Curriculum Vitae

NAME: Paul David Smolen, Ph.D.

PRESENT TITLE: Adjunct Associate Professor
Department of Neurobiology and Anatomy
University of Texas-Houston Medical School
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UNDERGRADUATE EDUCATION:

1980-1984 B.S. (Biophysics), University of California at Berkeley

GRADUATE EDUCATION:

1986-1990 Ph.D. (Biophysics), University of California at Davis

POSTGRADUATE TRAINING:

10/91 – 10/94	NIDDK, National Institutes of Health, Bethesda, MD (Advisor: Dr. John Rinzel)
12/94 – 5/96	Department of Neuroscience, University of Antwerp, Antwerp, Belgium(Advisor: Dr. Erik de Schutter)
5/96 – 6/99	Department of Neurobiology, University of Texas Medical School at Houston, TX (Advisor: Dr. John Byrne)

ACADEMIC APPOINTMENTS:

1999 – 2004	Research Scientist, Department of Neurobiology and Anatomy, University of Texas Medical School at Houston, Houston, TX
2004 – 2006	Senior Research Scientist, Department of Neurobiology and Anatomy, University of Texas Medical School at Houston, TX
2006 – 2008	Research Assistant Professor, Department of Neurobiology and Anatomy, University of Texas Medical School at Houston, TX
2009 - 2014	Adjunct Assistant Professor, Department of Neurobiology and Anatomy, University of Texas Medical School at Houston, TX
2014 - present	Adjunct Associate Professor, Department of Neurobiology and Anatomy, University of Texas Medical School at Houston, TX

TEACHING EXPERIENCE:

2008 – 2009	Mathematics Teacher, North Houston Early College High School, Houston, TX
2001	Adjunct Instructor, Developmental Mathematics, Houston Community College, Houston, TX

PROFESSIONAL ORGANIZATIONS:

1994 - Present Society for Neuroscience

1992 - 1997 Biophysical Society

HONORS AND AWARDS:

Phi Theta Kappa (junior college honors fraternity), Jacksonville, TX
Honors (top 15% GPA), University of California, Berkeley, Spring 1983
Research Fellowship, Department of Biochemistry and Molecular Biology, University of California, Davis, 1989-1991

SERVICE TO NATIONAL GRANT REVIEW PANELS AND STUDY SECTIONS:

2007 External Grant Reviewer, CSR Study Section, "Modeling and Analysis of Biological Systems", National Institutes of Health.

2006, 2013 External Grant Reviewer, Department of Science and Technology, India.

INVITED LECTURES AND SEMINARS:

"Principles of Gene Regulation Illustrated by Models of Common Motifs", Gordon Research Conference, Mount Holyoke College, MA, 2001.

"Transcriptional Feedback and Circadian Rhythm Maintenance", Institute of Molecular Biophysics, Florida State University, Tallahassee, FL, 2004.

"Generation of Circadian Rhythms in *Drosophila* and *Neurospora*", University of Montreal, Montreal, 2005.

"Modeling Circadian Rhythm Generation and Perturbation Responses", Humboldt University, Berlin, 2006.

"The Roles of Key Kinases in Long-Term Potentiation", Department of Computational and Applied Mathematics, Rice University, Houston, TX, 2007.

"Maintenance of Long-Term Potentiation, Assessment of Positive Feedback Mechanisms", Organization for Computational Neurosciences workshop, San Antonio, TX, 2008.

"Modeling LTP Maintenance, Roles of Protein Kinase C ζ and of Synaptic Tags", Institute of Molecular Biophysics, Florida State University, Tallahassee, FL, 2012.

SERVICE TO COMMUNITY:

External Reviewer for *Biophysical Journal*, *Journal of Neuroscience*, *Journal of Biological Chemistry*, *Learning and Memory*, *and Physical Review E.*

1997, 1998 and 2004 Laboratory demonstrations for undergraduates.
1998 and 2000 Judge for Houston Science Fair for secondary school students.
2009, 2010 Robotics Club Advisor, North Houston Early College High School.

CURRENT GRANT SUPPORT:

NIH Research Grant

1. Title: Modeling Gene Regulation Essential for Long-Term Plasticity
2. Grant Number: R01 NS073974
3. Period of Support: July 1, 2011 to June 30, 2016
4. Role: Co-Principal Investigator

PREVIOUS GRANT SUPPORT:

DARPA Research Grant

1. Title: Bio-spice: A Simulation and Analysis System for Modeling Nonlinear Dynamical Properties of Intracellular Signal Pathways and Genetic Networks
2. Grant number: N00014-01-1-1031
3. Period of support: August 8, 2001 to December 31, 2003
4. Role: Co-Project Leader-Project 1

NIH Program Project Grant

1. Title: Neural Models of Plasticity: Molecules to Networks
2. Grant number: P01 NS38310
3. Period of support: August 25, 1999 to May 31, 2005
4. Role: Co-Project Leader-Project 1

NIH Program Project Grant

1. Title: Neural Models of Plasticity: Molecules to Networks
2. Grant number: P01 NS38310
3. Period of support: July 15, 2005 to June 30, 2011
4. Role: Co-Project Leader-Project 1

PUBLICATIONS:

REFEREED ARTICLES IN JOURNALS:

1. Srivastava D., Smolen P., Betts G., and Bernhard S. (1989) Direct transfer of NADH between α-glycerol phosphate dehydrogenase and lactate dehydrogenase: fact or misinterpretation? *Proc. Natl. Acad. Sci. USA* 86: 6464-6468.

2. Smolen P., and Keizer J. (1990) Kinetics and thermodynamics of metabolite transfer between enzymes. *Biophys. Chem.* 38: 241-263.

3. Keizer J., and Smolen P. (1991) Bursting electrical activity in pancreatic β-cells caused by Ca^{2+}- and voltage-inactivated Ca^{2+} channels. *Proc. Natl. Acad. Sci. USA* 88: 3897-3901.

4. Smolen P., and Keizer J. (1992) Slow voltage-inactivation of Ca^{2+} currents and bursting mechanisms for the mouse pancreatic β-cell. *J. Membrane. Biol.* 127: 9-19.

5. Smolen P., Rinzel J., and Sherman A. (1993) Why pancreatic islets burst but single β-cells do not, the heterogeneity hypothesis. *Biophys. J.* 64: 1668-1680.

6. Smolen P., Terman D., and Rinzel J. (1993) Properties of a bursting model with two slow inhibitory variables. *SIAM J. Applied Math.* 53: 861-892.

7. Satin L., Tavalin S., and Smolen P. (1994) Inactivation of HIT cell Ca^{2+} current by a simulated burst of Ca^{2+} action potentials. *Biophys. J.* 66: 141-148.

8. Smolen P., and Sherman A. (1994) Phase-independent resetting in relaxation and bursting oscillators. *J. Theoret. Biol.* 169: 339-348.

9. Smolen P. (1995) A model for glycolytic oscillations based on skeletal muscle phosphofructokinase kinetics. *J. Theoret. Biol.* 174: 137-148.

10. Bertram R., Smolen P., Sherman A., Mears D., Atwater I., Martin F., and Soria B. (1995) A role for calcium release-activated current (CRAC) in cholinergic modulation of electrical activity in pancreatic β-cells. *Biophys. J.* 68: 2323-2332.

11. Sherman A., and Smolen P. (1997) Computer modeling of heterogenous β-cell populations. *Adv. Exp. Med. Biol.* 426: 275-284.

12. Smolen P., Baxter D.A., and Byrne J.H. (1998) Frequency selectivity, multistability and oscillations emerge from models of genetic regulatory systems. *Am. J. Physiol.* 274: C531 - C542.

13. Smolen P., Baxter D.A., and Byrne J.H. (1999) Effects of macromolecular transport and stochastic fluctuations on the dynamics of genetic regulatory systems. *Am. J. Physiol.* 277: C777-C790.

14. Smolen P., Baxter D.A., and Byrne J.H. (2000) Modeling transcriptional control in gene networks – methods, recent results, and future directions. *Bull. Math. Biol.* 62: 247-292.

15. Smolen P., Baxter D.A., and Byrne J.H. (2000) Mathematical modeling of gene networks. *Neuron*, 26: 567-580.

16. Smolen P., Baxter D.A., and Byrne J.H. (2001) Modeling circadian oscillations with interlocking positive and negative feedback loops. *J. Neurosci.* 21: 6644-6656.

17. Smolen P., Baxter D.A., and Byrne J.H. (2002) A reduced model clarifies the role of feedback loops and time delays in the *Drosophila* circadian oscillator. *Biophys. J.* 83: 2349-2359.

18. Smolen P., Baxter D.A., and Byrne J.H. (2003) Reduced models of the circadian oscillators in *Neurospora crassa* and *Drosophila melanogaster* illustrate mechanistic similarities. *OMICS: A Journal of Integrative Biology* 7: 337-354.

19. Smolen P., Hardin P.E., Lo B.S., Baxter D.A., and Byrne J.H. (2004). Simulation of *Drosophila* circadian oscillations, mutations, and light responses by a model with VRI, PDP-1, and CLK. *Biophys. J.* 86: 2786-2802.

20. Bertram R., Satin L., Zheng M., Smolen P., and Sherman A. (2004). Calcium and glycolysis mediate multiple bursting modes in pancreatic islets. *Biophys. J.* 87: 3074-3087.

21. Pettigrew D.B., Smolen P., Baxter D.A., and Byrne J.H. (2005). Dynamic properties of regulatory motifs associated with induction of three temporal domains of memory in *Aplysia*. *J. Comput. Neurosci.* 18: 163-181.

22. Mohamed H.A., Yao W., Fioravante D., Smolen P., and Byrne J.H. (2005). cAMP response elements in *Aplysia creb1, creb2*, and *Ap-uch* promoters: implications for feedback loops modulating long-term memory formation. *J. Biol. Chem.* 280: 27035-27043.

23. Fioravante D., Smolen P., and Byrne J.H. (2006). The 5-HT- and FMRFa- activated signaling pathways interact at the level of the Erk MAPK cascade: potential inhibitory constraints on memory formation. *Neurosci. Lett.* 396: 235-240.

24. Song H., Smolen P., Av-Ron E., Baxter D.A., and Byrne J.H. (2006). Bifurcation and singularity analysis of a molecular network for the induction of long-term memory. *Biophys. J.* 90: 2309-2325.

25. Smolen P., Baxter D.A., and Byrne J.H. (2006). A model of the roles of essential kinases in the induction and expression of late long-term potentiation. *Biophys. J.* 90: 2760-2765.

26. Song H., Smolen P., Av-Ron E., Baxter D.A., and Byrne J.H. (2007). Dynamics of a minimal model of interlocked positive and negative feedback loops of transcriptional regulation by CREB proteins. *Biophys. J.* 92: 3407-3424.

27. Smolen P. (2007). A model of late long-term potentiation simulates aspects of memory maintenance. *PLoS ONE*. 2: e445.

28. Smolen P., Baxter D.A., and Byrne J.H. (2008). Bistable MAP kinase activity, a plausible mechanism contributing to the maintenance of late long-term potentiation. *Am. J. Physiol. Cell Physiol.* 294(2): C503-15

29. Smolen P., Baxter D.A., and Byrne J.H. (2009). Interlinked dual-time feedback loops can enhance robustness to stochasticity and persistence of memory. *Phys. Rev. E Stat. Nonlin. Soft Matter Phys.* 79(3 Pt 1): 031902.

30. Zhang Y., Smolen P., Baxter D.A., and Byrne J.H. (2010). The sensitivity of memory consolidation and reconsolidation to inhibitors of protein synthesis and kinases: computational analysis. *Learn. Mem.* 17: 428-439.

31. Zhang Y., Liu R.Y., Heberton G.A., Smolen P., Baxter D.A., and Byrne J.H. (2012). Computational design of enhanced learning protocols. *Nat. Neurosci*. 15: 294-297.

32. Smolen P., Baxter D.A., and Byrne J.H. (2012). Molecular constraints on synaptic tagging and maintenance of long-term potentiation: a predictive model. *PLoS Comput. Biol*. 8: e1002620.

33. Liu R.Y., Zhang Y., Baxter D.A., Smolen P., Cleary L.J., and Byrne J.H. (2013). Deficit in long-term plasticity is rescued by a computationally predicted stimulus protocol. *J. Neurosci*. 33: 6944-6949.

34. Zhang Y., Smolen P., Baxter D.A., and Byrne J.H. (2014). Computational analyses of synergism in small molecular network motifs. *PLoS Comput. Biol*. 10: e1003524.

35. Smolen P., Baxter D.A., and Byrne J.H. (2014). Simulations suggest pharmacological methods for rescuing long-term potentiation. *J. Theoret. Biol.*, 360: 243-250.

36. Zhou L., Zhang Y., Liu R.Y., Smolen P., Cleary L.J., and Byrne J.H. (2015). Rescue of impaired long-term facilitation at sensorimotor synapses of *Aplysia* following siRNA knockdown of CREB1. *J. Neurosci.*, 35: 1617-1626.

37. Smolen P. (2015). Modeling maintenance of long-term potentiation in clustered synapses: long-term memory without bistability.
Neural Plast., dx.doi.org/10.115/2015/185410.

38. Smolen P., Zhang Y., and Byrne J.H. (2016). The right time to learn: mechanisms and optimization of spaced learning. *Nat. Rev. Neurosci*. 17: 77-88.

INVITED ARTICLES IN JOURNALS:

1. Keizer, J., and Smolen, P. (1992). Mechanisms of metabolite transfer between enzymes: diffusional *vs*. direct transfer. *Curr. Top. Cell. Regul.* 33: 391-405.

2. Satin L., and Smolen P. (1994). Electrical bursting and calcium oscillations in pancreatic β-cells. *Endocrine J.* 2: 677-687.

3. Smolen P., and Byrne J.H. (2003). Support of progress in clinical neurology by models of genetic regulation. *Arch. Neurol.* 60: 1053-1057.

BOOK CHAPTERS AND DISSERTATION:

1. Smolen P. (1990). Thermodynamic and kinetic consequences of transient interactions between cognate enzymes. Ph. D. dissertation, Dept. of Biochemistry and Biophysics, University of California, Davis, CA.

2. De Schutter E., Smolen P. (1998). Calcium dynamics in large neuronal models. In: *Methods in Neuronal Modeling: from Ions to Networks*. Editors, C. Koch and I. Segev. MIT Press.

3. Smolen P., Baxter D.A., and Byrne J.H. (2004). Mathematical modeling and analysis of intracellular signaling pathways. In: *From Molecules to Networks, An Introduction to Cellular and Molecular Neuroscience*, Editors, J.H. Byrne and J.L. Roberts. Elsevier.

4. Smolen P., Baxter D.A., and Byrne J.H. (2008). Modeling and analysis of intracellular signaling pathways. In: *From Molecules to Networks: An Introduction to Cellular and Molecular Neuroscience (2nd Edition),* Editors, J.H. Byrne and J.L. Roberts. Elsevier.
5. Smolen, P., and Byrne, J.H. (2009). Circadian rhythm models. In: *New Encyclopedia of Neuroscience, Vol. 2*. Editor, Squire, L.R. Elsevier.
6. Smolen P., Baxter D.A., and Byrne J.H. (2014). Modeling and analysis of intracellular signaling pathways. In: *From Molecules to Networks, An Introduction to Cellular and Molecular Neuroscience (3rd Edition)*. Editors, J.H. Byrne and Roberts, J.L. Elsevier.
7. Smolen P., and Byrne, J. H. (2016). Circadian rhythm models. In: *Reference Module in Neuroscience and Biobehavioral Psychology*. Editor, J. Stein. Elsevier.

ABSTRACTS (Since 1996):

1. Smolen, P., Byrne, J.H. and Baxter, D.A. Computational models of cAMP-dependent activation and repression of gene transcription involved in long-term memory formation. *Soc. Neurosci. Abstr.*, 22:1880, 1996.
2. Smolen, P., Baxter, D.A. and Byrne, J.H. Dependence of transcription rate on stimulus pattern and frequency modeled by competition between transcriptional activator and repressor. *Soc. Neurosci. Abstr.*, 23:983, 1997.
3. Smolen, P., Baxter, D.A. and Byrne, J.H. Modeling clarifies the roles of delays and feedback in circadian oscillators. *Soc. Neurosci. Abstr.*, 25:867, 1999.
4. Smolen, P., Baxter, D.A., and Byrne, J.H. Complex dynamics generated by models of positive and negative feedback interactions within the MAP kinase pathway. *Soc. Neurosci. Abstr.*, 26:407, 2000.
5. Pettigrew, D.B., Smolen, P., Baxter, D.A. and Byrne, J.H. Spaced, but not massed, stimulation induces long-term facilitation in an intracellular model of *Aplysia* sensory neurons. *Soc. Neurosci. Abstr.*, 27: 2535, 2001.
6. Smolen, P., Fioravante D., Chin, J., Baxter, D.A. and Byrne, J.H. Computational model of molecular processes underlying long-term facilitation in *Aplysia*. *Soc. Neurosci. Abstr.*, 27: 2535, 2001.
7. Smolen, P.D., Baxter, D.A. and Byrne, J.H. Simplified models clarify the functions of feedback loops and time delays in circadian oscillators. Program No. 321.12. *2002 Abstract Viewer/Itinerary Planner*, Washington, DC: Society for Neuroscience, 2002. CD-ROM.
8. Smolen, P., Waxham, M.N., Baxter, D.A. and Byrne, J.H. Simulation of nuclear CaM kinase IV (CaMKIV) activation during L-LTP induction predicts tight binding with CaM-Ca_4 and suggests CaMKIV activation is not significant in some induction protocols. *2004 Abstract Viewer/Itinerary Planner*, San Diego, CA: Society for Neuroscience, 2004. CD-ROM.
9. Smolen, P.D., Baxter, D.A. and Byrne, J.H. A predictive model of the roles of essential kinases in the induction and expression of late long-term potentiation. Program No. 496.1. *2005 Abstract Viewer/Itinerary Planner*. Washington, DC: Society for Neuroscience.

10. Byrne, J.H., Fioravante, D., Mohamed, H.A., Smolen, P. and Yao, W. cAMP response elements in the promoter regions of *Aplysia creb1*, *creb2*, and *uch*: implications for feedback loops modulating the formation of long-term memory. Program No. 503.1. *2005 Abstract Viewer/Itinerary Planner.* Washington, DC: Society for Neuroscience.
11. Song, H., Smolen, P., Av-Ron, E., Baxter, D.A. and Byrne, J.H. Nonlinear dynamics of a minimal model of interlocked positive and negative feedback loops of CREBs: deterministic and stochastic analysis. Presentation No. 669.7. *2006 Abstract Viewer/Itinerary Planner*. Atlanta, GA: Society for Neuroscience.
12. Smolen, P., Baxter, D.A. and Byrne, J.H. Modeling suggests persistent activation of MAP kinase may contribute to long-term memory formation. Presentation No. 221.1. *2007 Abstract Viewer/Itinerary Planner*. San Diego, CA: Society for Neuroscience.
13. Smolen, P., Baxter, D.A. and Byrne, J.H. Interlinked dual-time feedback loops can enhance robustness to stochasticity and persistence of memory. Presentation No. 334.8. *2008 Abstract Viewer/Itinerary Planner*. Washington, D.C.: Society for Neuroscience 2008.
14. Zhang, Y., Smolen, P.D., Baxter, D.A. and Byrne, J.H. Positive feedback and the sensitivity of memory consolidation and reconsolidation to protein synthesis or kinase inhibition: A computational study. *Soc. Neurosci. Abstr.*, 2010.
15. Zhang, Y., Liu, R. Y., Smolen, P., Baxter, D. A., and Byrne, J. H. Novel enhanced learning protocol is predicted by computational designs. *Soc. Neurosci. Abstr.*, 2011.
16. Liu, R.Y., Zhang, Y., Heberton, G., Smolen, P., Cleary, L. J., Baxter, D. A. and Byrne J. H. A training protocol based on optimal dynamics of PKA/ERK pathways in *Aplysia* sensory neurons enhances long-term memory (LTM). *Soc. Neurosci. Abstr.*, 2011.
17. Smolen, P. D., Baxter, D. A. And Byrne; J. H. Molecular constraints on synaptic tagging and LTP maintenance: a predictive model. *Soc. Neurosci. Abstr.*, 2012.
18. Zhou, L. Zhang, Y., Liu, R.Y., Baxter, D.A., Smolen, P., Cleary, L.J., and Byrne, J.H. Rescuing impaired long-term facilitation (LTF) at sensorimotor (SN-MN) synapses of *Aplysia* following siRNA knock down of CREB1. *Soc. Neurosci. Abstr.*, 2013.
19. Smolen, P., Baxter, D.A., and Byrne, J.H. Simulations suggest pharmacological methods for rescuing long-term potentiation. *Soc. Neurosci. Abstr.*, 2014.