

Patrick A. Fletcher

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Education

Ph.D, Mathematics (Biomathematics), August 2015. Florida State University, Tallahassee, Florida, USA. Dissertation title: *Theoretical, Computational, and Experimental Topics in Anterior Pituitary Cell Signaling*

M.Sc, Mathematics (Mathematical Biology), November 2008. University of British Columbia, Vancouver, Canada. Thesis title: *Modeling electrical spiking, bursting and calcium dynamics in gonadotropin releasing hormone (GnRH) secreting neurons*

B.S, Integrated Sciences (Mathematics and Biology), May 2005. University of British Columbia, Vancouver, Canada.

Publications

- [1] S. S. Stojilkovic, R. M. Prévide, A. Sherman, and **P. A. Fletcher**. *Pituitary transcriptomics with focus on corticotrophs*. Manuscript submitted for publication, Jan 2022.
- [2] **P. A. Fletcher**, R. M. Prévide, K. Smiljanic, A. Sherman, S. L. Coon, and S. S. Stojilkovic. *Transcriptomic heterogeneity of sox2-expressing pituitary cells*. *bioRxiv*, Dec 2021. [10.1101/2021.12.10.472137](https://doi.org/10.1101/2021.12.10.472137).
- [3] M. Kučka, A. E. Gonzalez-Iglesias, M. Tomić, R. M. Prévide, K. Smiljanic, S. J. Sokanovic, **P. A. Fletcher**, A. Sherman, T. Balla, and S. S. Stojilkovic. *Calcium-prolactin secretion coupling in rat pituitary lactotrophs is controlled by pi4-kinase alpha*. *Frontiers in Endocrinology*, 12, Dec 2021. [10.3389/fendo.2021.790441](https://doi.org/10.3389/fendo.2021.790441).
- [4] I. Marinelli, **P. A. Fletcher**, A. S. Sherman, L. S. Satin, and R. Bertram. *Symbiosis of electrical and metabolic oscillations in pancreatic β -cells*. *Frontiers in Physiology*, 12, Dec 2021. [10.3389/fphys.2021.781581](https://doi.org/10.3389/fphys.2021.781581).
- [5] **P. A. Fletcher**, I. Marinelli, R. Bertram, L. S. Satin, and A. Sherman. *Pulsatile basal insulin secretion is driven by glycolytic oscillations*. Manuscript submitted for publication, Nov 2021.
- [6] I. Marinelli*, V. S. Parekh*, **P. A. Fletcher**, B. Thompson, J. Ren, X. Tang, T. L. Saunders, J. Ha, R. Bertram, A. Sherman, and L. S. Satin. *Slow oscillations persist in pancreatic β -cells lacking phosphofructokinase m*. Manuscript submitted for publication, Aug 2021.
- [7] I. Marinelli*, B. Thompson*, V. S. Parekh, **P. A. Fletcher**, L. Gerardo-Giorda, A. Sherman, L. S. Satin, and R. Bertram. *Oscillations in $k(atp)$ conductance drive slow calcium oscillations in pancreatic β -cells*. Manuscript submitted for publication, Aug 2021.

- [8] D. Asuzu*, R. Alvarez*, **P. A. Fletcher***, D. Mandal, K. Johnson, W. Wu, A. Elkahloun, P. Clavijo, C. Allen, D. Maric, A. Ray-Chaudhury, S. Rajan, Z. Abdullaev, A. Kosanam, D. Nwokoye, K. Aldape, L. Nieman, C. Stratakis, S. S. Stojilkovic, and P. Chittiboina. *Pituitary adenomas evade apoptosis via noxa deregulation in cushing's disease*. Manuscript submitted for publication, Jun 2021.
- [9] J. C. Chang, **P. A. Fletcher**, J. Han, T. L. Chang, S. Vattikuti, B. Desmet, A. Zirikly, and C. C. Chow. *Sparse encoding for more-interpretable feature-selecting representations in probabilistic matrix factorization*. arXiv preprint arXiv:2012.04171, Oct 2020.
- [10] K. Wang, K. Kretschmannova, R. Prévède, K. Smiljanic, Q. Chen, **P. A. Fletcher**, A. Sherman, and S. Stojilkovic. *Cell-type-specific expression pattern of proton-sensing receptors and channels in pituitary gland*. Biophysical Journal, 119(11):2335–2348, Oct 2020. [10.1016/j.bpj.2020.10.013](https://doi.org/10.1016/j.bpj.2020.10.013).
- [11] M. M. Janjic, R. M. Prévède, **P. A. Fletcher**, A. Sherman, K. Smiljanic, D. Abebe, I. Bjelobaba, and S. S. Stojilkovic. *Divergent expression patterns of pituitary gonadotropin subunit and gnrh receptor genes to continuous gnrh in vitro and in vivo*. Scientific Reports, 9(1):1–14, Dec 2019. [10.1038/s41598-019-56480-1](https://doi.org/10.1038/s41598-019-56480-1).
- [12] **P. A. Fletcher**, K. Smiljanic, R. Maso Prévède, J. Iben, T. Li, M. B. Rokic, A. Sherman, S. L. Coon, and S. S. Stojilkovic. *Cell type-and sex-dependent transcriptome profiles of rat anterior pituitary cells*. Frontiers in Endocrinology, 10, Sept 2019. [10.3389/fendo.2019.00623](https://doi.org/10.3389/fendo.2019.00623).
- [13] **P. A. Fletcher**, A. Sherman, and S. S. Stojilkovic. *Common and diverse elements of ion channels and receptors underlying electrical activity in endocrine pituitary cells*. Molecular and Cellular Endocrinology, 463:23–36, March 2018. [10.1016/j.mce.2017.06.022](https://doi.org/10.1016/j.mce.2017.06.022).
- [14] **P. A. Fletcher**, H. Zemkova, S. S. Stojilkovic, and A. Sherman. *Modeling the diversity of spontaneous and agonist-induced electrical activity in anterior pituitary corticotrophs*. Journal of Neurophysiology, 117(6):2298–2311, 2017. [10.1152/jn.00948.2016](https://doi.org/10.1152/jn.00948.2016).
- [15] **P. A. Fletcher**, R. Bertram, and J. Tabak. *From global to local: exploring the relationship between parameters and behaviors in models of electrical excitability*. Journal of Computational Neuroscience, 40(3):331–345, 2016. [10.1007/s10827-016-0600-1](https://doi.org/10.1007/s10827-016-0600-1).
- [16] A. E. Gonzalez-Iglesias, **P. A. Fletcher**, J. A. Arias-Cristancho, R. Cristancho-Gordo, C. V. Helena, R. Bertram, and J. Tabak. *Direct stimulatory effects of oxytocin in female rat gonadotrophs and somatotrophs in vitro: Comparison with lactotrophs*. Endocrinology, 156(2):600–612, 2015. [10.1210/en.2014-1543](https://doi.org/10.1210/en.2014-1543).
- [17] **P. A. Fletcher**, F. Clément, A. Vidal, J. Tabak, and R. Bertram. *Interpreting frequency responses to dose-conserved pulsatile input signals in simple cell signaling motifs*. PLOS ONE, 9(4):1–10, 04 2014. [10.1371/journal.pone.0095613](https://doi.org/10.1371/journal.pone.0095613).
- [18] M. N. Schulson, D. R. L. Scriven, **P. A. Fletcher**, and E. D. W. Moore. *Couplons in rat atria form distinct subgroups defined by their molecular partners*. Journal of Cell Science, 124(7):1167–1174, 2011. [10.1242/jcs.080929](https://doi.org/10.1242/jcs.080929).
- [19] **P. A. Fletcher**, D. R. Scriven, M. N. Schulson, and E. D. Moore. *Multi-image colocalization and its statistical significance*. Biophysical Journal, 99(6):1996 – 2005, 2010. [10.1016/j.bpj.2010.07.006](https://doi.org/10.1016/j.bpj.2010.07.006).

- [20] **P. A. Fletcher** and Y.-X. Li. *An integrated model of electrical spiking, bursting, and calcium oscillations in gnRH neurons*. Biophysical Journal, 96(11):4514 – 4524, 2009. [10.1016/j.bpj.2009.03.037](https://doi.org/10.1016/j.bpj.2009.03.037).
- [21] M. W. Richter, **P. A. Fletcher**, J. Liu, W. Tetzlaff, and A. J. Roskams. *Lamina propria and olfactory bulb ensheathing cells exhibit differential integration and migration and promote differential axon sprouting in the lesioned spinal cord*. Journal of Neuroscience, 25(46):10700–10711, 2005. [10.1523/JNEUROSCI.3632-05.2005](https://doi.org/10.1523/JNEUROSCI.3632-05.2005).

* These authors contributed equally to the work.

Presentations

- 2022 *Sox2+ stem cells and astroglia in the postnatal pituitary: a single cell transcriptomics perspective* DEMGEO Research Conference, NICHD, NIH
- 2020 *The heterogeneity of Sox2-expressing cells in the pituitary gland at single-cell transcriptome resolution*. DEMGEO Research Conference, NICHD, NIH
- 2019 *The dependence of glycolytic oscillations on calcium oscillations in models of pancreatic beta cells*. Society for Mathematical Biology Annual Meeting, Montreal Canada
- 2017 *Feature-Based Parameter Estimation in a Model of Anterior Pituitary Cell Electrical Activity*. SIAM Dynamical Systems, Snowbird UT
- 2016 *Modeling electrical activity in pituitary corticotrophs*. SIAM Life Sciences, Boston, MA
- 2014 *Real-Time Model calibration and prediction testing in pituitary cells using GPU and dynamic clamp*. SIAM Life Sciences, Charlotte, NC
- 2013 *How do cells detect the frequency of pulsatile chemical signals?* SIAM Dynamical Systems, Snowbird UT
- 2012 *Periodic forcing of simple models of cell signaling pathway components*. FSU biomathematics seminar, Tallahassee, FL
- 2011 *Modeling frequency-dependent FSH transcription and secretion*. Workshop in Mathematical Neuroendocrinology, INRIA, Paris, France

Experience

Postdoctoral Fellowship

10/15–present: Laboratory of Biological Modeling, NIDDK, NIH. Supervisor: Arthur Sherman

- Analysis of single-cell RNA sequencing data in anterior pituitary cells
- Modeling electrical activity and response to hormones in pituitary cells and pancreatic beta cells
- Time series analysis of video microscopy data from pancreatic islets
- Development of numerical simulation tools for parallel computation using graphics processing units (GPUs)

Research Assistantships

01/11–08/15: Department of Mathematics, Florida State University. Supervisor: Richard Bertram

- Investigating the generation and decoding of pulsatile hormone patterns using mathematical models
- Performing calcium imaging experiments and mathematical modeling to study the response of pituitary cells to oxytocin
- Developing software for parallel numerical simulation of biophysical models of neuronal activity on graphics processing units (GPUs), for the purpose of rapid model calibration and studying how features of model solutions depend on model parameters

02/12, 07/12: INRIA Rocquencourt, France. Supervisor: Frédérique Clément - Studied pulsatile forcing of non-linear systems inspired by intracellular signaling pathways

10/05–08/09: University of British Columbia.

- Department of Cellular and Physiological Sciences. Supervisor: Ed Moore - Quantified spatial patterning and its statistical significance in fluorescence microscopy images of signaling proteins involved in excitation-contraction coupling in cardiac myocytes.
- Department of Mathematics. Supervisor: Yue-Xian Li - Modeled electrical activities, calcium dynamics, and G-protein signaling of GnRH neurons and pituitary cells.
- Department of Mathematics. Supervisor: Eric Cytrynbaum - Compared a model of *E. coli* cell division machinery to experimental data.
- Department of Zoology. Supervisor: Jane Roskams - Quantified patterns of blood vessel growth and neurite outgrowth in fluorescence microscopy images of spinal cord explants.

Teaching Assistantships

08/09–12/14: **Florida State University**, Department of Mathematics

- Lecturer. **Courses taught:** Calculus 1 and 3, Pre-calculus algebra, Biocalculus Laboratory
- Teaching assistant. Supervised computer laboratories in Pre-calculus algebra, and trigonometry

09/06–05/08: **University of British Columbia**, Department of Mathematics - Tutoring, grading homework assignments

Awards

04/14: Distinguished Teaching Assistant award.

Languages and Programming Skills

Bilingual: English, French

Programming: MatLab, Python, R, XPPAUT, C/C++, OpenCL, CUDA

Course Delivery systems: Blackboard, WebAssign

Professional Service

Review Editor for Frontiers: Computational Physiology and Medicine

Referee for papers submitted to Mathematical Biosciences, Journal of Theoretical Biology, PLOS Computational Biology, PLOS ONE, Nature Communications, Journal of Neuroendocrinology, Computer Methods and Programs in Biomedicine.

Leadership

05/17: **Co-organizer**, Minisymposium for SIAM Dynamical Systems conference, titled *State and Parameter Estimation in Models of Cellular Electrical Activity*.

03/11–08/15: **President, Vice-President, Treasurer**, Kiteboarding Association at FSU. Responsible for activities of the club including organization of club trips, competitions and community service events, budget request presentations, purchasing and negotiation with industry contacts for kiteboard equipment, instruction of beginners, and repairing equipment.

01/11–04/11: **Co-organizer of the Graduate Student Seminar**, FSU Mathematics Department. Select, organize and schedule speakers and participants for the graduate student run seminar.

References

Available upon request.