Research Briefings

Computational modelling of neural networks

WE USE COMPUTATIONAL MODELS TO HELP UNDERSTAND THE NEUROENDOCRINE SYSTEMS THAT WE STUDY EXPERIMENTALLY.

THIS INVOLVES:

1) TRANSLATING BIOLOGICAL STATEMENTS INTO EQUATIONS

2) USING THESE TO GENERATE THEORETICAL "DATA" THAT CAN BE COMPARED WITH OBSERVATIONS

3) "FITTING" THE MODEL BY VARYING ITS PARAMETERS TO ENSURE THAT IT MATCHES OBSERVATIONAL DATA

4) USING THE MODEL TO GENERATE NEW AND UNEXPECTED PREDICTIONS.

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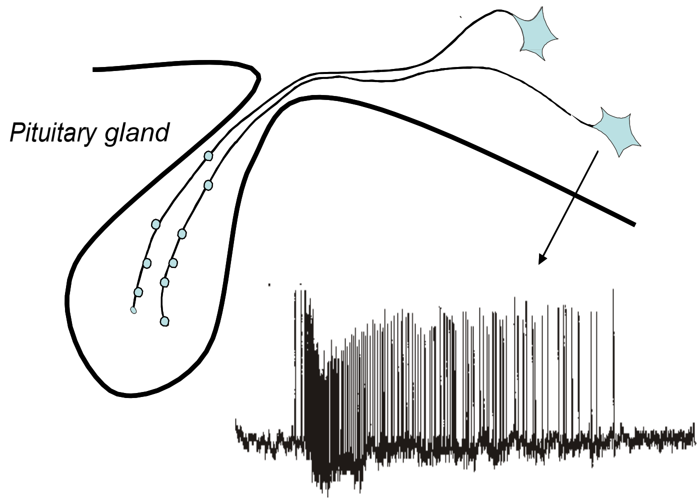
COMPUTATIONAL MODELS

Our science is not about facts, but about explanations; rational accounts of phenomena, embedded in a framework of theory, which include a wide range of observations and which are predictive of behaviour in circumstances as yet untested. We all seek to explain the world of observations using a set of logically interacting components, and we all simplify by recognising that some observations are important while others can be reasonably neglected. Formulating such explanations mathematically ensures their logical consistency, and makes them open to structured analysis; it is a stringent test of their intellectual coherence. We have used computational models to help understand several of the neuroendocrine systems that we study experimentally.

THE MILK-EJECTION REFLEX

When young suckle, they are rewarded intermittently with a let-down of milk that results from reflex secretion of the hormone oxytocin. Oxytocin is made by neurons in one small part of the hypothalamus (in the supraoptic and paraventricular nuclei), and this is one of the neuroendocrine systems that we have studied extensively. Oxytocin is secreted in response to action potentials (spikes) that are generated in the cell bodies, and which are propagated down to nerve endings at the pituitary gland. During suckling, every 5 minutes or so, every oxytocin cell discharges a brief, intense burst of spikes that release a pulse of oxytocin from the pituitary, which acts at the myoepithelial cells of the mammary gland. Oxytocin is also secreted during parturition to stimulate contractions of the uterus.

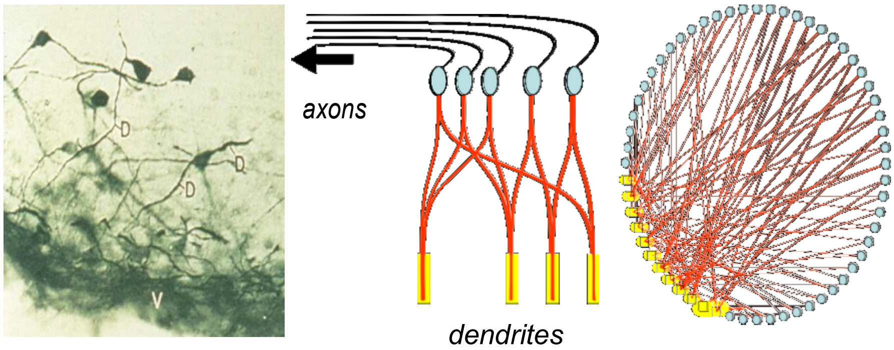


Oxytocin cells in the hypothalamus fire short intense bursts of action potentials during suckling; the inset shows a typical burst, lasting about 2 seconds.

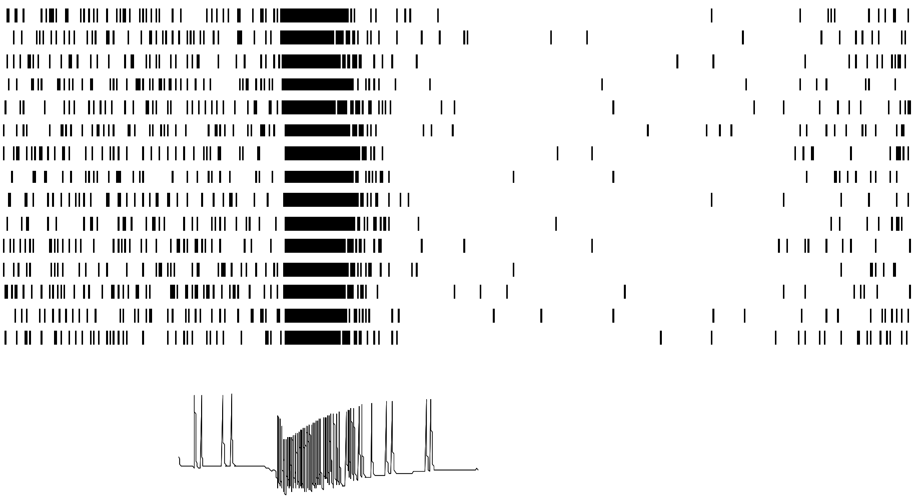
MODELLING THE REFLEX

Exactly how these bursts are generated has been a major problem in neuroendocrinology since this behaviour was first described, more than 30 years ago. To resolve this, we developed a computational model that incorporates basic observations of the physiology of oxytocin cells. In the model, oxytocin released from the dendrites of oxytocin cells acts on dendrites of adjacent cells to excite them in a positive-feedback manner. The interplay between the neuronal properties and the topology of the connections between cells leads to the emergence of synchronised bursts that are identical to bursts observed in real cells.

We have also used computational models to analyse the behaviour of vasopressin cells, and to help understand the hypothalamic networks that control the secretion of growth hormone, and the secretion of luteinising hormone. Both growth hormone and luteinising hormone are also released in pulses, but different mechanisms are involved in generating the pulses.



Dendrites of supraoptic neurons form “bundles” at the base of the supraoptic nucleus. The model represents each neurone as having an axon that projects to the posterior pituitary and two dendrites (red) that form bundles (yellow) with the dendrites of a few other neurons. The oxytocin cell population (blue cells) is thus randomly interconnected (right).



The model contains 1000 neurons, which display brief intermittent bursts very like those of oxytocin cells during suckling. The figure shows the bursts in just a few of these – each row shows the spike activity of a single model cell (spikes are the vertical lines). Below these is the detailed model representation of one of these bursts in a single cell.

Selected References

MacGregor DJ, Leng G (2013) Spike Triggered Hormone Secretion in Vasopressin Cells; a Model Investigation of Mechanism and Heterogeneous Population Function. PLoS Comput Biol 9(8): e1003187. doi:10.1371/journal.pcbi.1003187

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