Out-of-equilibrium thermodynamics of an active poroelastic system

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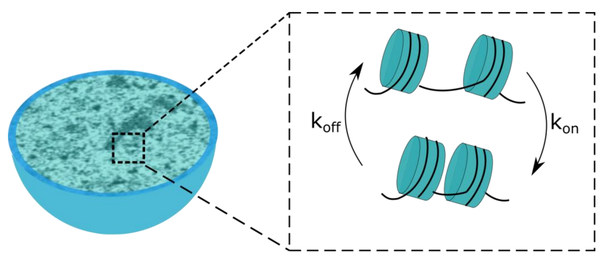
ABSTRACT

Living systems dissipate energy constantly as they perform essential functions. Because of their ordered and self-organized dynamics, these processes frequently result in complex behaviors that can be classified as non-thermal processes. However, it can often be challenging to tell whether a process' dynamics are significantly different from those of a thermally driven process.

Here, we present an active-poroelastic theoretical framework to represent chromatin as an active-elastic solid coupled to a permeating fluid. Based on experimental data suggesting large-scale correlated mobility of chromatin inside the nuclei of live differentiated cells, we include the active stress into a two-fluid model that accounts for the spatiotemporal dynamics of the nucleus. This system is affected by both passive thermal fluctuations and active scalar events, such as condensation and decondensation, which we name spikes. The coupled set of equations showing the presence of emergent processes is simulated in this instance.

ACTIVE POROELASTIC SYSTEM

Throughout the cell cycle, the chromatin in the nucleus undergoes different stages of compaction. The condensation and decondensation of these areas of chromatin is mediated by proteins called **histones**.



Spikes are the compaction or decompaction events of the histones. The wrapping and the unwrapping of the **nucleosomes** translate into pressure pulses.

We present a theoretical model for nonlinear wave propagation in an active poroelastic medium, which is the nucleus:

- The nucleus is considered as an **active gel** in which the package chromatin is embedded in an aqueous media and belongs to the solid component.
- The chromatin is quite compressible. A change in the volume fraction of the chromatin fiber in one location can be adjusted by solvent movement in or out of that region.
- Gene expression is a **stochastic process** in which random fluctuations affect the transcription of messenger RNA as fluctuations in the cell's automatisms.

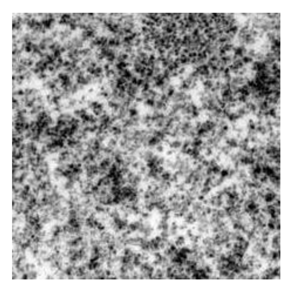


Image of the interior of the cell nucleus under electron microscopy.

Compaction - decompaction $\phi = \nabla u$

Spikes scalar activity can be defined as a change in the form's osmotic pressure:

$$\Pi(x,y,t) = K\phi(x,y,t) - \widetilde{\alpha}(x,y,t)$$

Π osmotic pressure
K osmotic constant
ζ mesh size
ϕ compactation
τ activation time

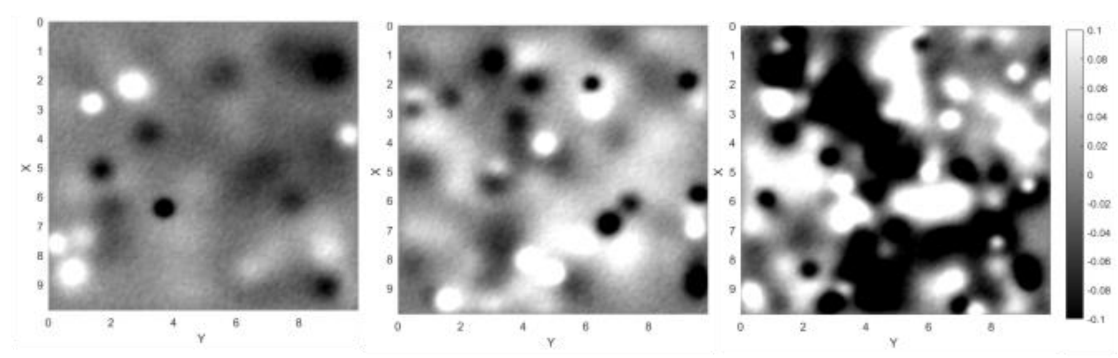
Where α is the **activity function** $\widetilde{\alpha}(x,y,t) = \sum_i s_i \delta(x-x_i)\delta(y-y_i)\theta(t)e^{-t/\tau}$

We arrive at a **diffusion equation**:

Noise term $\langle \xi(t) \rangle = 0$, $\langle \xi(t'), \xi(t) \rangle = 2k_B T \delta(t-t')$

$$\boxed{\frac{\partial \phi(x,y,t)}{\partial t} = D\nabla^2 \phi(x,y,t) + \alpha(x,y,t) + \sigma \xi(t)}$$

with $D = K\dfrac{(1-\phi_0)^2}{\zeta/\phi_0}$



Coupling distance

$$l \lesssim \sqrt{D\tau}$$

$$l \lesssim (1-\phi)\sqrt{\frac{\phi K \tau}{\zeta}}$$

RESULTS

We study the spatial and temporal structure of the system through the **Fourier transform**.

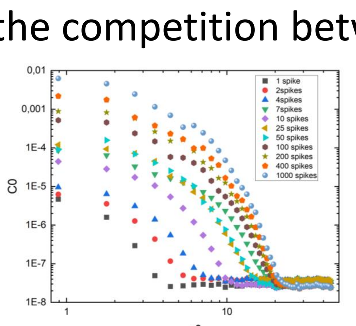
$$i\omega\phi(\vec{q},\omega) = -Dq^2\phi(\vec{q},\omega) + \sum_i^{t \in [t_i, t_i+\tau_{act}]} s_i e^{(x_i+y_i)\omega} + \sigma$$

$$E_{noise} = \frac{1}{T}\int \Phi^2_{noise} dx^2$$

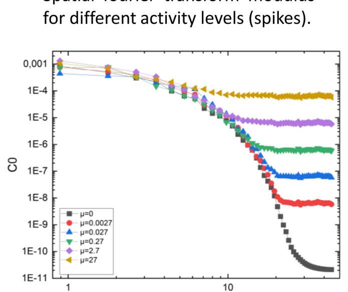
$$E_{spikes} = \frac{1}{T}\int \Phi^2_{spikes} dx^2$$

Ratio between noise and spike energy: $\dfrac{E_{noise}}{E_{spikes}} \sim \dfrac{\Delta\mu}{kT}$

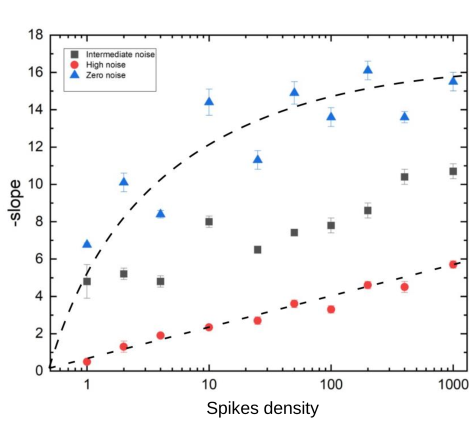
- **Spatial structure**: different behaviors are observed when varying noise and activity levels and the competition between them.



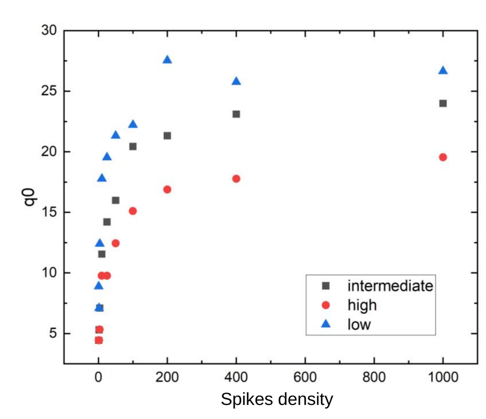
Spatial fourier transform modulus for different activity levels (spikes).



Spatial fourier transform modulus for different noise levels.

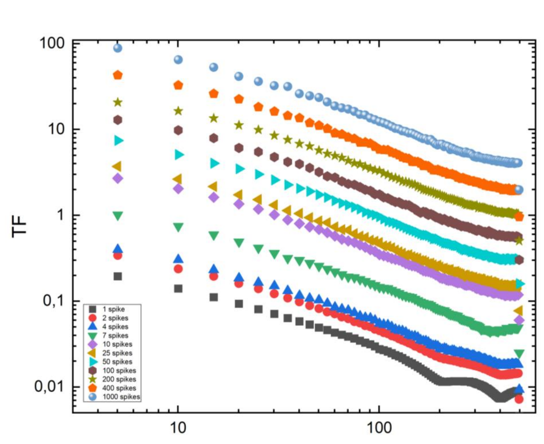


Fourier transform slopes as a function of the number of spikes for different noise levels.

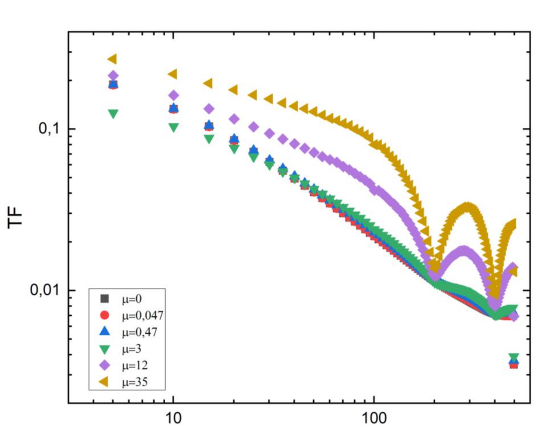


Cutoff frequency for the Fourier transform as a function of the number of spikes for different noise levels

- **Temporal structure:** for high noise levels vs. activity, structure factor type behaviors appear.



Temporal fourier transform modulus for different activity levels (spikes).

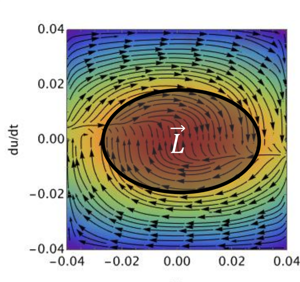


Temporal fourier transform modulus for different noise levels.

THERMODYNAMICS

Aiming to study of the dissipated energy, the tool of the **detailed broken balance** is used. The total current J is calculated with the components normal and parallel to the curve $\vec{L}$:

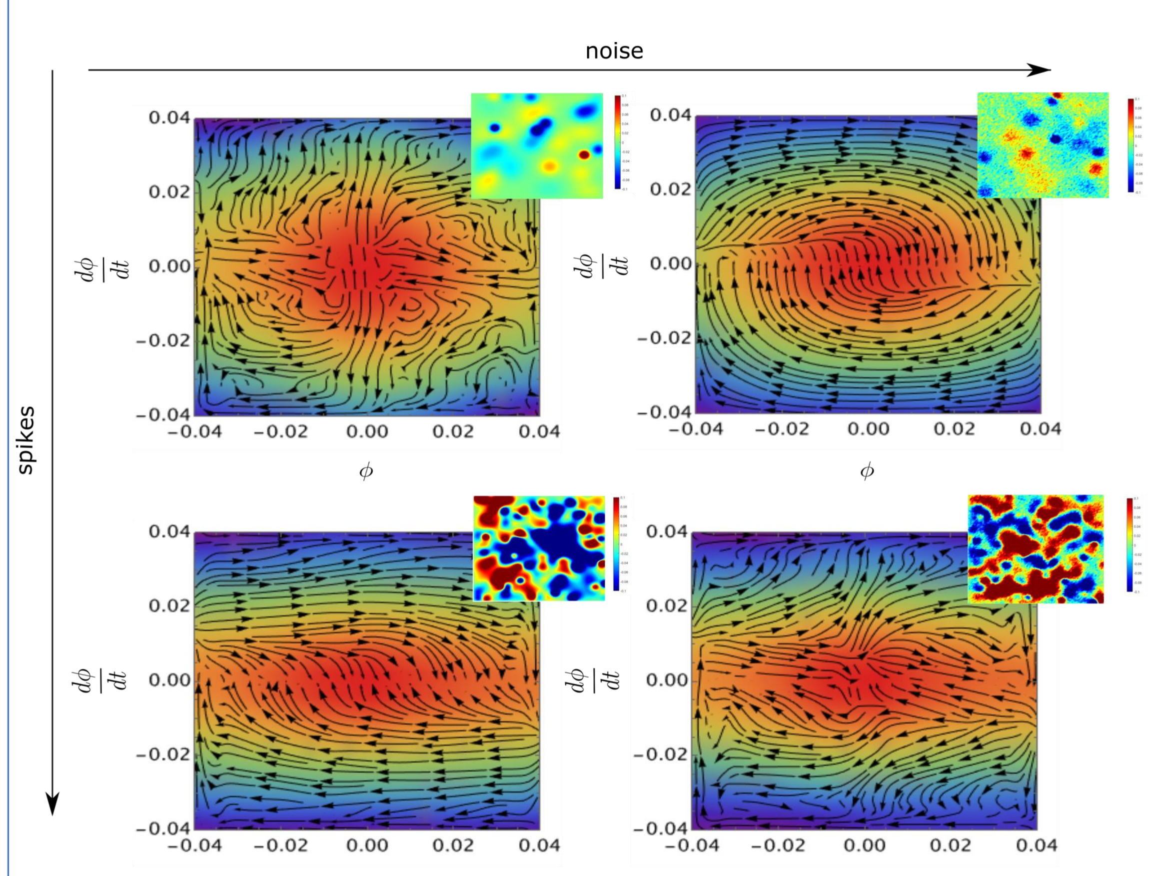
$$J = J_N + J_P = \left| \oint \vec{j} \times d\vec{L} \right| + \left| \oint \vec{j} \cdot d\vec{L} \right|$$



The **entropy production rate**, which is commonly connected to the energy dissipation in the system, is a measure to assess the time-irreversibility of a process.

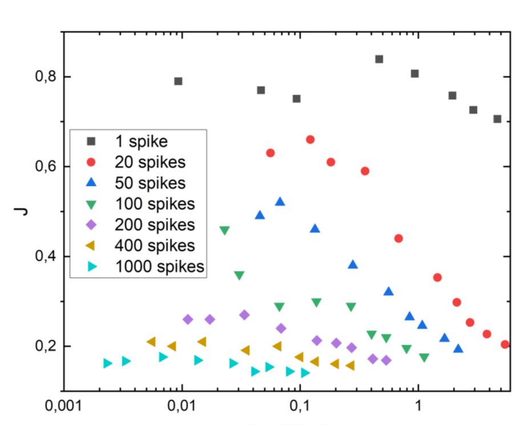
Thermodynamic Uncertainity Relation (TUR) $\dot{S} \geq \dfrac{2k_b \langle J \rangle^2}{\tau_{obs} Var(J)}$

The probability currents and entropy production are calculated by varying the activity and noise level:



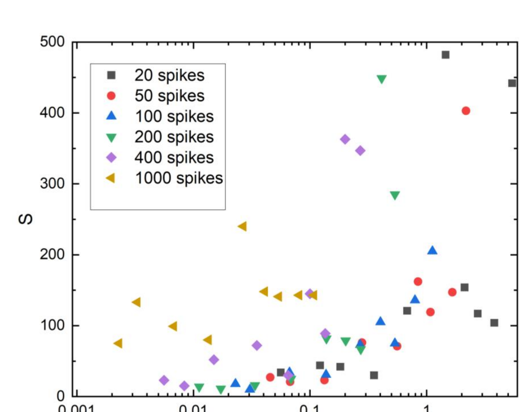
Broken detailed balance in phase space ϕ and $\frac{d\phi}{dt}$ for different noise and activity levels

- **Probability currents**



Probability currents as a function of the ratio between energies for different number of spikes

- **Entropy Production**



Entropy production as a function of the ratio between energies for different number of spikes

CONCLUSIONS

A continuous active poroelastic system representing the cell nucleus has been modelled:

- A simple poroelastic model based on two-fluid dynamics is able to form coupling patterns similar to experimental results.
- Different types of patterns are observed depending on the compactness and noise of the system, showing signs of competition and cooperation between activity and noise.
- A consistent way has been found to quantify the energy dissipated by the system through the probability currents in a phase space and the thermodynamic uncertainty relation.
- Entropy production increases exponentially as noise increases due to the loss of spatial structure.

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