Simulation Methods with Applications to Cell Cycle Models			
The goals of this project are to develop hybrid deterministic-stochastic methods for simulating models of molecular regulatory networks in cells, to design efficient simulation algorithms, and to test the modeling methodology on cell cycle regulation in yeast. Role: CoPI			
NIH-NCI	R01-CA201092	PI: William Baumann	August 2016 – July 2020
Optimizing Targeted Breast Cancer Therapy by Mathematical Modeling and Experimental Studies			
The goals of this project are to the responsiveness of breast cancer cells to endocrine therapy by experimental studies (carried out by Ayesha Shajahani at Georgetown Univ Medical College) and by mathematical modeling (carried out by Bill Baumann and JJT at Virginia Tech). Role: CoPI			
NSF-MCB	MCB-1615287	PI: Kathleen Ryan (UC Berkeley)	September 2016 – August 2019
Collaborative Research: Identifying and modeling the advantages of regulating protein abundance in Caulobacter crescentus			
The goals of this project are to understand the advantages of periodic synthesis and degradation of proteins during the cell division cycle of a bacterium by a combination of experimental studies (carried out by Kathleen Ryand at Univ Calif Berkeley) and by mathematical modeling (carried out by Yang Cao and JJT at Virginia Tech). Role: CoPI			

NIH-NCI	U54 CA149147	PI: Robert Clarke (GUMC)	April 2010 – February 2015
Title: ER-related Activities Affect Breast Cancer Susceptibility and Responsiveness to Endocrine Therapy			
The goals of this Cancer Systems Biology Center were to study the molecular basis of breast cancer cell responsiveness to endocrine therapy and the mechanisms by which these cancer cells become resistant to therapy, by a combination of experimental studies (carried out at Georgetown Univ Medical College), big-data analysis (carried out at GUMC and VT-NoVa), and mathematical modeling (carried out at VT Blacksburg, by Bill Baumann and JJT).			
NIH-GMS	R01 GM095955	PI: T.M. Murali	January 2011 – December 2015
Title: Integrating Top-Down and Bottom-Up Models in Systems Biology with Application to Cell Cycle Control in Budding Yeast			
The goals of this project were to combine top-down analysis of signaling networks in yeast cells (Murali group) with bottom-up mathematical modeling (Tyson group), in order to derive novel extensions to the deterministic cell-cycle models in the literature, and then to test these models experimentally (Peccoud lab) by characterizing the phenotypes of novel mutant strains of budding yeast. Role: CoPI			
NSF-DMS	DMS-1225160	PI: John Tyson	September 2012 – August 2015
Title: Integrated Dynamics of Temporal and Spatial Controls in the Cell Division of *Caulobacter crescentus*			
The goal of this project was to build deterministic and stochastic models of the spatiotemporal interactions of the genes, mRNAs and proteins that control growth, division and differentiation of an alpha-proteobacterium.			