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ABSTRACT

Astrocytes regulate neuronal information processing through a variety of spatio-temporal calcium signals. Advances in calcium imaging started to reveal astrocytic activities, but the complexity of the recorded data strongly call for computational analysis tools. Their development is hindered by the lack of reliable annotations that are essential for their evaluation and for the design of learning-based methods. To overcome the labeling problem, we present a framework to simulate realistic astrocytic calcium signals in 3D+time lattice light sheet microscopy (LLSM) images by closely modeling calcium kinetics in real astrocytes.



on Biomedical Imaging



Determination of \mathbf{X}_{c}

Determination of \mathbf{X}_{c}



The three calcium puff sites of the wave



Simulation of Astrocytic Calcium Dynamics in Lattice Light Sheet Microscopy Images

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Simulation (microscale)

 $\text{ if } \mathbf{x} \in \mathcal{A},$

•
$$g(\mathbf{x}) = \begin{cases} \gamma e^{-\left(\frac{\|\mathbf{x}-\mathbf{x}_{0}\|}{2\sigma^{2}}\right)} \\ 0 \end{cases}$$

 $\frac{c \parallel^2}{2}$ otherwise.

 $\frac{\partial f_{\rm e}(\mathbf{x},t)}{\partial t} = \operatorname{div} \left(c(\|\nabla f_{\rm e}(\mathbf{x},t)\|) \nabla f_{\rm e}(\mathbf{x},t) \right)$

 \mathcal{A} : set of points belonging to astrocytes

•
$$\Delta t_{\mathrm{e}}\left(\sum_{n=1}^{N_{c}} \mu \mathbb{1}_{\mathcal{O}_{t}}(n) - \alpha\right)$$

 $\mathbb{1}_{\mathcal{O}_t}$: indicator function of the subset \mathcal{O}_t \mathcal{O}_t : set of open IP₃Rs at time *t*

$$\Delta_{t_e}$$
: temporal resolution N_c : number of IP $_3$ Rs in a cluste

Anisotropic Perona-Malik diffusion

: sequence simulating one calcium event $div(\cdot)$: divergence operator ${\mathcal E}$: set of points belonging to astrocytes' edges

 $f_{\mathbf{e}}(\mathbf{x}, t_0) = g(\mathbf{x}) + \beta \, \mathbb{1}_{\mathcal{E}}(\mathbf{x}),$

 β : maximum intensity $c(u) = \exp\left(-\left(\frac{u}{\kappa}\right)^{2}\right)$: conductivity function

$$f_{\rm e}(\mathbf{x}, t + \Delta t_{\rm e}) = f_{\rm e}(\mathbf{x}, t) + \Delta t_{\rm e} \frac{\partial f_{\rm e}(\mathbf{x}, t)}{\partial t} + \Delta t_{\rm e} \left(\sum_{n=1}^{N_c} \mu \, \mathbb{1}_{\mathcal{O}_t}(n) - \alpha\right)$$
(1)



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RESULTS

Figure 1



Maximum intensity projections of calcium puff (a) and waves (b)-(c) from real 3D+time lattice light sheet microscopy images ($\Delta t = 0.5 s$).

Maximum intensity projections of calcium puff (a) and waves (b)-(c) from our simulated 3D+time lattice light sheet microscopy images ($\Delta t = 0.5 s$)

Figure 2



Traces of the epicenters of calcium puffs present in real (a) and synthetic (b) 2D+time lattice light sheet microscopy images ($\Delta t = 0.01 s$)

CONCLUSIONS

Contributions

- Generation of 3D+time LLSM images depicting astrocytic activity. First simulator of its kind
- Driven by a calcium kinetic model that we adapted from nanoscale to microscale
- Image background made of **real astrocytic ramifications**
- Simulation of **experimental conditions** of LLSM acquisitions (*e.g.*, noise and blur)
- Implementation as an ImageJ plugin with parameters and user interface

Results

- Variety of synthetic datasets that realistically represents the complexity of experimental data
- Helpful to develop computerized learning-based methods to analyze astrocytic calcium signals in 3D+time images





REFERENCES

- A. Denizot et al., "Simulation of calcium signaling in fine astrocytic processes: Effect of spatial properties on spontaneous activity," PLoS Computational Biology, 2019
- M. Ducros et al., "Lattice light sheet microscopy and photostimulation in brain slices," Neural Imaging and Sensing, 2019
- M. Arizono *et al.*, " Structural basis of astrocytic Ca²⁺ signals at tripartite synapses," *Nature Communications*, 2020
- E. Bindocci *et al.*, "Three-dimensional Ca²⁺ imaging advances understanding of astrocyte biology," Science, 2017
- M. Santello et al., "Astrocyte function from information processing to cognition and cognitive impairment," *Nature Neuroscience*, 2019