Lancaster University

Complex Oscillatory Systems: Modeling and Analysis
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Membrane potential of a biological cell: stochastic or deterministic?

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Intro

Every living ce ll continuously maintains its membrane potential by carefully adjusting the concentrations of different ions inside thus to avoid the osmotic pressure increase. In most approaches voltage is clamped and part of data explained as noise. We study the role of K^+, Cl^-, Ca^{2+}, and ATP in voltage behaviour and possible indications of their deterministic impact in non-excitable cells.

Methods

- Jurkat cells (human T-lymphocytes),
- whole cell **free-running voltage** patch clamp,
- alteration of the extracellular solution: standard (SB) or non-standard bath (high K^+ or low Cl^-) [1],
- alteration of the intrapipette solution (ATP or/and Ca^{2+}) [1],
- Data analysis
  - Preprocessing;
  - Wavelet transform:

$$W(s,t) = \int \Psi(s, u-t) f(u) du \tag{1}$$

W – wavelet transform, $\Psi(s,t)$ – mother wavelet, $f(u)$ – time series

  - Bispectrum and time-dependent biamplitude ans biphase [2]:

$$\begin{aligned} B(s_1, s_2) &= \left| \int W(s_1, u) W(s_2, u) W^*(s_3, u) dt \right| \\ A(s_1, s_2, u) &= \left| W(s_1, u) W(s_2, u) W^*(s_3, u) \right| \\ \phi(s_1, s_2, u) &= \phi(s_1, u) + \phi(s_2, u) - \phi(s_3, u) \end{aligned} \tag{2}$$

where s_1 and s_2 scale, $\frac{1}{s_3} = \frac{1}{s_1} + \frac{1}{s_2}$, $\phi(s,u)$ – time-dependent wavelet phase,

  - Surrogate testing [3]

Results

- Mean membrane voltages and standard deviations (as a measure of fluctuations)

	SB K^+	high K^+	SB Cl^-	low Cl^-
intrapipette	$\langle V \rangle \pm \langle \sigma \rangle [mV]$	$\langle V \rangle \pm \langle \sigma \rangle [mV]$	$\langle V \rangle \pm \langle \sigma \rangle [mV]$	$\langle V \rangle \pm \langle \sigma \rangle [mV]$
i	-32.6 ± 1.7	-9.22 ± 0.37	-3.71 ± 0.96	14.6 ± 1.43
i + Ca^{2+}	-31.1 ± 2.9	-9.28 ± 0.71	0.61 ± 0.68	23.2 ± 1.23
i + ATP	-32.3 ± 2.1	-9.15 ± 0.51	-6.07 ± 1.28	8.71 ± 2.15
i + Ca^{2+} + ATP	-35.2 ± 1.5	-13.0 ± 0.5	-15.1 ± 1.37	4.84 ± 2.08

Table 1: Means and mean standard deviations for SB and non-SB solutions for K^+ and Cl^-, i stays for the basic intrapipette solution.

- Time-averaged wavelet power (0.01-10Hz, as a measure of fluctuations)

	SB K^+	high K^+	SB Cl^-	low Cl^-
intrapipette	WP [$10^{-7} \times V^2$]	WP [$10^{-7} \times V^2$]	WP [$10^{-7} \times V^2$]	WP [$10^{-7} \times V^2$]
i	2.22	0.108	1.67	2.35
i + Ca^{2+}	6.25	0.703	0.57	1.68
i + ATP	4.88	0.293	2.13	6.05
i + Ca^{2+} + ATP	2.43	0.253	2.23	5.31

Table 1: Time-averaged wavelet power (WP) within 0.01-10Hz frequency band for SB and non-SB solutions for K^+ and Cl^-, i stays for the basic intrapipette solution.

- Significant changes in voltages and standard deviations and time-averaged wavelet power (0.01-10Hz)

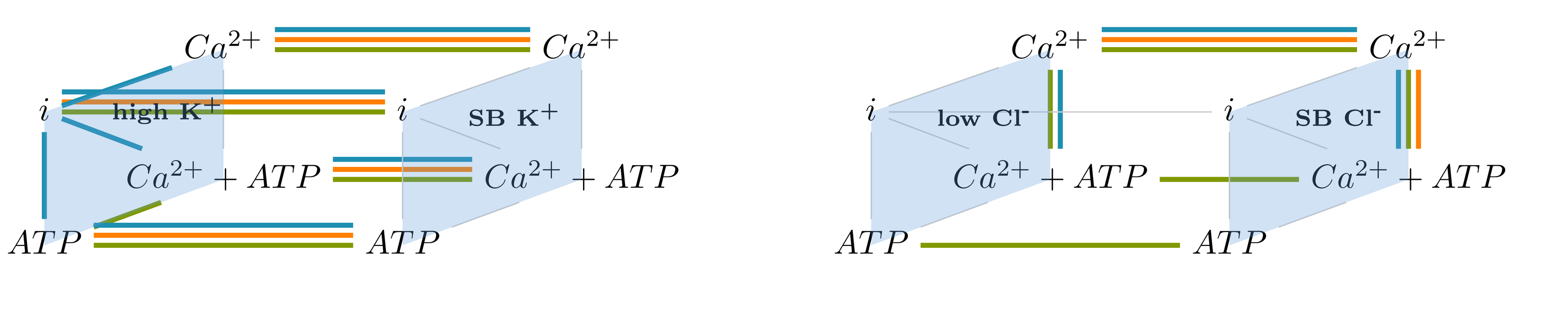

Fig. 1: Significant changes in voltage, standard deviation, time-average wavelet power

Results

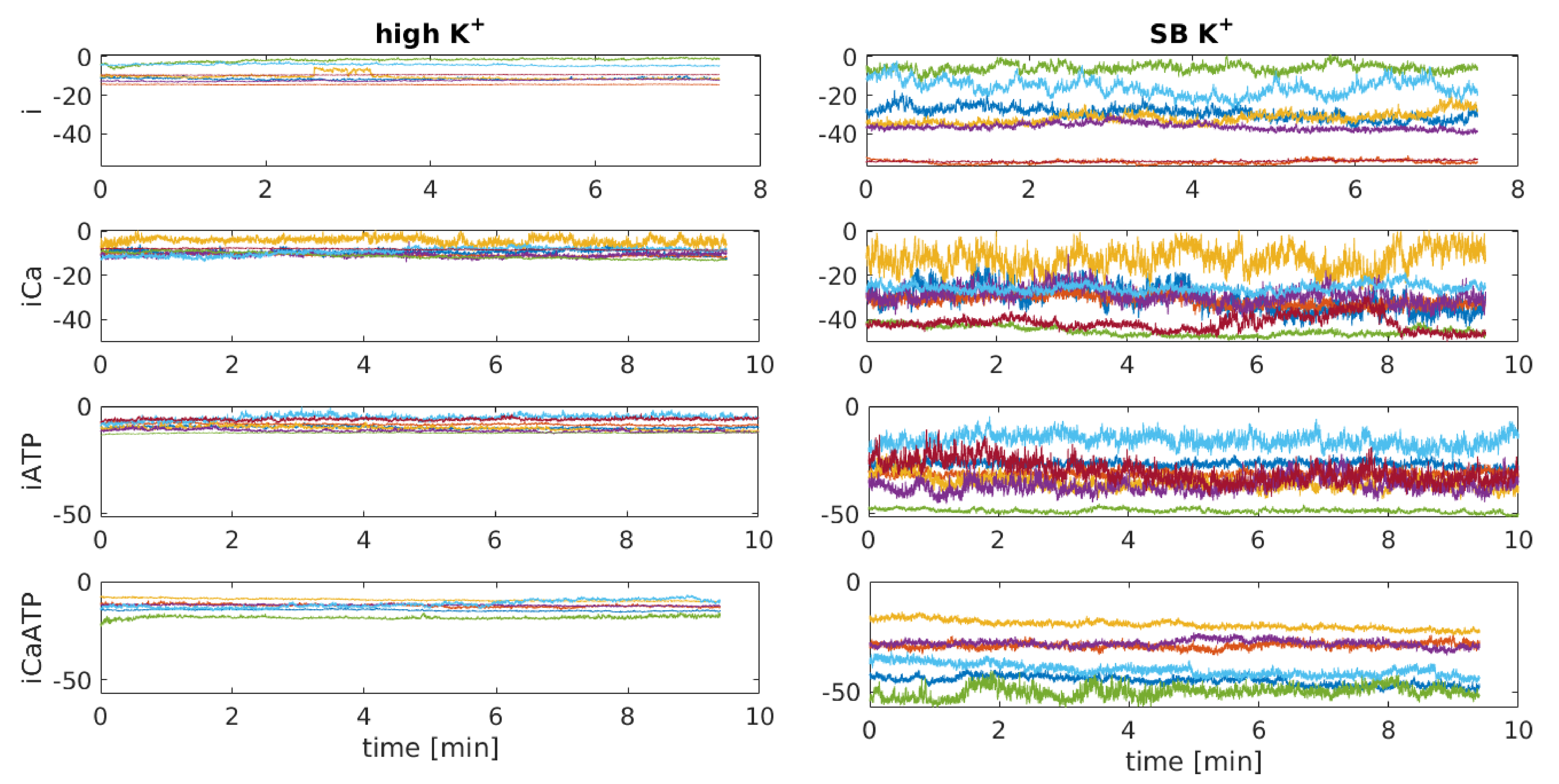

Fig. 2: Original time series for K^+ experiment, Adding ext. K^+ made voltage less negative and reduced fluctuations

Standard bath, K^+-permeable cell, ATP:

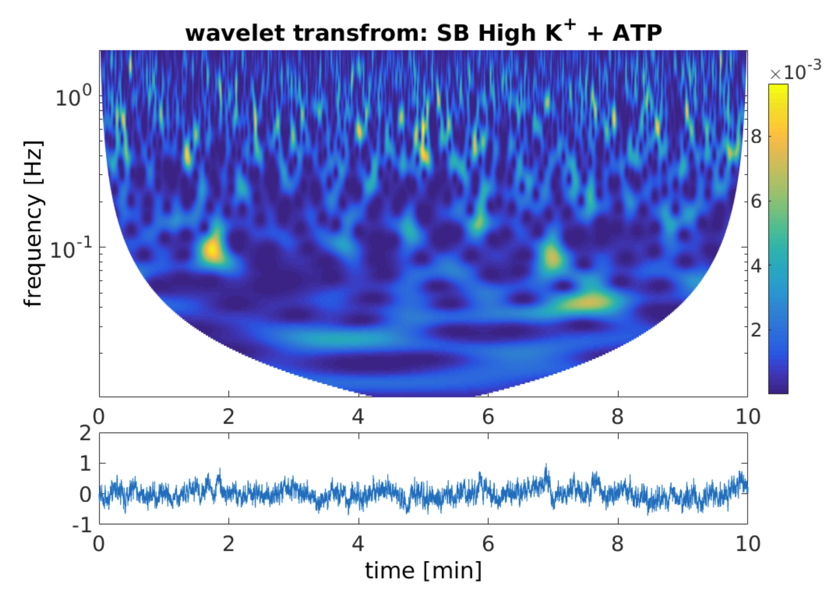

Fig. 3: Original dataset and its wavelet transform

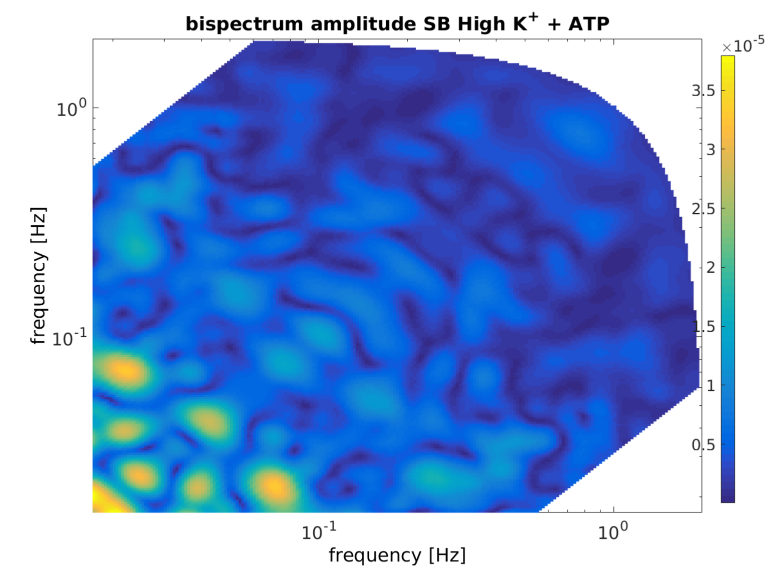

Fig. 4: Maxima in bispectrum indicate possible coupling

Coupling between frequencies s_1 and s_2 can be identified by peaks in the amplitude or observing the dynamics of phase $\phi(s_1, s_2)$, where if the phase is constant a coupling exists.

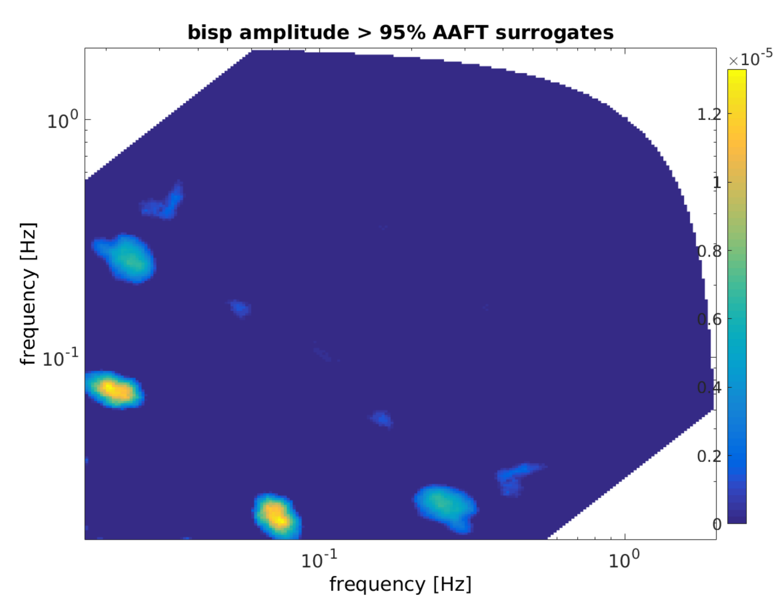

Fig. 5: bispectrum > 95% of 200 AAFT surrogates

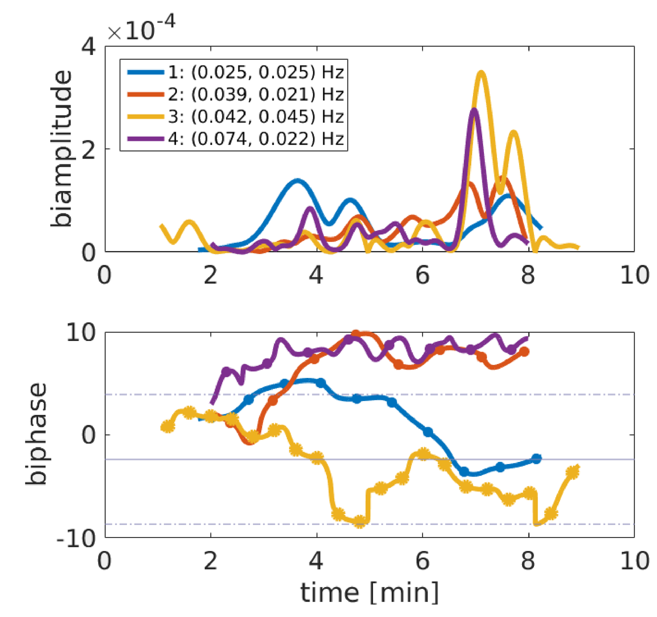

Fig. 6: Biamplitude and biphases for maxima in bispectrum

Summary

- Ions of K^+, Cl^-, Ca^{2+} and ATP influence membrane potential: increasing ext. K^+ depolarises the membrane and decreases the fluctuations; decreasing the ext. Cl^- depolarises the membrane and increases the fluctuations,
- Some indications of deterministic dynamics, nevertheless longer recordings could help to further elucidate the dynamics of the membrane potential.

References

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