Modelling Oscillations in Human Immune & Neuroimmune Cells: How Cells Time Inflammation

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Summary

This PhD sits at the intersection of biology, physics, and computing. We study human immune and neuroimmune effector cells [1-2]—innate myeloid-lineage sentinels that sit within tissues, along blood vessels and barriers, and at nerve interfaces. When tissue is stressed, these cells sense extracellular nucleotides (e.g., ATP/UTP) and respond with rhythmic changes in intracellular calcium and membrane voltage (V_m). These oscillations act like timing signals that regulate early inflammatory genes. Computational physiology turns those processes into compact ordinary differential equations (ODEs) that we can simulate and test against real data. You will build small, interpretable models that explain how ligand-gated receptors, intracellular Ca^{2+} (calcium) cycling, and Ca^{2+}-activated K^+ (potassium) channels generate oscillations—and how oscillation patterns control cytokine transcription.

You do not need a biology degree. If you enjoy differential equations, coding, and problem-solving, we will teach you the physiology.

Project scope and applications

- **General immune relevance:** Danger-signal nucleotides appear in infection, injury, ischemia, and mechanical stress. Understanding how they gate oscillations clarifies early inflammatory decisions (e.g., IL-6 bursts), with implications for host defence, wound healing, cardiovascular and sterile inflammation.
- **Neuroimmune relevance:** Similar mechanisms operate at neural interfaces (meninges, perivascular spaces, peripheral nerves, enteric tissues), shaping pain, neuroinflammation, and barrier immunity.
- **Wide application:** The resulting human-centric model will be reusable across myeloid effector contexts (vascular, mucosal, brain-border, and peripheral-nerve tissues), provide in-silico pharmacology for receptor/channel modulators, and suggest stimulation protocols to steer cytokine output.

What you'll do

- Develop ODE-based models that reproduce Ca^{2+}/V_m oscillations evoked by short nucleotide pulses.
- Parameterise human ligand-gated receptor kinetics using our generalised Hodgkin–Huxley (gHH) framework [3]; integrate with ER Ca^{2+} cycling and a lightweight Ca^{2+}→transcription module.
- Validate against published human datasets; generate pharmacology/stimulation predictions; open-source all code and figures.

What you'll learn

- Translate biology into compact ODE models (ligand-gated receptors, ER Ca^{2+} handling, Ca^{2+}-activated K^+ channels).
- Use gHH framework [3] to capture human receptor currents with a small, interpretable parameter set.
- Fit models with feature-based metrics (oscillation frequency, phase-lag, initial depolarisation) and make falsifiable predictions.
- Write reproducible scientific code (Python/Julia/MATLAB, Git) and communicate to mixed computational/experimental audiences.

What you'll bring (ideal)

- Background in mathematics, physics, chemistry, engineering, computer science, computational neuroscience/physiology, biophysics, or related fields.
- Strong numerics in Python/Julia/MATLAB, comfort with ODEs and scientific computing.
- Curiosity about ion channels, calcium signalling, immunophysiology, and neuroinflammation.

Training & environment

You will gain depth in ion-channel modelling, Ca^{2+} dynamics, feature-based model fitting, and open-science workflows. The project is tightly scoped for early results yet broad enough for high-impact publications and collaborations. You will have the opportunity to work with a diverse team of world-leading experts in computational and experimental neuroscience/physiology at several research institutions in the UK and abroad.

Why this project?

You will create a human-centric, mechanistic model linking extracellular danger signals to oscillatory dynamics and cytokine output—useful across immune and neuroimmune settings, including cardiovascular, barrier, and neural interfaces. The gHH foundation provides a tractable, data-first alternative to large, opaque Markov schemes.

How to apply

Please contact **Dr Alireza Poshtkohi** (a.poshtkohi@herts.ac.uk) or **Professor Volker Steuber** (v.steuber@herts.ac.uk) directly if you are interested in this project.

References

1. A. Poshtkohi *et al.*, *Mathematical Modelling of PI3k/Akt Pathway in Microglia*, Neural Computation, 36:4 (2024). doi: 10.1162/neco_a_01643
2. A. Poshtkohi *et al.*, *Mathematical Modelling of Human P2X-mediated Plasma Membrane Electrophysiology and Calcium Dynamics in Microglia*, PLoS Computational Biology, 17:11 (2021). doi: 10.1371/journal.pcbi.1009520
3. A. Poshtkohi *et al.*, *Generalised Hodgkin–Huxley Model Captures Human P2X and AMPA Receptor Currents*, The Journal of Physiology, **in press** (2025). doi: 10.1113/JP288880