Simularium

Software to collaboratively model biological systems

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The Simularium Viewer: an interactive online tool for sharing spatiotemporal biological models

Blair Lyons, Eric Isaac, Na Hyung Choi, Thao P. Do, Justin Domingus, Janet Iwasa, Andrew Leonard, Megan Riel-Mehan, Emily Rodgers, Lisa Schaefbauer, Daniel Toloudis, Olivia Waltner, Lyndsay Wilhelm & Graham T. Johnson

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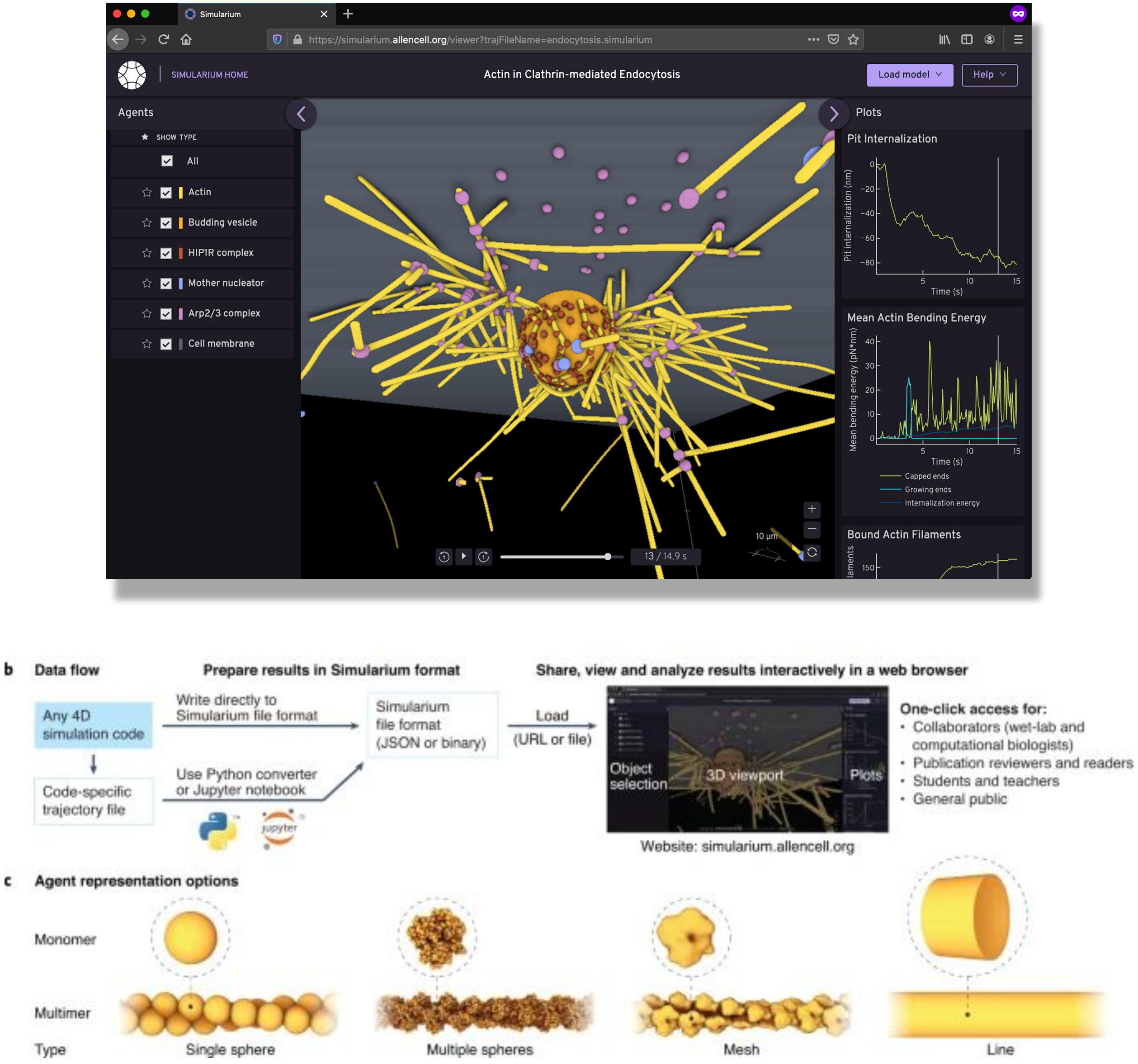
2124 Accesses | **54** Altmetric | Metrics

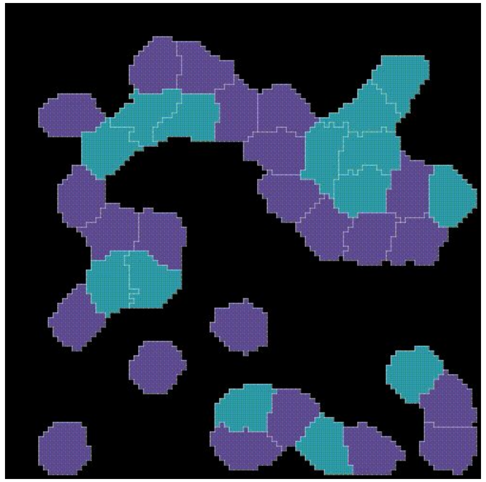
To the Editor – We present the Simularium Viewer, a user-friendly, open-source application that makes it easy to share and interrogate interactive three-dimensional (3D) visualizations of biological simulation trajectories directly in a web browser at https://simularium.allencell.org. The primary goal of the Simularium project is to facilitate collaborations among experimental and computational biologists by removing challenges to sharing, accessing and comparing simulation results. As a new arrow in the modeling community's quiver, the Simularium Viewer provides a platform to share simulation outputs in an easy-to-use interface that requires no computational expertise from end users. With a relatively small effort, any modeling researcher can use our conversion package to save their data as a Simularium file and generate a link that anyone can use to interactively investigate their simulation trajectories and related plots immediately in a browser, instead of spending time downloading, installing and learning to use tools specific to any given model.

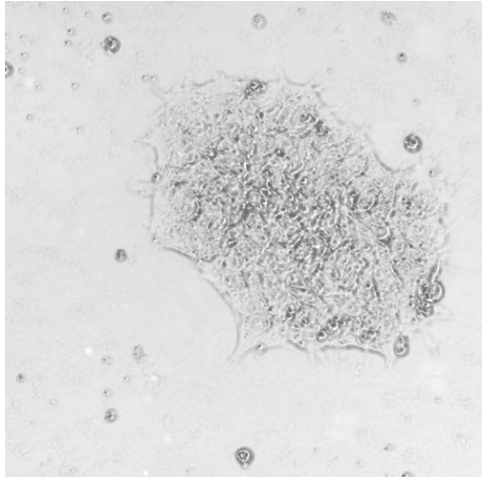


Simulations can provide biological insight when used in combination with wet lab experiments

cellular potts model
of growing cells

modeled in ARCADE
by Jessica Yu



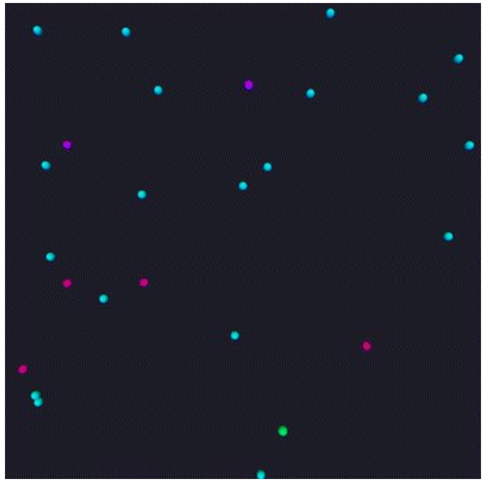


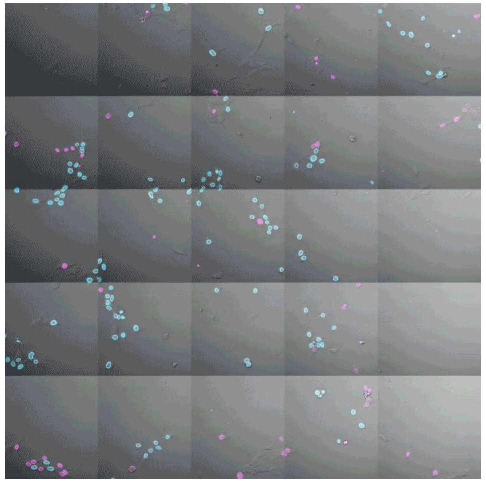
time lapse of growing IPSCs

AICS line 54 (CAAX-RFP)
acquired by Sara Carlson
(clip shows 6 hours)

center-based model
of growing cells

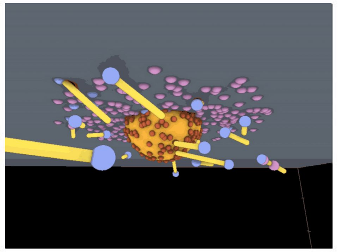
modeled in PhysiCell
by Julie Cass and Blair Lyons





time lapse of growing IPSCs

AICS lines 13 (laminB1-GFP)
and 34 (laminB1-RFP)
acquired by Irina Mueller
(clip shows ? hours)



15s

Actin in Clathrin-mediated Endocytosis

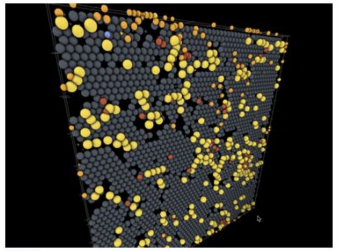
Matthew Akamatsu et al.

Principles of self-organization and load adaptation by the actin cytoskeleton during clathrin-mediated endocytosis. *eLife* (2020)

A CytoSim model of a branched actin network internalizing an endocytic pit against membrane tension.

Software used to generate this data is available here.

Please note that the use of this software is subject to third party licensing requirements, which are currently available here.



v4.1 24h

SARS-CoV-2 Dynamics in Human Lung Epithelium

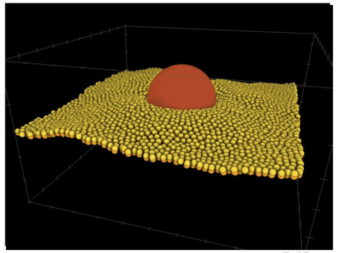
Michael Getz et al.

Rapid community-driven development of a SARS-CoV-2 tissue simulator. *bioRxiv* (2020)

A PhysiCell model of SARS-CoV-2 dynamics in human lung epithelium.

Software used to generate this data is available here.

Please note that the use of this software is subject to third party licensing requirements, which are currently available here.



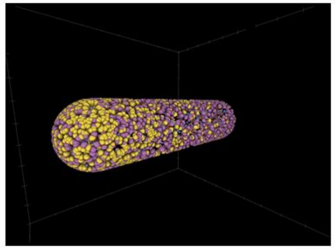
5.48ms

Membrane Wrapping a Nanoparticle

Mohsen Sadeghi et al.

Particle-based membrane model for mesoscopic simulation of cellular dynamics. *J Chem Phys* (2018)

A model of a coarse-grained particle-based membrane wrapping a nanoparticle.



100s

Spatiotemporal oscillations in the E. coli Min system

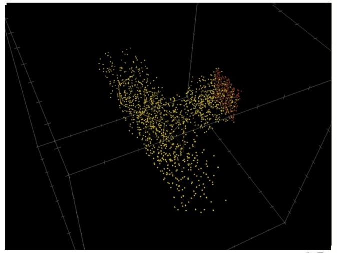
Steve Andrews et al.

Detailed Simulations of Cell Biology with Smoldyn 2.1. *PLoS Computational Biology* (2010)

A Smoldyn example model of the E. coli Min system, which is used to find the cell center during cell division.

Software used to generate this data is available here. The input data file is here.

Please note that the use of this software is subject to third party licensing requirements, which are currently available here.



1.5s

Sequestration of CaMKII in dendritic spines

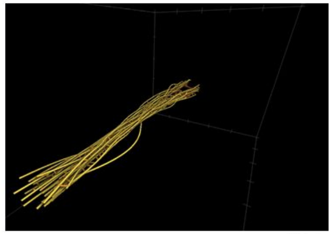
Shahid Khan et al.

Sequestration of CaMKII in dendritic spines in silico. *J Comp Neuro* (2011)

A Smoldyn model of a dendritic spine with CaMKII and molecules of the postsynaptic density at the spine tip.

Software used to generate this data is available here. The input data file is here.

Please note that the use of this software is subject to third party licensing requirements, which are currently available here.



33min

Actin Bundle Dynamics with α–Actinin and Myosin: Low Myosin Activity

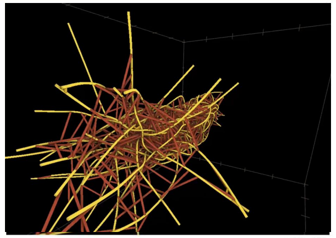
Chandrasekaran et al.

Remarkable structural transformations of actin bundles are driven by their initial polarity, motor activity, crosslinking, and filament treadmilling. *PLoS Computational Biology* (2019)

A MEDYAN model of interacting actin filaments, α–actinin crosslinkers, and myosin motors. Low myosin activity maintains the bundle structure.

Software used to generate this data is available here. The outputs that were visualized can be downloaded here.

Please note that the use of this software is subject to third party licensing requirements, which are currently available here.



33min

Actin Bundle Dynamics with α–Actinin and Myosin: High Myosin Activity

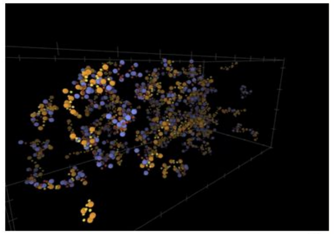
Chandrasekaran et al.

Remarkable structural transformations of actin bundles are driven by their initial polarity, motor activity, crosslinking, and filament treadmilling. *PLoS Computational Biology* (2019)

A MEDYAN model of interacting actin filaments, α–actinin crosslinkers, and myosin motors. High myosin activity causes formation of an aster-like structure.

Software used to generate this data is available here. The outputs that were visualized can be downloaded here.

Please note that the use of this ... requirements, which are curren...



1s

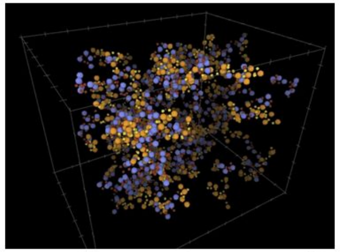
Condensate Formation: Below Ksp

Aniruddha Chattaraj et al.

The solubility product extends the buffering concept to heterotypic biomolecular condensates. *eLife* (2021)

A SpringSaLaD model of liquid-liquid phase separation below Ksp where no condensate forms.

Software used to generate this data is available here.



0.4s

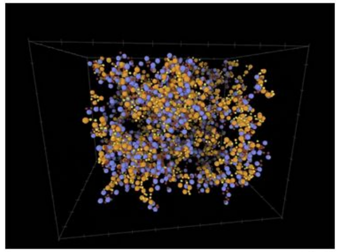
Condensate Formation: At Ksp

Aniruddha Chattaraj et al.

The solubility product extends the buffering concept to heterotypic biomolecular condensates. *eLife* (2021)

A SpringSaLaD model of liquid-liquid phase separation at Ksp where condensate forms.

Software used to generate this data is available here.



0.4s

Condensate Formation: Above Ksp

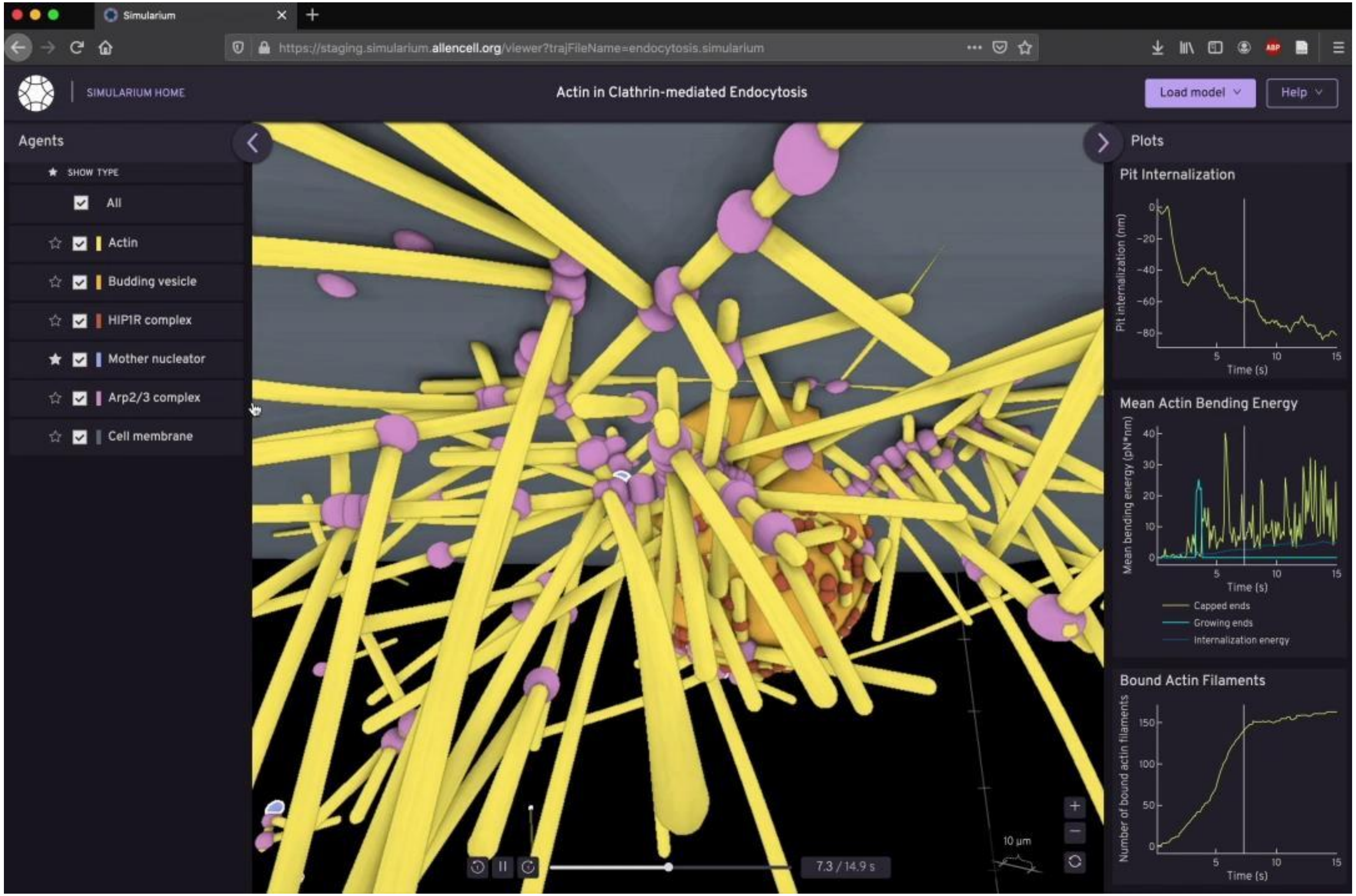
Aniruddha Chattaraj et al.

The solubility product extends the buffering concept to heterotypic biomolecular condensates. *eLife* (2021)

A SpringSaLaD model of liquid-liquid phase separation above Ksp where condensate forms.

Software used to generate this data is available here.

simularium.allencell.org

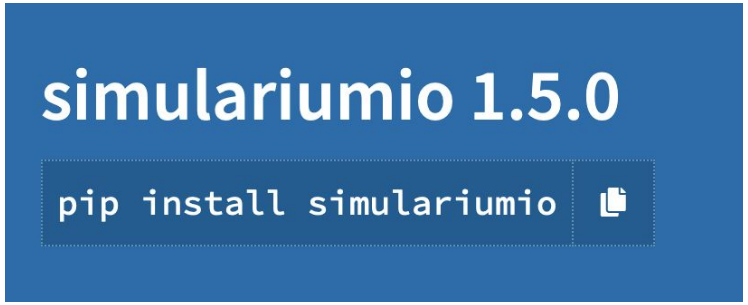


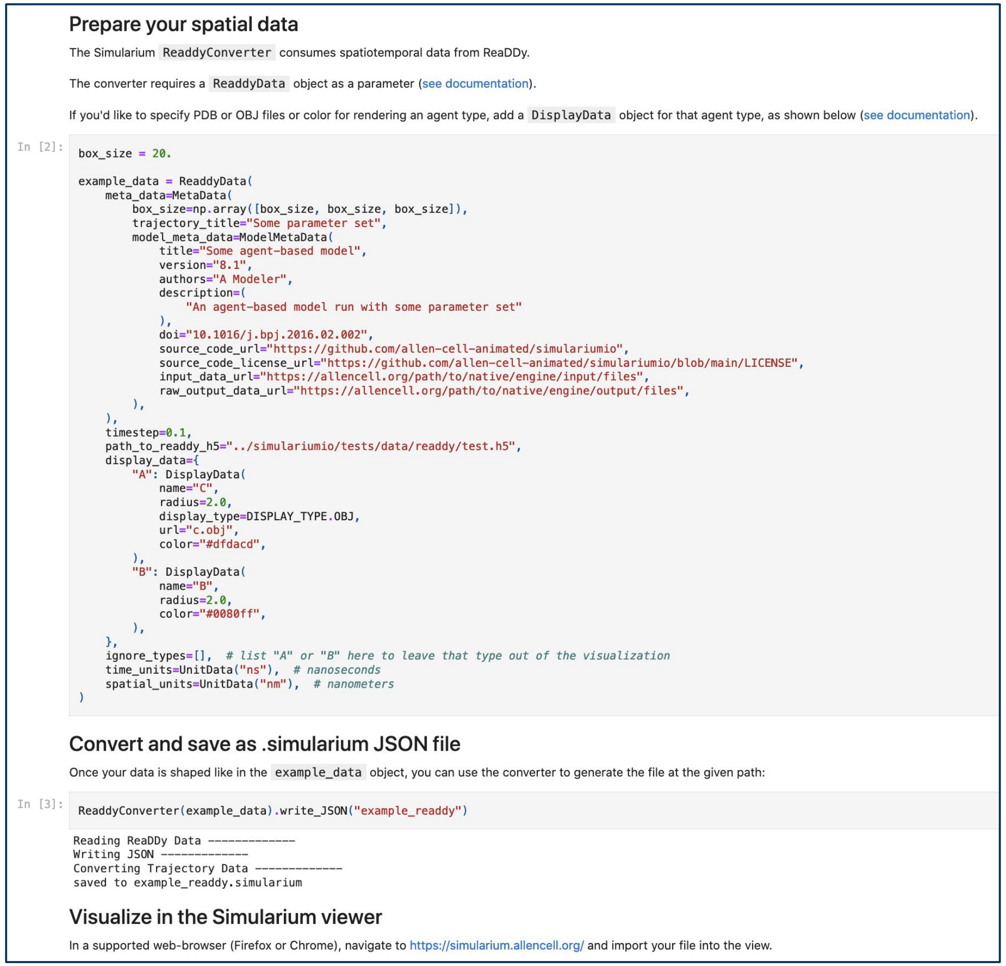
simularium.allencell.org

How Simularium works

1. **Convert data from simulation engines**

CytoSim
MCell
MEDYAN
PhysiCell
ReaDDy
Smoldyn
SpringSaLaD
Molecular dynamics (MDAnalysis)





Prepare your spatial data

The Simularium `ReaddyConverter` consumes spatiotemporal data from ReaDDy.

The converter requires a `ReaddyData` object as a parameter (see documentation).

If you'd like to specify PDB or OBJ files or color for rendering an agent type, add a `DisplayData` object for that agent type, as shown below (see documentation).

In [2]:

```
box_size = 20.

example_data = ReaddyData(
    meta_data=MetaData(
        box_size=np.array([box_size, box_size, box_size]),
        trajectory_title="Some parameter set",
        model_meta_data=ModelMetaData(
            title="Some agent-based model",
            version="8.1",
            authors="A Modeler",
            description=(
                "An agent-based model run with some parameter set"
            ),
            doi="10.1016/j.bpj.2016.02.002",
            source_code_url="https://github.com/allen-cell-animated/simulariumio",
            source_code_license_url="https://github.com/allen-cell-animated/simulariumio/blob/main/LICENSE",
            input_data_url="https://allencell.org/path/to/native/engine/input/files",
            raw_output_data_url="https://allencell.org/path/to/native/engine/output/files",
        ),
    ),
    timestep=0.1,
    path_to_readdy_h5="../simulariumio/tests/data/readdy/test.h5",
    display_data={
        "A": DisplayData(
            name="C",
            radius=2.0,
            display_type=DISPLAY_TYPE.OBJ,
            url="c.obj",
            color="#dfdacd",
        ),
        "B": DisplayData(
            name="B",
            radius=2.0,
            color="#0080ff",
        ),
    },
    ignore_types=[],  # list "A" or "B" here to leave that type out of the visualization
    time_units=UnitData("ns"),  # nanoseconds
    spatial_units=UnitData("nm"),  # nanometers
)
```

Convert and save as .simularium JSON file

Once your data is shaped like in the `example_data` object, you can use the converter to generate the file at the given path:

In [3]:

```
ReaddyConverter(example_data).write_JSON("example_readdy")
```

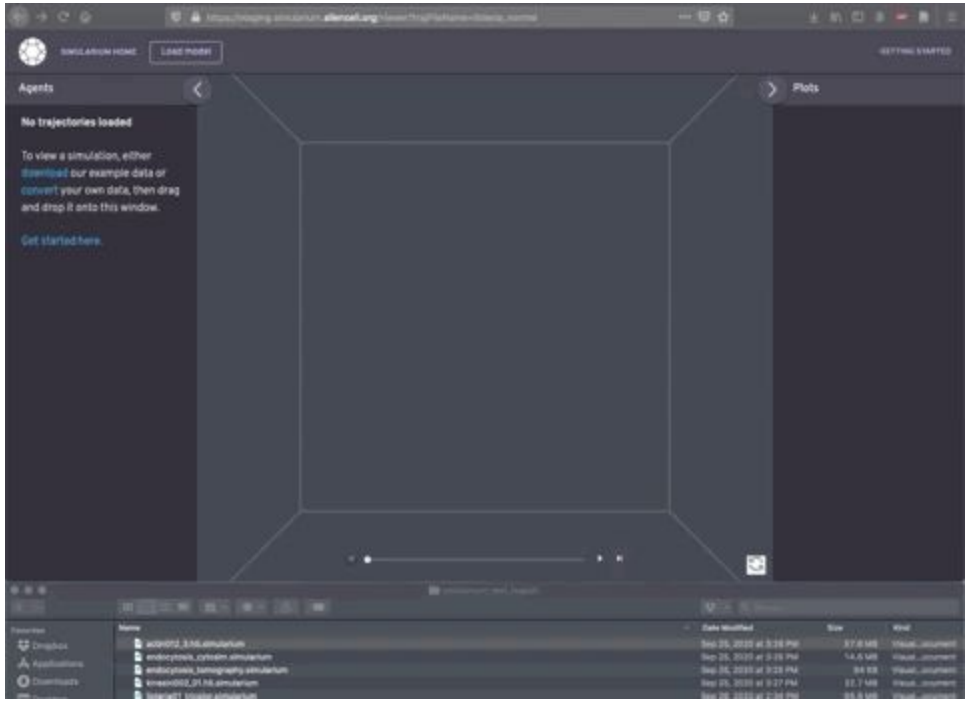
```
Reading ReaDDy Data -------------
Writing JSON -------------
Converting Trajectory Data -------------
saved to example_readdy.simularium
```

Visualize in the Simularium viewer

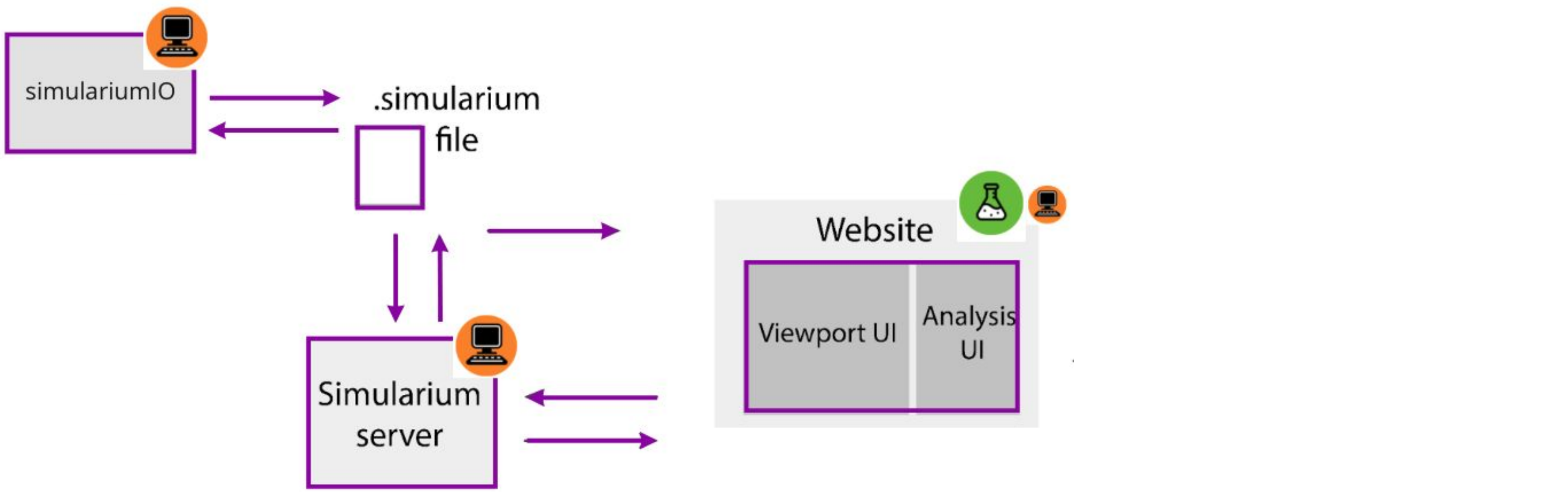
In a supported web-browser (Firefox or Chrome), navigate to https://simularium.allencell.org/ and import your file into the view.

How Simularium works

1. **Convert data from simulation engines**
2. **Load file in viewer at simularium.allencell.org/viewer**

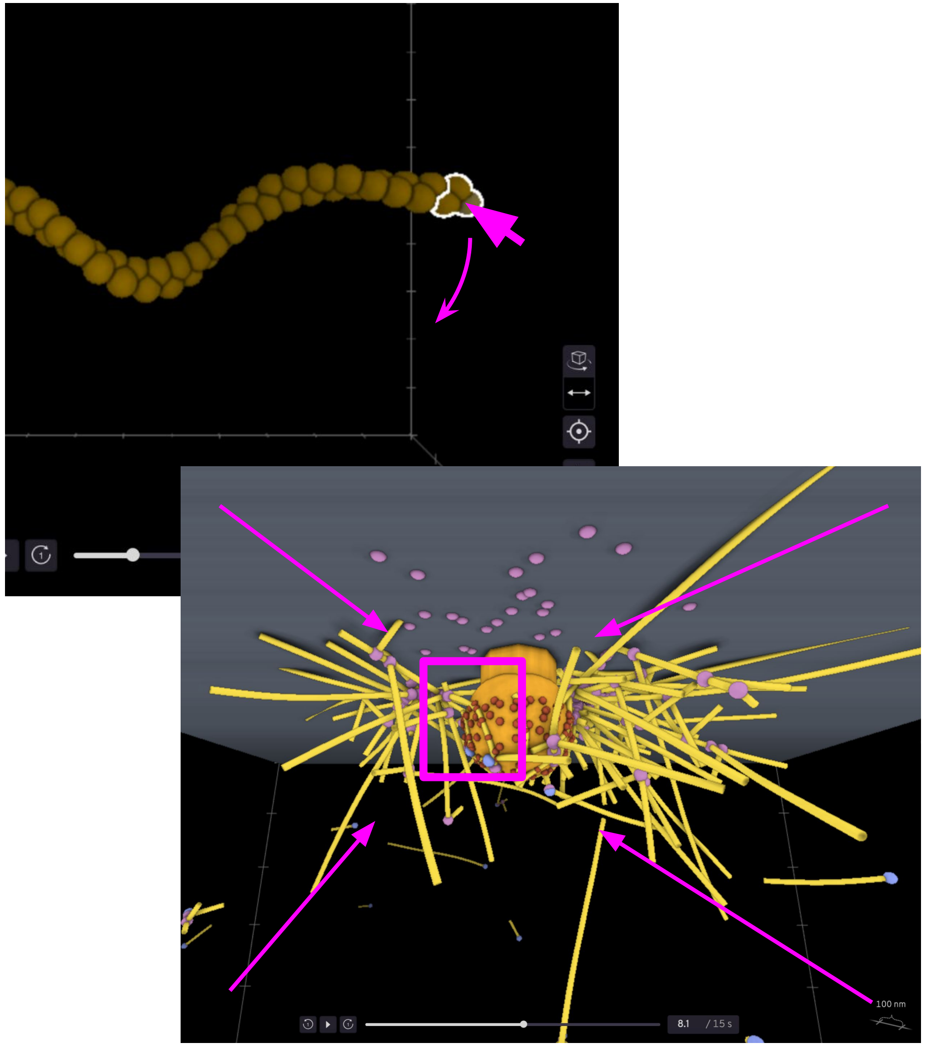


How Simularium works

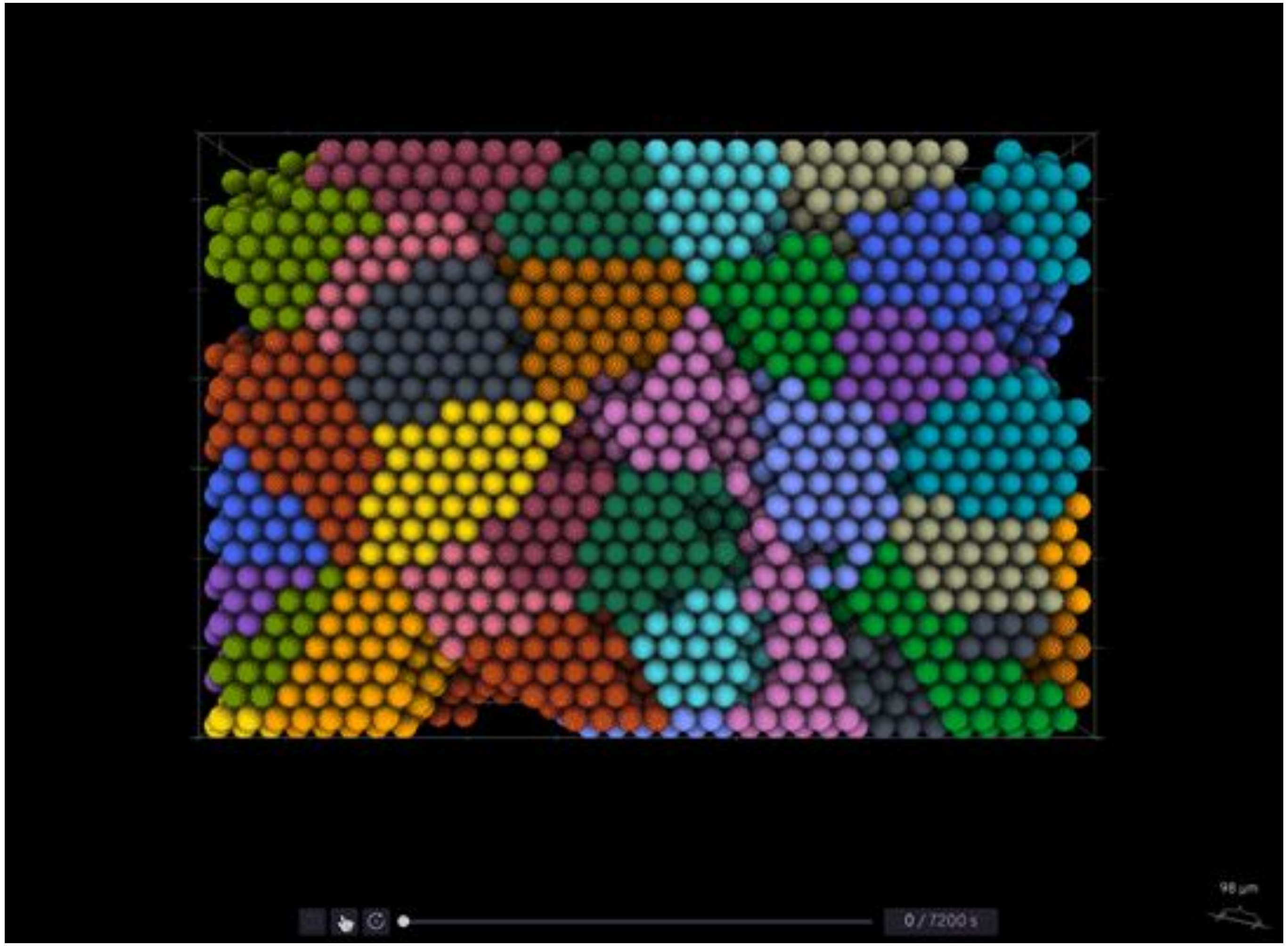


Opportunities

- Change parameters on simulations running live
  - to encourage input on assumptions and parameters from experimentalists
- Click and drag an agent as it simulates
  - for use in a classroom to build mechanistic intuition
- Zoom in to regions in 3D space
  - to steer model resolution interactively for exploration
- Simulate the same model with different methods
  - to help researchers compare the validity of different modeling frameworks



AICS PhysiCell modeling



Acknowledgments

We'd like to thank the following people for their contributions to Simularium

- **For training and development with their simulation engines:**
Johannes Schöneberg, Moritz Hoffmann, Christoph Fröhner, Frank Noé, François Nédélec, Adam Husar, Tom Bartol, Jacob Czech, Leslie Loew, Aniruddha Chattaraj, Michael Blinov, Ann Cowen, Ion Moraru, Garegin Papoian, Steve Andrews, Paul Macklin, Randy Heiland, Ryan Spangler, Eran Agmon, and James Faeder

- **For providing example data:**
Mohsen Sadeghi, Matthew Akamatsu, Daniel Serwas, Leslie Loew, Aniruddha Chattaraj, Jessica Yu, Julie Cass, and Jonathan Alberts

- **For their guidance over Simularium's goals and progress as part of the project advisory committee:**
Ron Vale, Torsten Moeller, Omar Quintero, Tom Goddard, and David Goodsell

- **For their input on how Simularium could be used for education:**
Omar Quintero, Derek Applewhite, Le Paliulis, Erin Dolan, Lalitha Jayant, and Carlos Goller

- **For participating in user tests to improve the Viewer and other prototypes:**
Matthew Akamatsu, Lindsay Case, Alyssa Harker, Kristen Verhey, Daniel Cortes, Andrew Nguyen, Cuncheng Zhu, and Karthik Vegesna

- **For discussion on how building and analyzing simulations could help them in their research or teaching:**
Julian Berro, Jiongyi Tan, Margot Quinlan, Lam Nguyen, Tamara Bidone, Glen Hocky, Christian Suarez, Simon Freedman, Carolyn Moores, Matt Akamatsu, Dave Kovar, Tom Pollard, Will Hancock, Michio Tomishige, Kimberly Tanner, Naina Phadnis, Sabrice Guerrier, Christina Vizcarra, Sarah Goodwin, Kathy Perkins, Kristen Verhey, David Frischer, Josh Sandquist, Melinda Owens, Brian Young, Ann Miller, and Jennifer Sallee

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Ludovic Autin and Ivan Viola

- **For inspiration and/or comments on manuscripts:**
Rick Horwitz, Julie Theriot