

Neurotransmitter release in the brain

1 Introduction

The human brain consists of around 100 billion neurons each making 1000-10,000 synaptic connections. The activity of the brain is electrical but the connections between neurons are primarily chemical, across a specialised structure called the synapse. At the synapse, vesicles containing neurotransmitter fuse with the cell membrane and release their contents into the synaptic cleft. The transmitter molecules (typically 10,000-100,000 molecules per vesicle in our systems) diffuse across the synaptic cleft, where some of them engage with receptors triggering another wave of electrical activity in the post synaptic cell, while the remainder are taken back up by membrane-bound transporter proteins so they can be broken down or re-packaged. It is of interest experimentally to measure how this process changes with age or drugs. For example, do aging or drugs affect the concentration of neurotransmitter released from the vesicles and the rate of re-uptake?

2 Experimental measurements

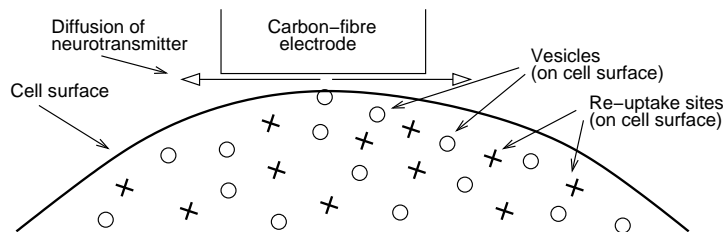


Figure 1: Experimental set-up showing vesicles and re-uptake sites distributed discretely across the cell surface.

This release of the neurotransmitter can be detected using microelectrodes, with a typical experimental set-up as shown in Figure 1. The neurotransmitter molecules are oxidised electrochemically at the surface of the electrode, which results in an electric current. A typical current profile detected from the brain of a snail (*Lymnaea stagnalis*) is shown in Figure 2, from data provided by Dr. O'Hare (Imperial College London). The spikes correspond to neurotransmitter-release events.

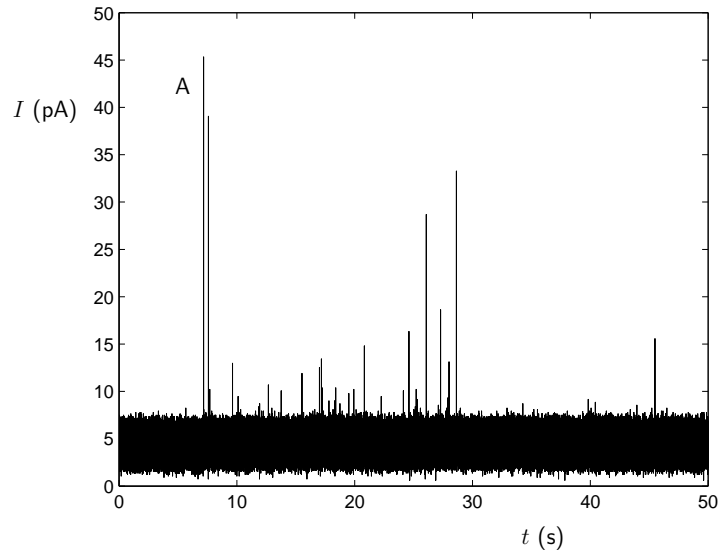


Figure 2: Current produced over a 50 second interval from a snail, showing spikes due to releases of neurotransmitter.

3 Mathematical modelling

We would like to be able to relate the size of the spikes in current response back to key parameters of the process, such as the total concentration released from the vesicle and the rate of re-uptake. This requires a theoretical model.

3.1 Scheme of work

- Introduction of the problem.
- Partial differential equation model of vesicle release, re-uptake and oxidation at the electrode.
- Analytical and numerical solution of the model.
- Comparison to experimental results.
- Further investigations into the effect of discrete re-uptake sites.