Model of membrane-potential fluctuations

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Gist

Temporal behaviour of the membrane potential in non-excitable cells is usually overlooked. We propose a model which accounts for (a) time-variability of membrane's constituents, as well as (b) active transport mechanisms. The properties of membrane potential's behaviour may provide useful indicators of cellular dynamics.

Model

Space is divided into three compartments: bulk A, membrane M, and bulk B.

Modified Poisson-Nernst-Planck approach [1]

$$\frac{\partial c_m}{\partial t} = -\nabla \mathbf{J}_m, \quad \mathbf{J}_m = -D_m \left(\nabla c_m - \frac{z_m e}{k_B T} c_m \mathbf{E} \right) + \mathbf{j}_m,$$

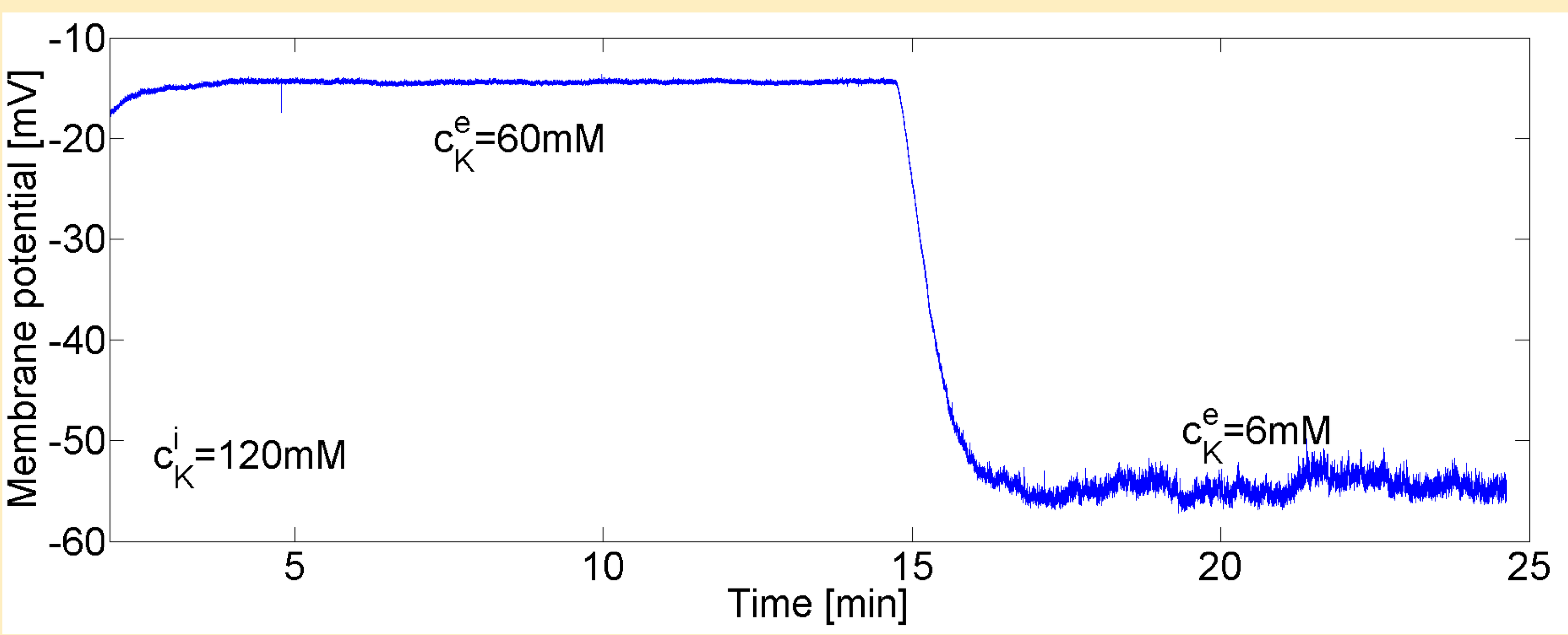
$$\nabla \varepsilon \mathbf{E} = -\nabla(\varepsilon \nabla \phi) = 4\pi\varrho = 4\pi \sum_m z_m c_m,$$

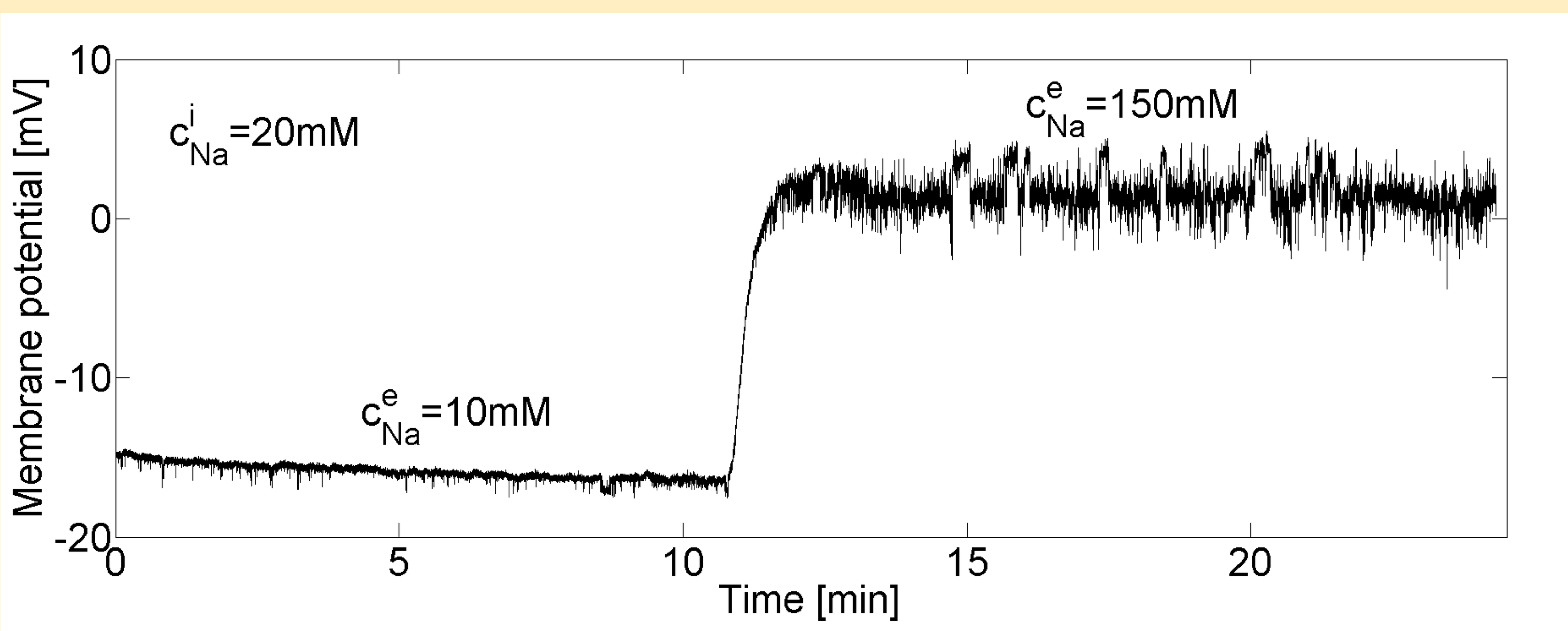
z_m	charge of m-th ion species in the solution ($z_1 = 1$ for permeable ions, $z_2 = -1$ for impermeable)
c_m	local instantaneous concentration
$D_m(\mathbf{r}, t)$	diffusivity (time dependence defines variability, spatial dependence distinguishes compartments)
$\mathbf{j}_m$	current due to active transport in compartment M.
$\mathbf{E}$, ϕ	local electric field and potential

$D_1 = 1$ in compartment M is corrupted by the white gaussian noise with $\sigma = 0.1$ (a.u.). $D_2 = 1$ reduces to zero in compartment M, reflecting impermeability of that ion.

Biological motivation

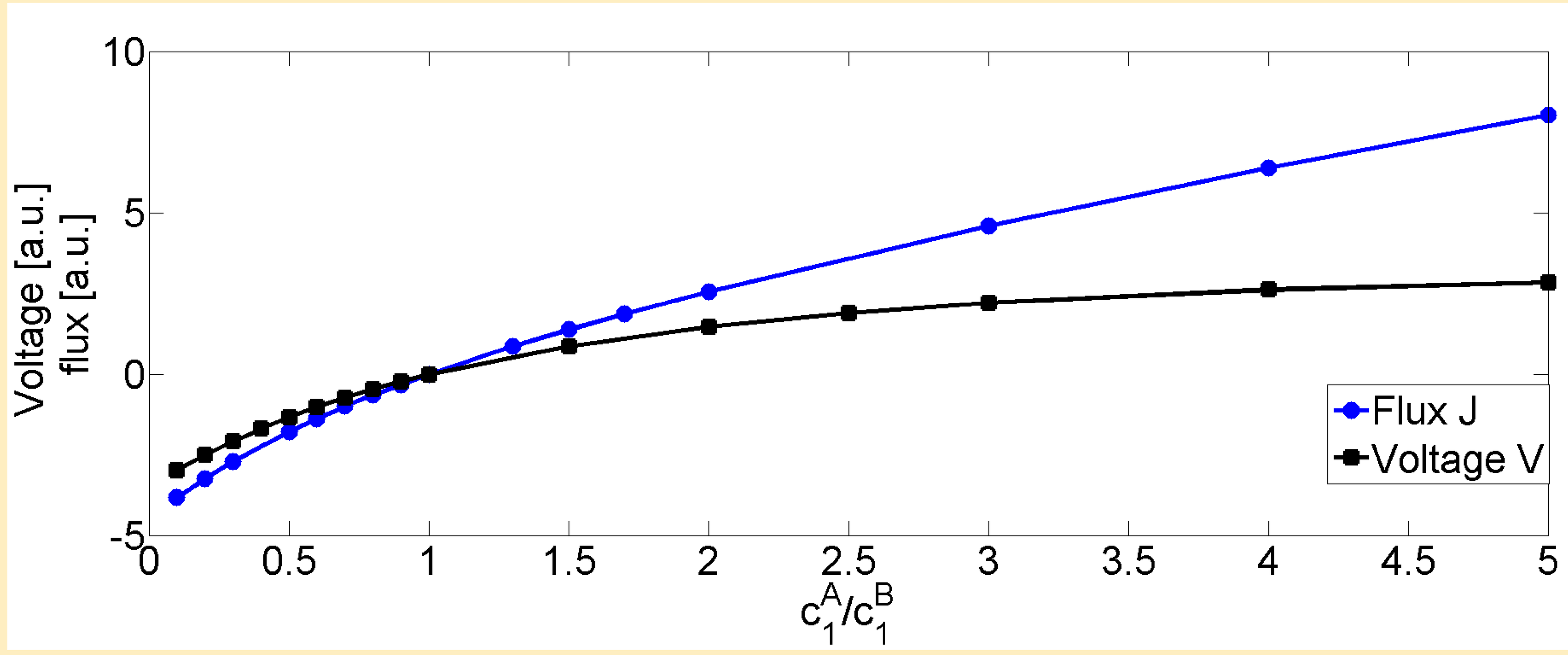
Whole-cell voltage patch-clamp recordings from the human Jurkat T-lymphocytes [2,3].

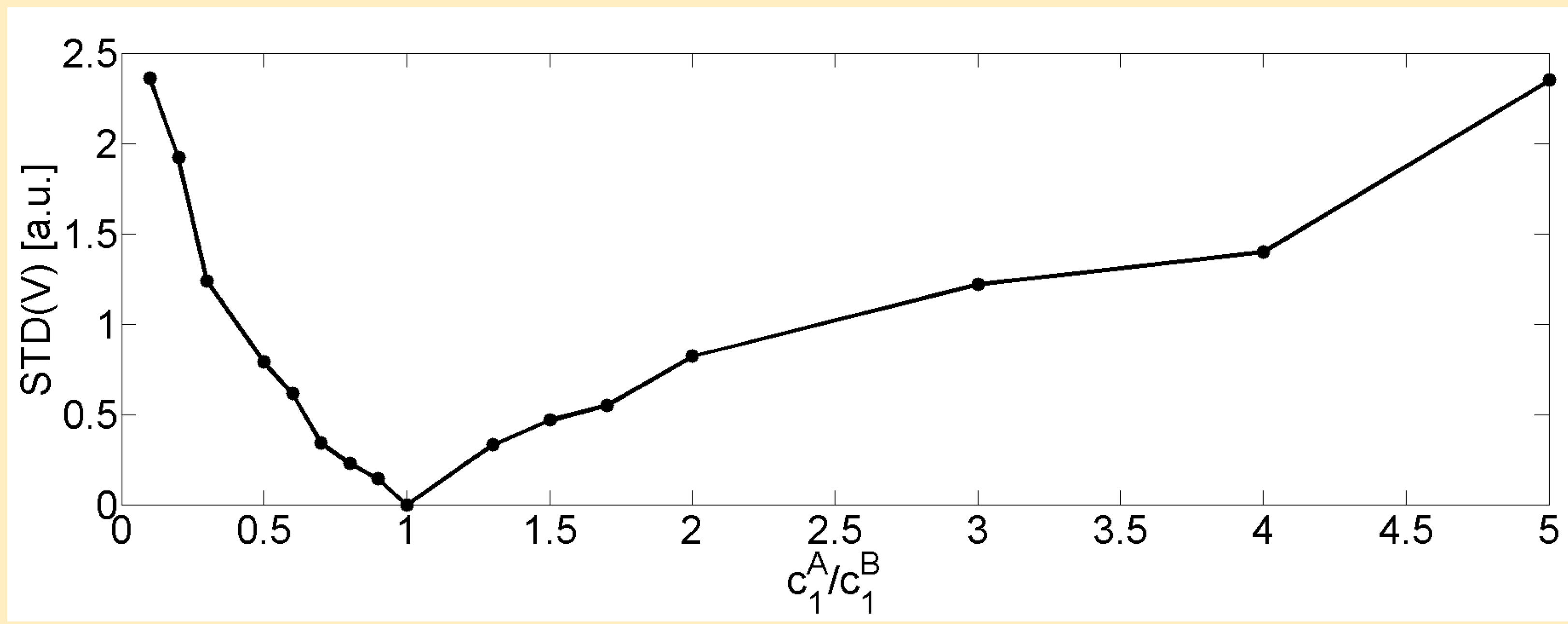




Numerical simulations

Two-ion mixture, the positive being permeable and negative being impermeable.





Discussion

Voltage fluctuation magnitude is coupled with the ionic flux' magnitude. Flux, induced by larger concentration gradient, causes larger variations of ionic densities nearby the membrane. These variations magnify the charge density fluctuations. Therefore, the electric field and consequently membrane potential fluctuations increase. That effect is capable to explain the change of fluctuation magnitude in the simulated example and in the experimental data provided.

Further work

- More ionic species in solutions.
- Account for Ca^{2+}- and voltage-gated permeation.
- Hydration effects.
- Simulations with realistic active transport terms.

References

[1] B. Nadler *et al.* *Ionic diffusion through confined geometries: from Langevin equations to partial differential equations*. J. Phys.: Condens. Matter **16** S2153 (2004).

[2] S. Patel, *The role of membrane potential dynamics in cell behaviours: investigating the membrane potential dynamics in the Jurkat and HMEC-1 cell lines using the continuous wavelet transform*, PhD thesis, Division of Biomedical and Life Sciences, Lancaster University, 2015.

[3] A. K. Pidde *et al.* Membrane potential of a biological cell: stochastic or deterministic?, in *ESGCO*, Lancaster University, 2016.