



# Simulation of Astrocytic Calcium Dynamics in Lattice Light Sheet Microscopy Images

Anaïs Badoual, Misa Arizono, Audrey Denizot, Mathieu Ducros, Hugues Berry, U Valentin Nägerl, Charles Kervrann

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## ABSTRACT

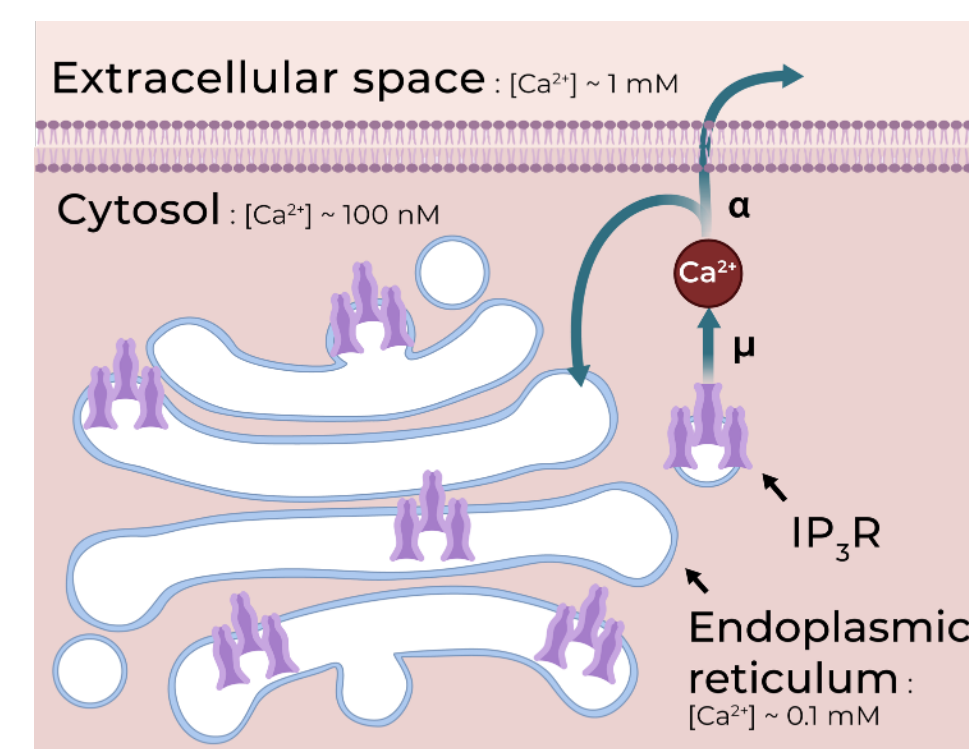
Astrocytes regulate neuronal information processing through a variety of **spatio-temporal calcium signals**. Advances in calcium imaging started to reveal astrocytic activities, but the complexity of the recorded data strongly call for computational analysis tools. Their development is hindered by the 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.

## METHOD

### Simulation of Calcium Puffs

#### Kinetic model (nanoscale)

- Stimulus at time  $t_0$  and location  $\mathbf{x}_c$  of an astrocyte triggering a  $\gamma$  variation of  $[Ca^{2+}]$



- Cytosolic calcium fluxes:

- Brownian motion

#### Simulation (microscale)

$$g(\mathbf{x}) = \begin{cases} \gamma e^{-\left(\frac{\|\mathbf{x} - \mathbf{x}_c\|^2}{2\sigma^2}\right)} & \text{if } \mathbf{x} \in \mathcal{A}, \\ 0 & \text{otherwise.} \end{cases}$$

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

$$\Delta t_e \left( \sum_{n=1}^{N_c} \mu \mathbb{I}_{\mathcal{O}_t}(n) - \alpha \right)$$

$\mathbb{I}_{\mathcal{O}_t}$  : 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 IP3Rs in a cluster

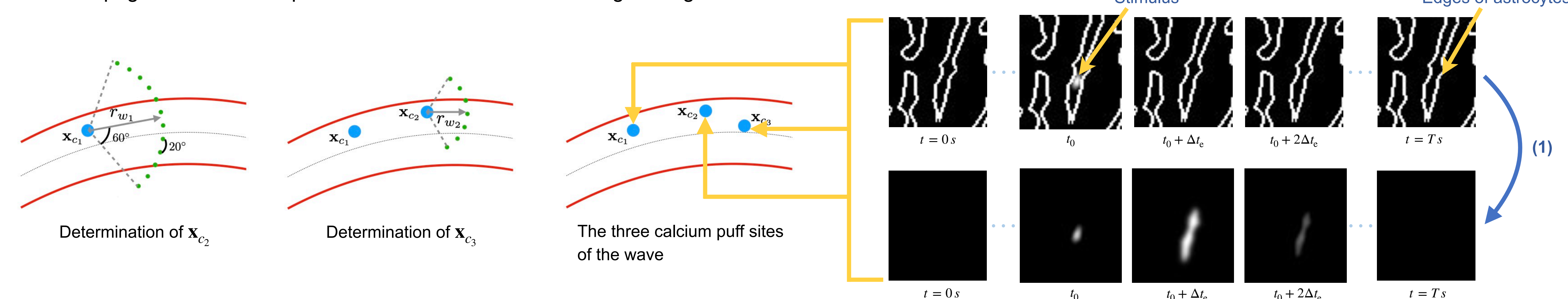
$$\begin{cases} \frac{\partial f_e(\mathbf{x}, t)}{\partial t} = \text{div} \left( c(\|\nabla f_e(\mathbf{x}, t)\|) \nabla f_e(\mathbf{x}, t) \right) \\ f_e(\mathbf{x}, t_0) = g(\mathbf{x}) + \beta \mathbb{I}_{\mathcal{E}}(\mathbf{x}), \end{cases} \quad \text{Anisotropic Perona-Malik diffusion}$$

$f_e$  : sequence simulating one calcium event  
 $\text{div}(\cdot)$  : divergence operator  
 $\mathcal{E}$  : set of points belonging to astrocytes' edges  
 $\beta$  : maximum intensity  
 $c(u) = \exp\left(-\left(\frac{u}{\kappa}\right)^2\right)$  : conductivity function

$$f_e(\mathbf{x}, t + \Delta t_e) = f_e(\mathbf{x}, t) + \Delta t_e \frac{\partial f_e(\mathbf{x}, t)}{\partial t} + \Delta t_e \left( \sum_{n=1}^{N_c} \mu \mathbb{I}_{\mathcal{O}_t}(n) - \alpha \right) \quad (1)$$

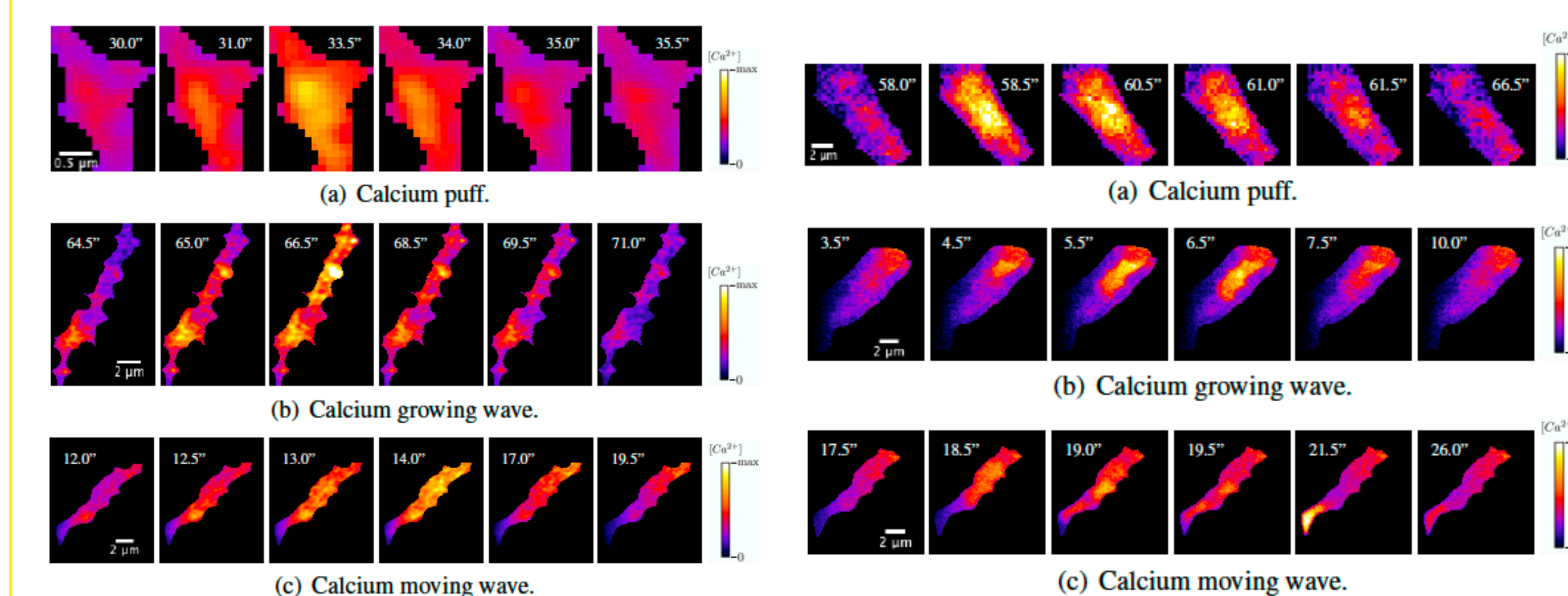
### Simulation of Calcium Waves

- Propagation of calcium puffs from a IP3R cluster to the neighboring ones



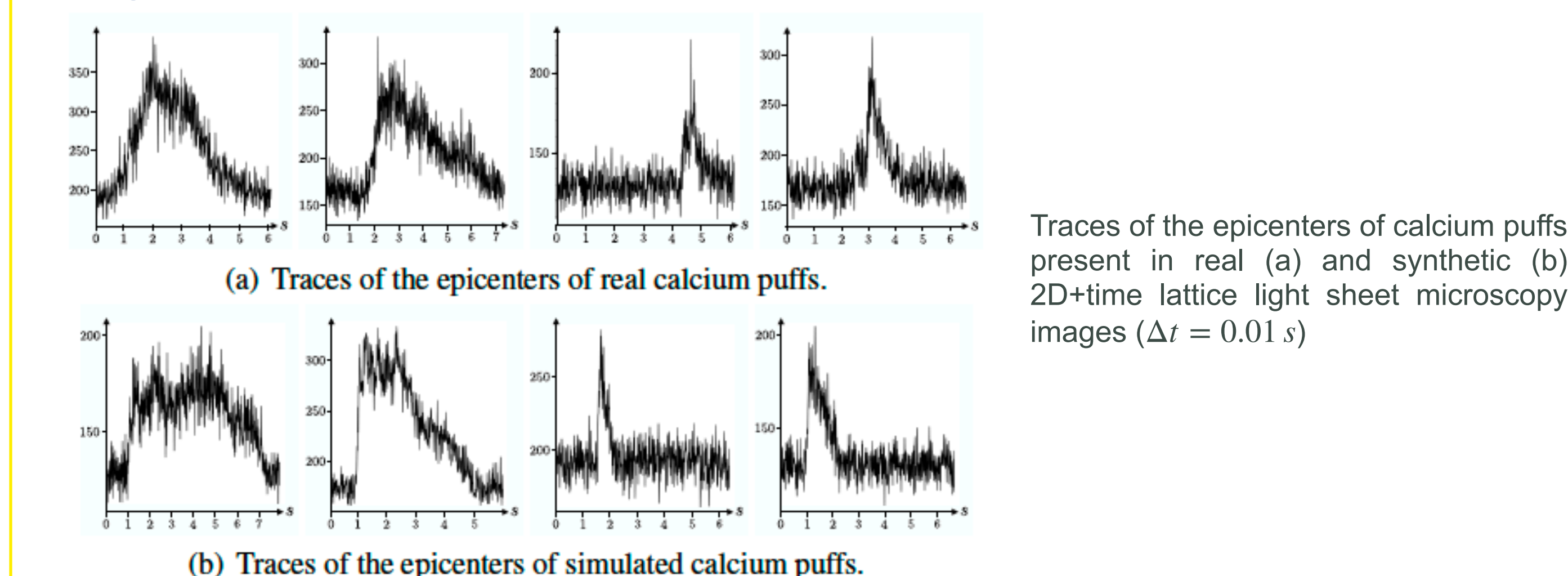
## RESULTS

### Figure 1



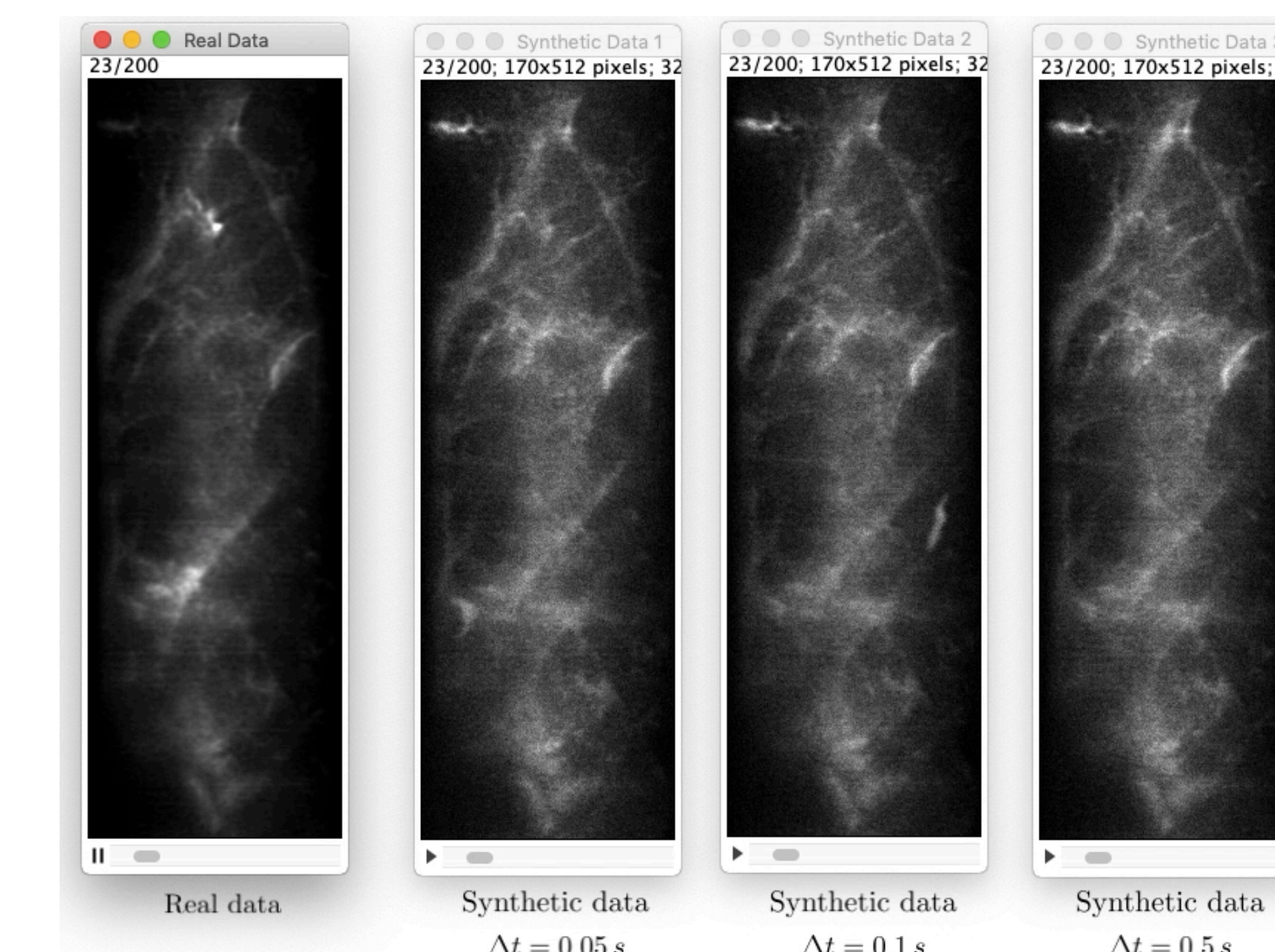
Maximum intensity projections of calcium puff (a) and waves (b)-(c) from real 3D+time lattice light sheet microscopy images ( $\Delta t = 0.5$  s).

### Figure 2

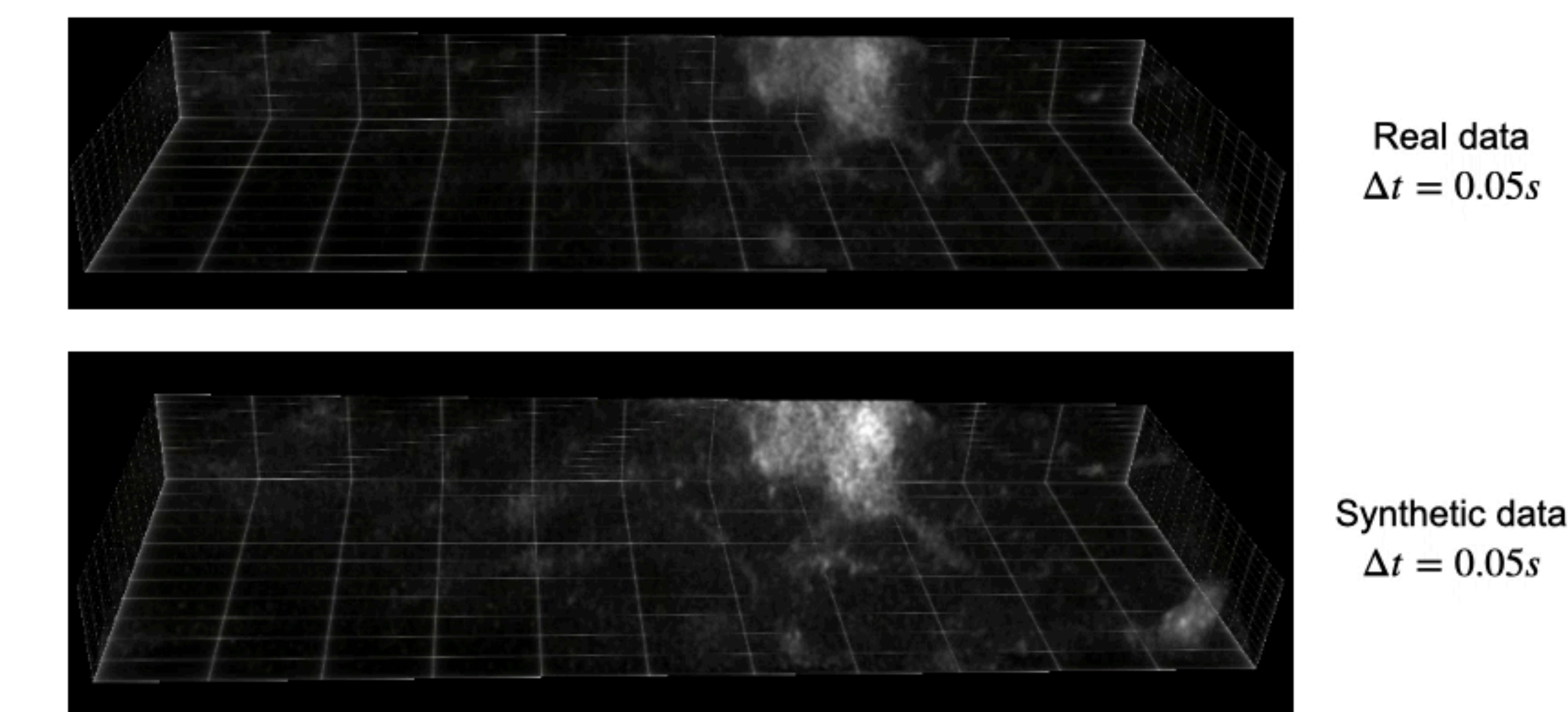


Traces of the epicenters of calcium puffs present in real (a) and synthetic (b) 2D+time lattice light sheet microscopy images ( $\Delta t = 0.01$  s).

### Video 1: 2D+time sequences



### Video 2: 3D+time sequences



## 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

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