New Tools for Understanding and Engineering the Brain

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McGOVERN INSTITUTE FOR BRAIN RESEARCH AT MIT

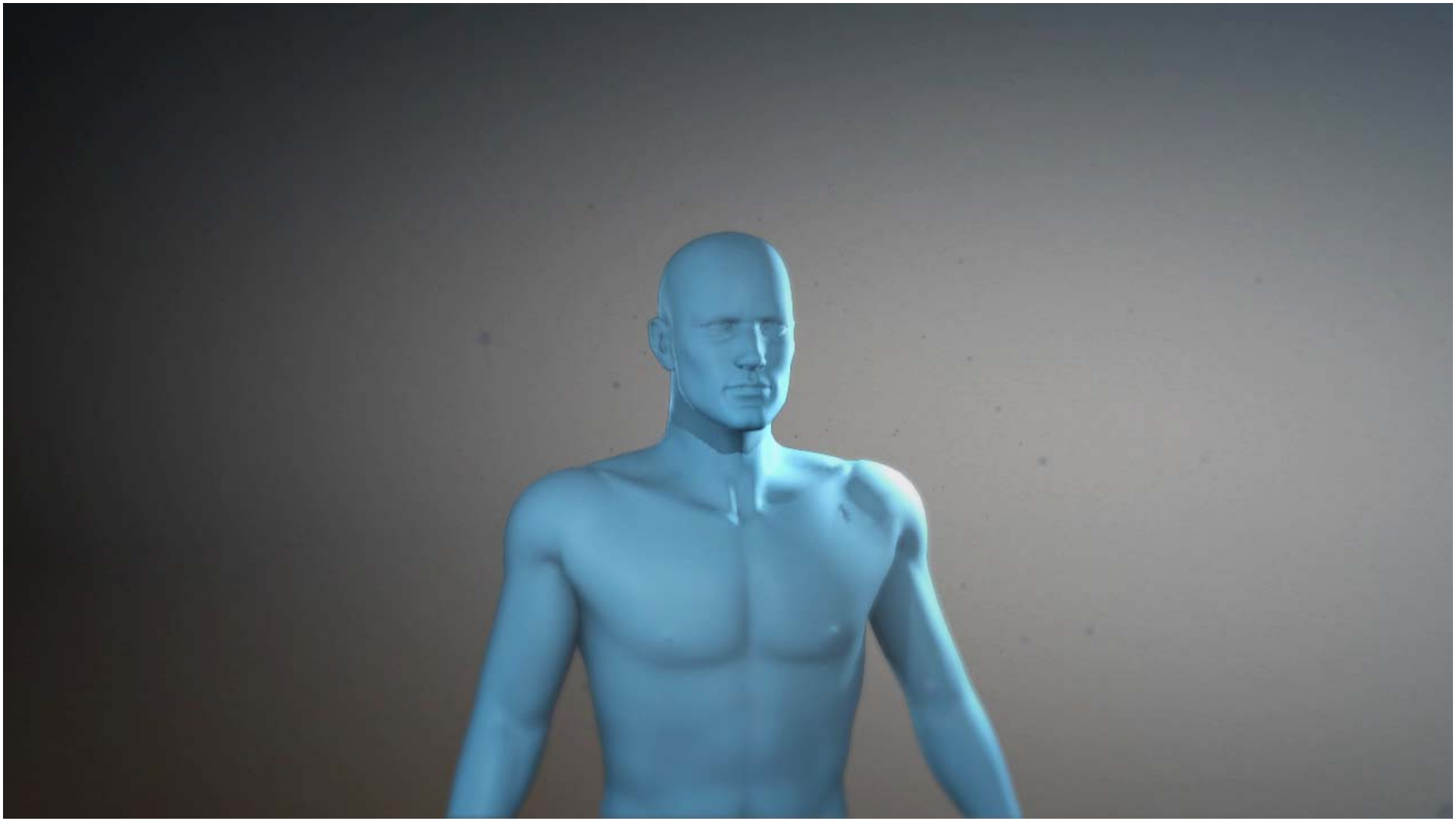
MIT BE BIOLOGICAL ENGINEERING

brain+cognitive sciences

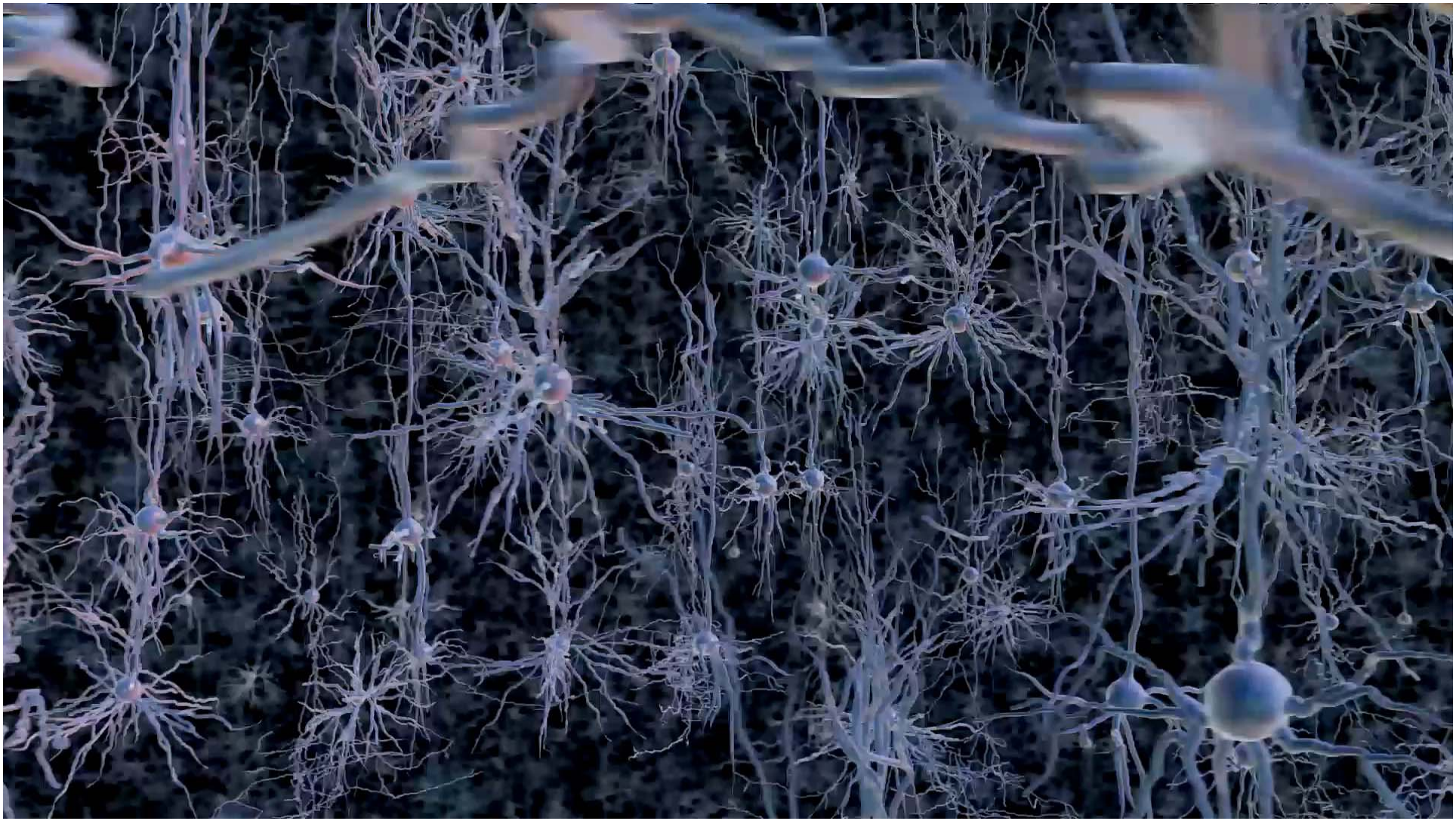
CNBE MIT CENTER FOR NEUROBIOLOGICAL ENGINEERING

NYSCF The New York Stem Cell Foundation NYSCF-Robertson Investigator

Space: Nanoscale building blocks, spanning centimeters



Time: Millisecond events, spanning seconds to years



What data do we need, to make detailed models of brain computations?

Map the **wires**

Map the **molecules** along those wires, and at connections

Need **dynamical** observations

Test with **causal** perturbation

1 billion people

Alzheimer's disease

obesity

sleep disorders

schizophrenia

depression

attention deficit disorder

stroke

ALS

anxiety

addiction

epilepsy

tinnitus

multiple sclerosis

spinal cord injury

autism

vision loss

migraine

traumatic brain injury

hearing loss

Parkinson's disease

chronic pain

Science 30 July 2010:
Vol. 329 no. 5991 pp. 502-504
DOI: 10.1126/science.329.5991.502

Is Pharma Running Out of Brainy Ideas?

Brain drugs:

Take **9 years**

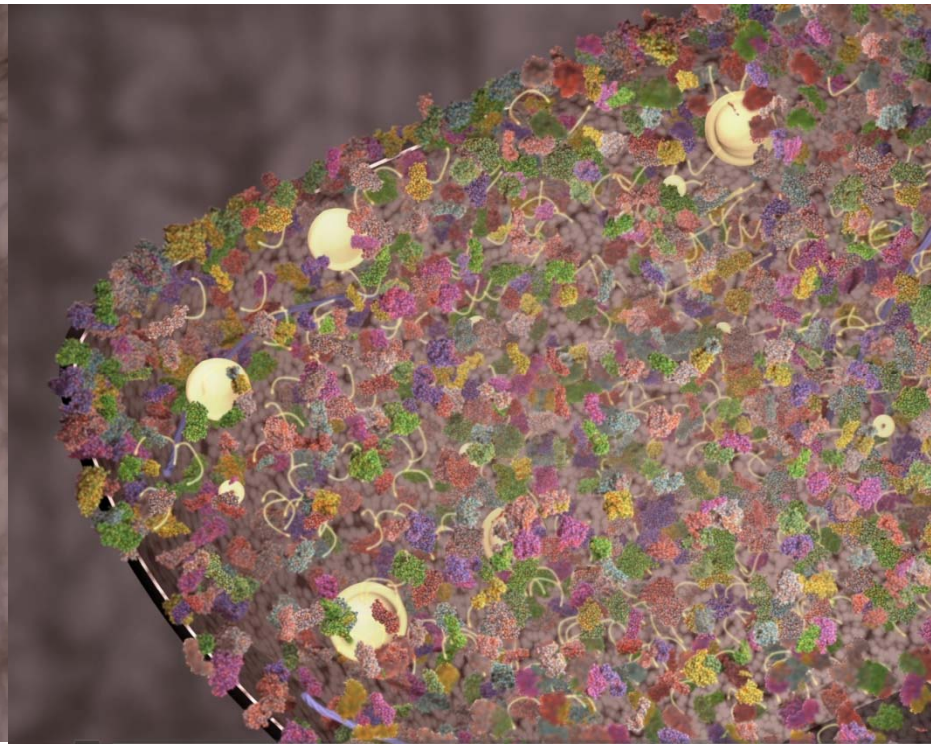
Fail 92% of the time

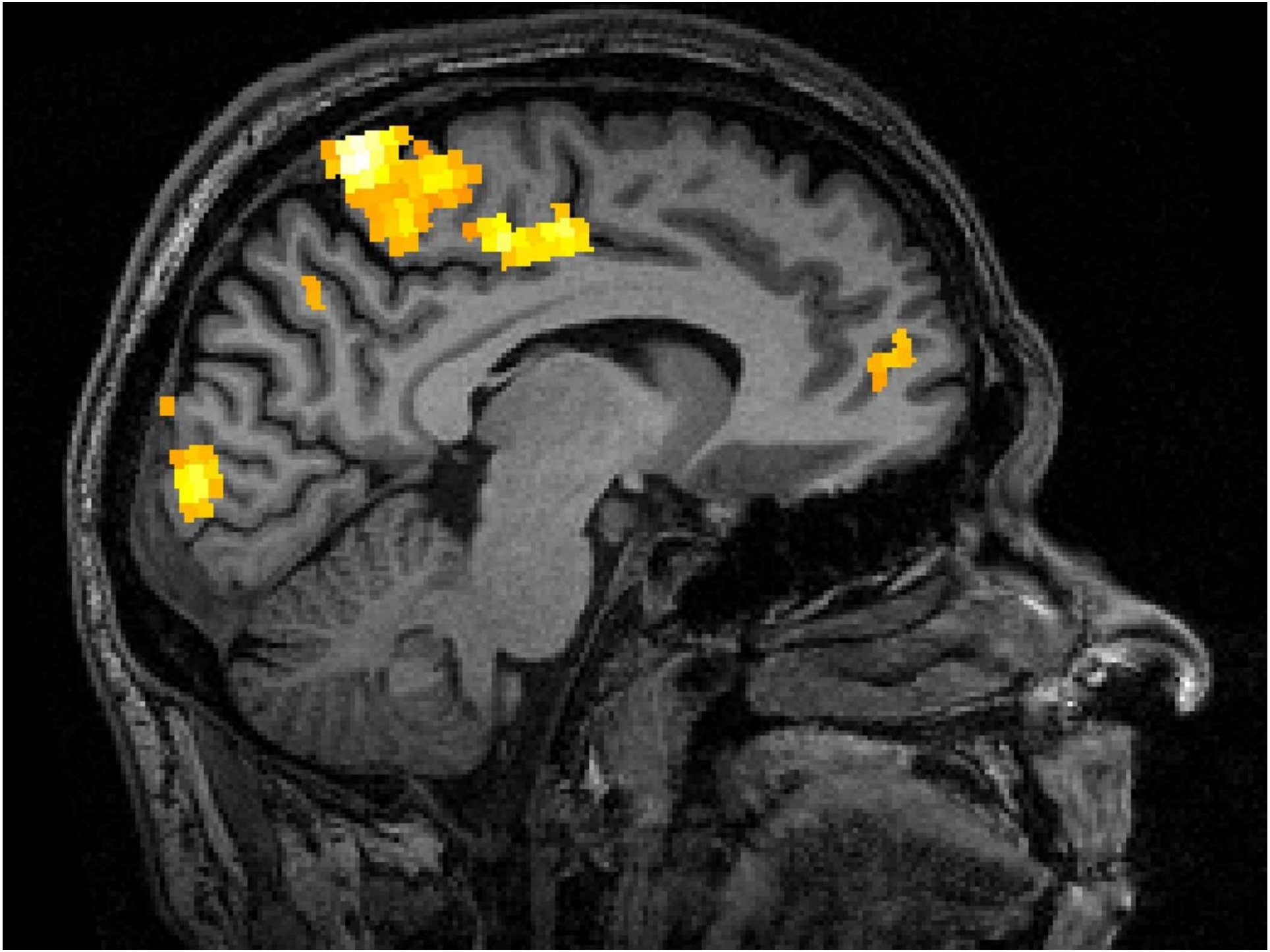
Cost $1 billion each

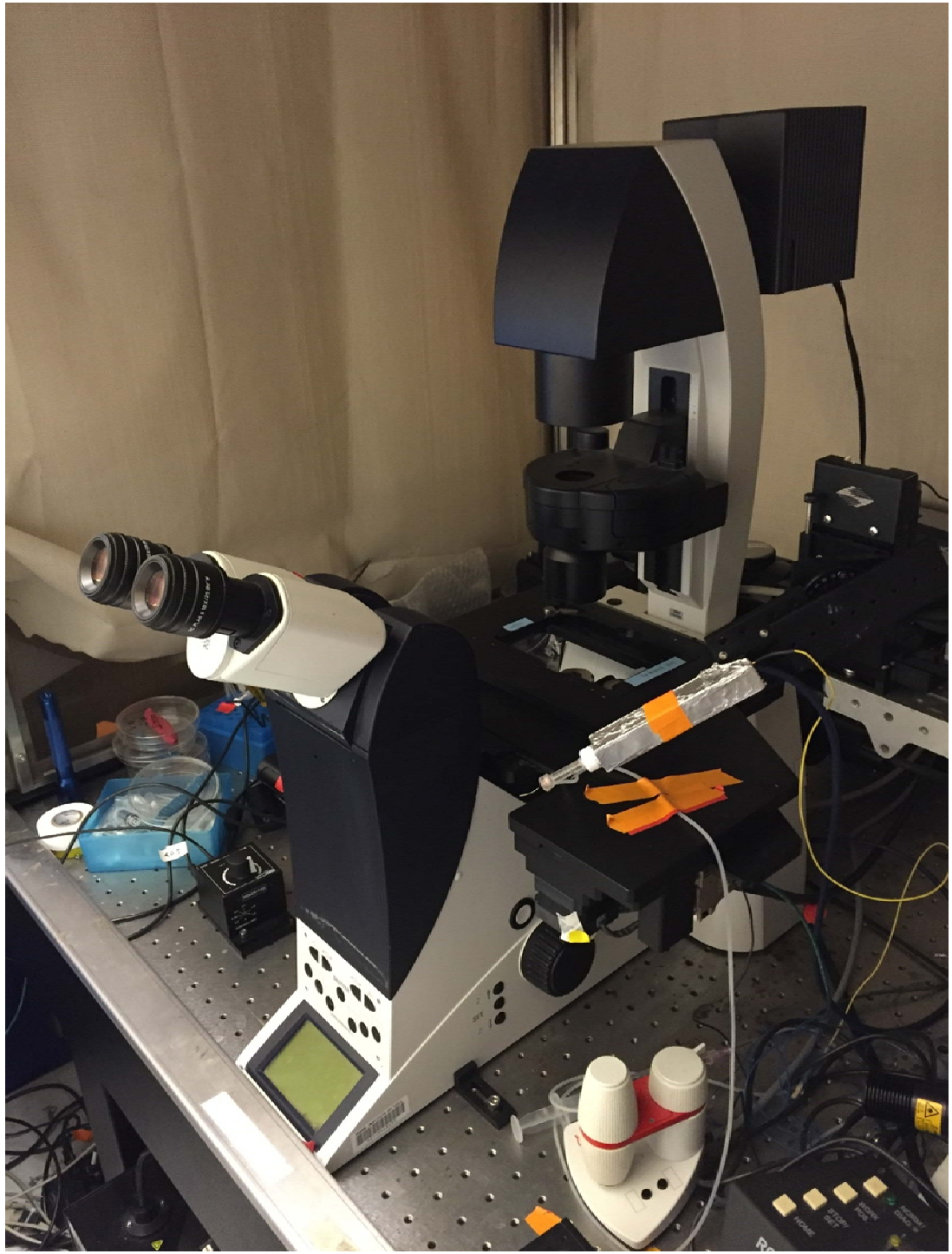
Partial success

How are neurons organized into networks?

How are biomolecules organized within neurons?



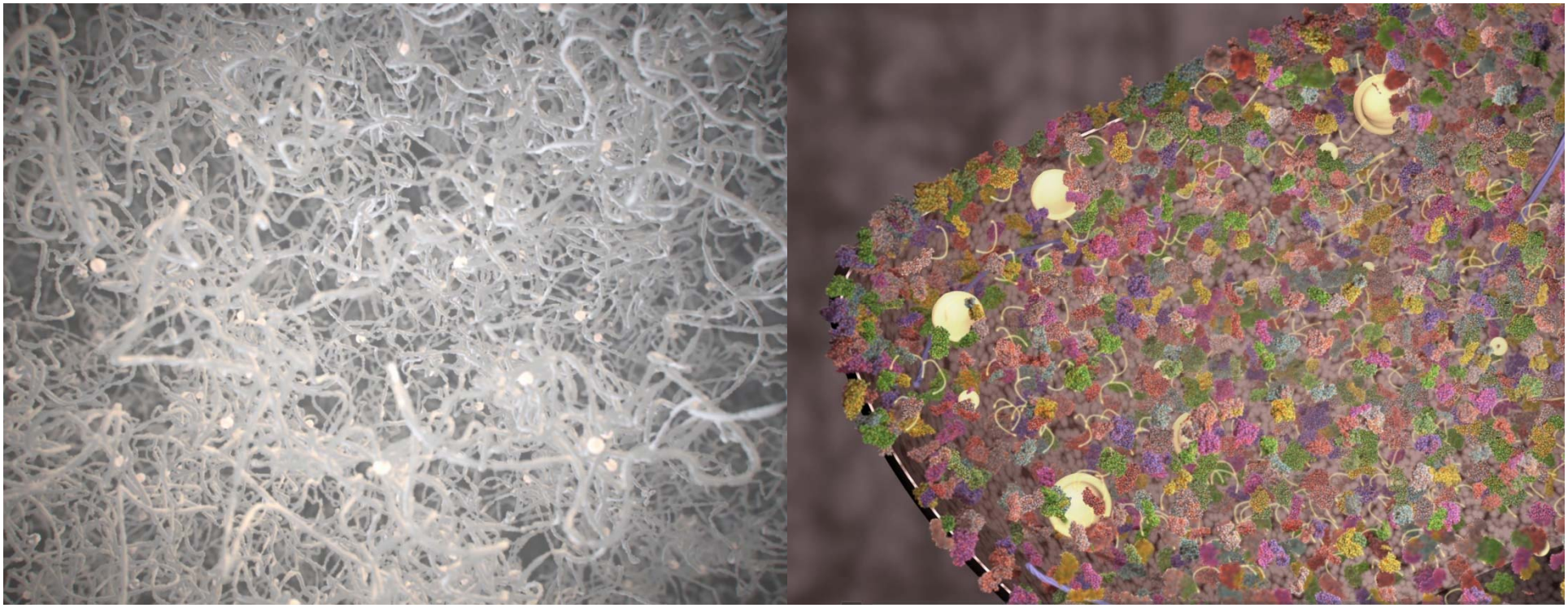




Expansion Microscopy

Can we install polymer chains of a swellable material…

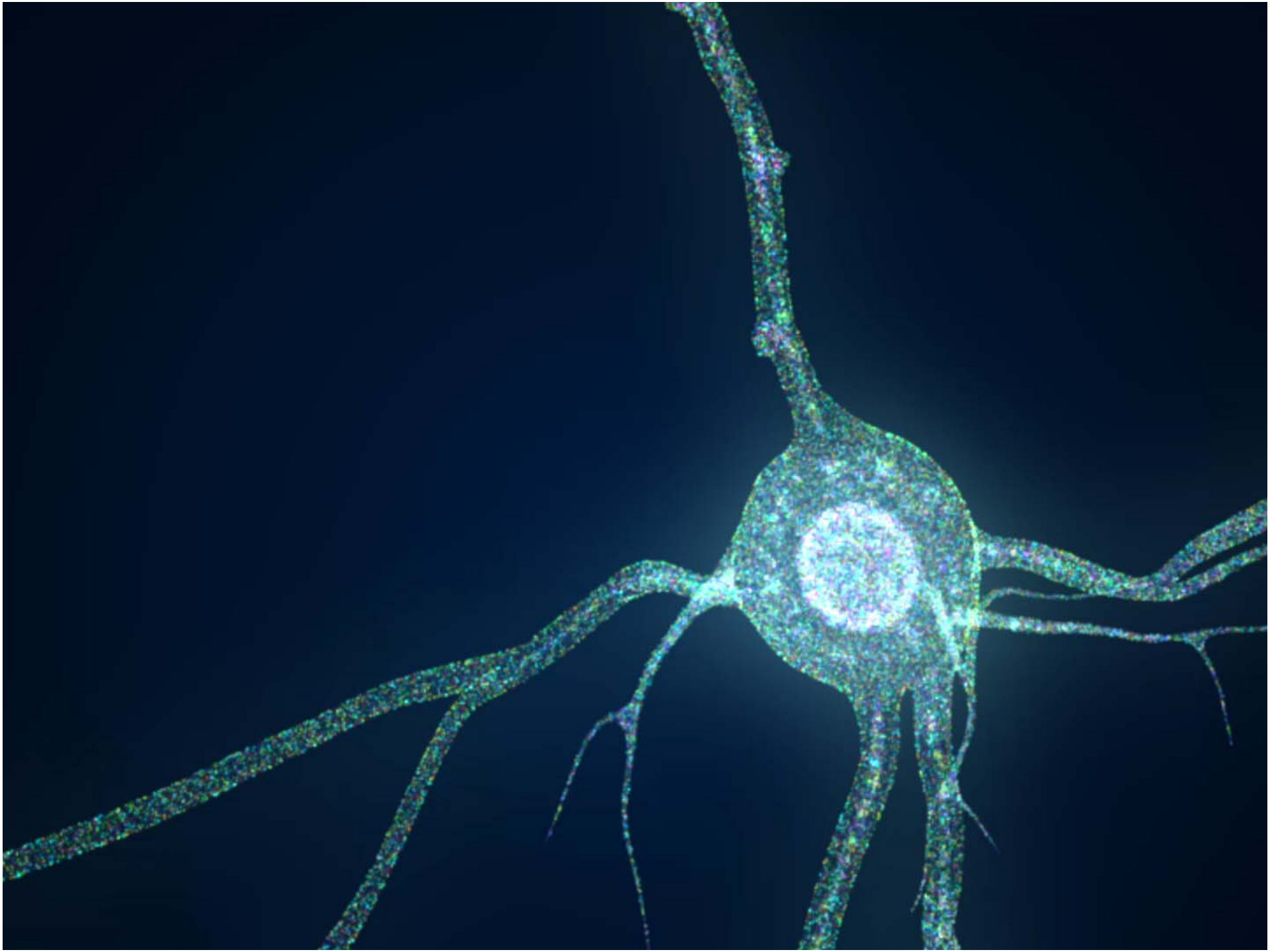
…throughout cells, winding their way around biomolecules?

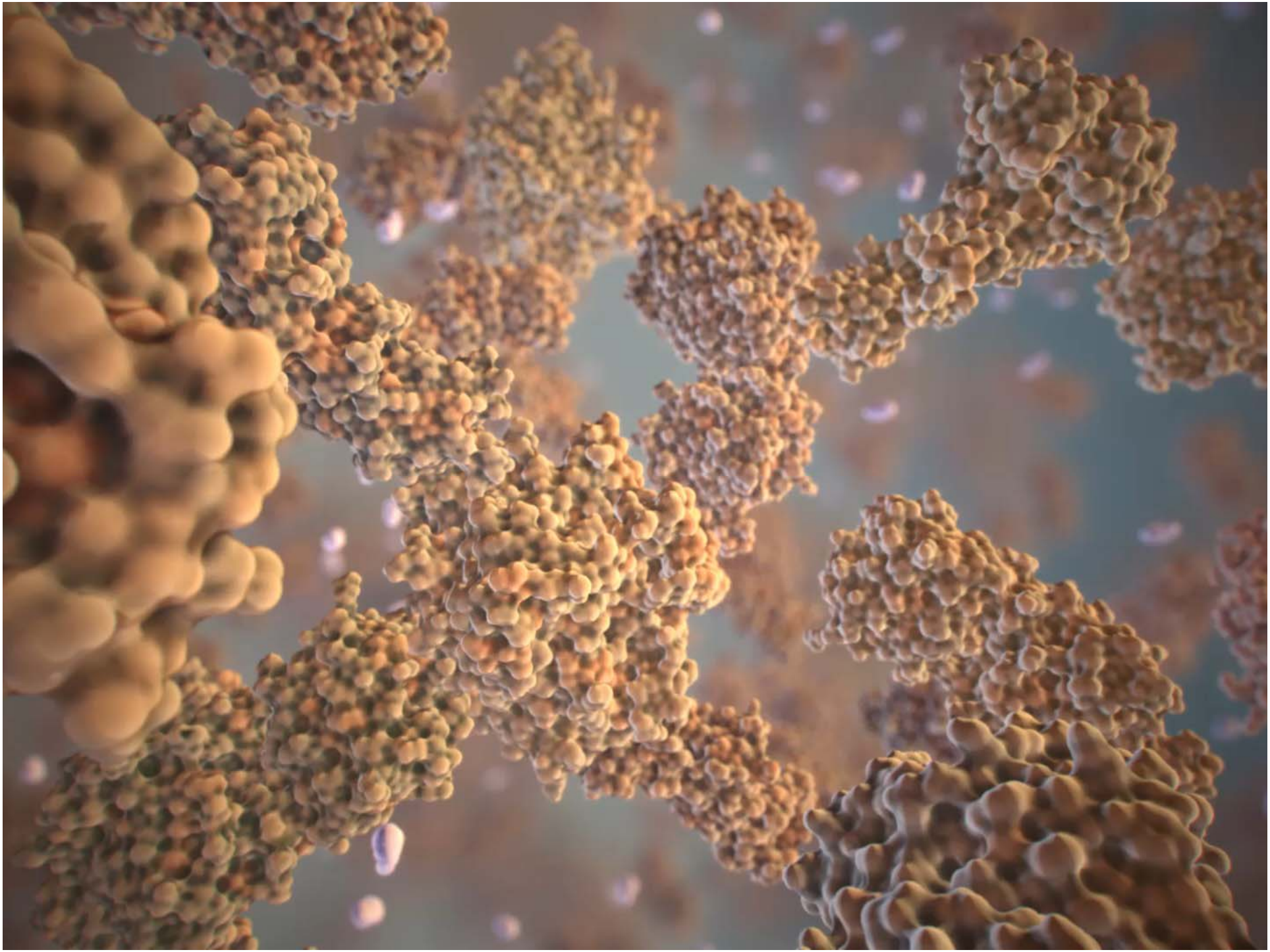


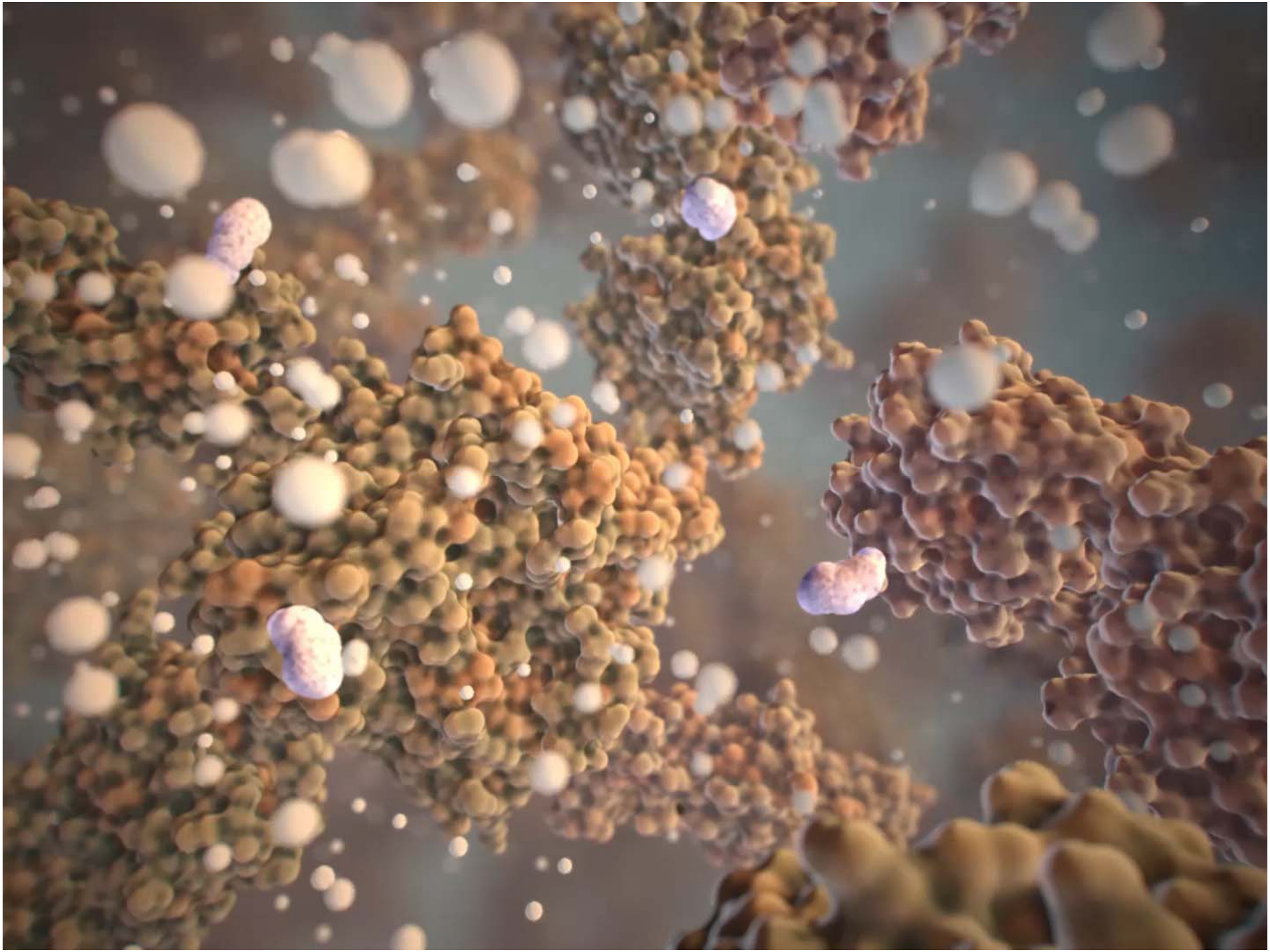
Chen*, Tillberg*, Boyden (2015) *Science* 347(6221):543-548; Tillberg*, Chen*, et al. (2016) *Nature Biotechnology* 34:987–992; Chen*, Wassie*, et al. (2016) *Nature Methods* 13(8):679-84.

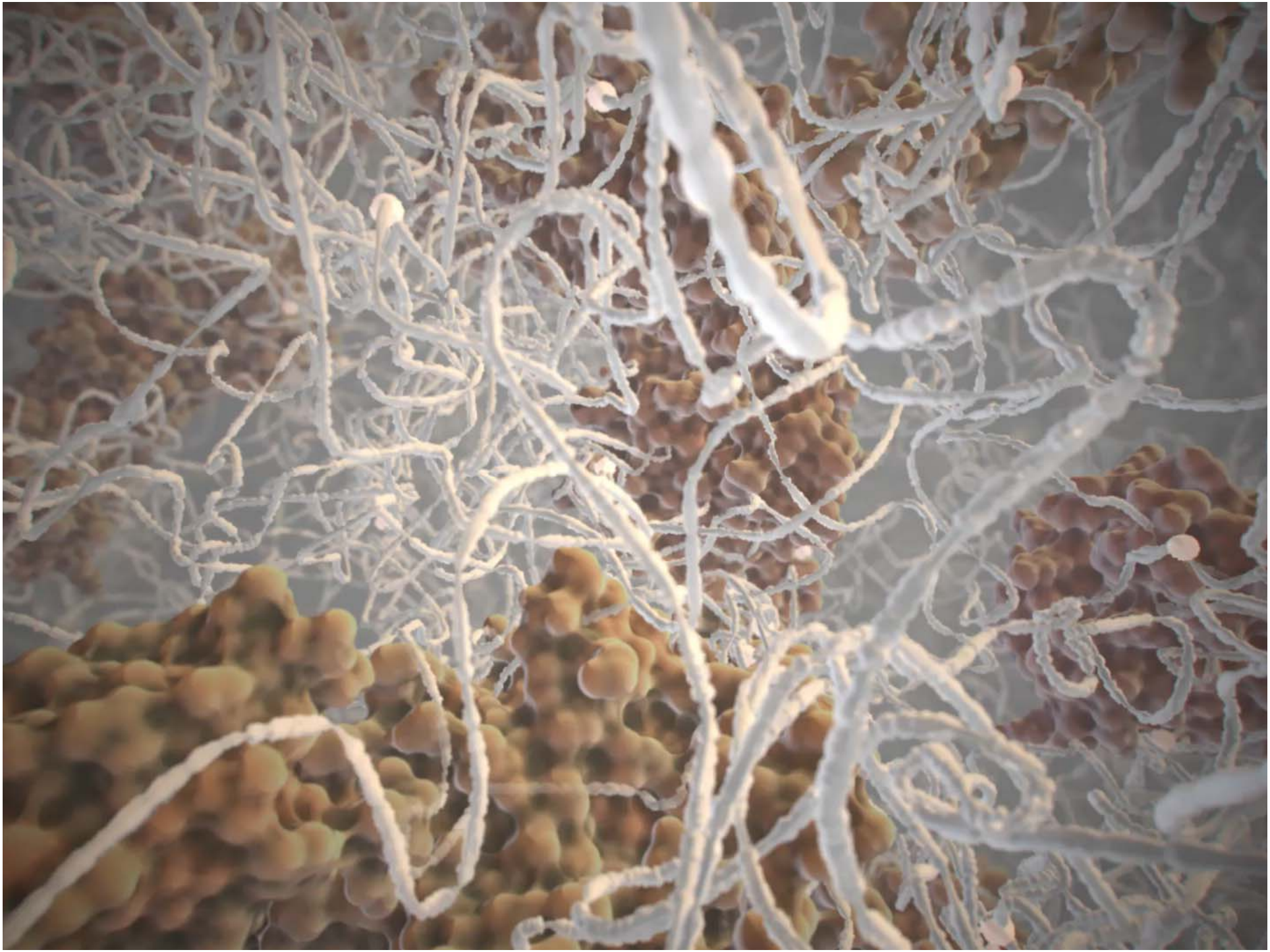
Protocols and resources at: http://expansionmicroscopy.org

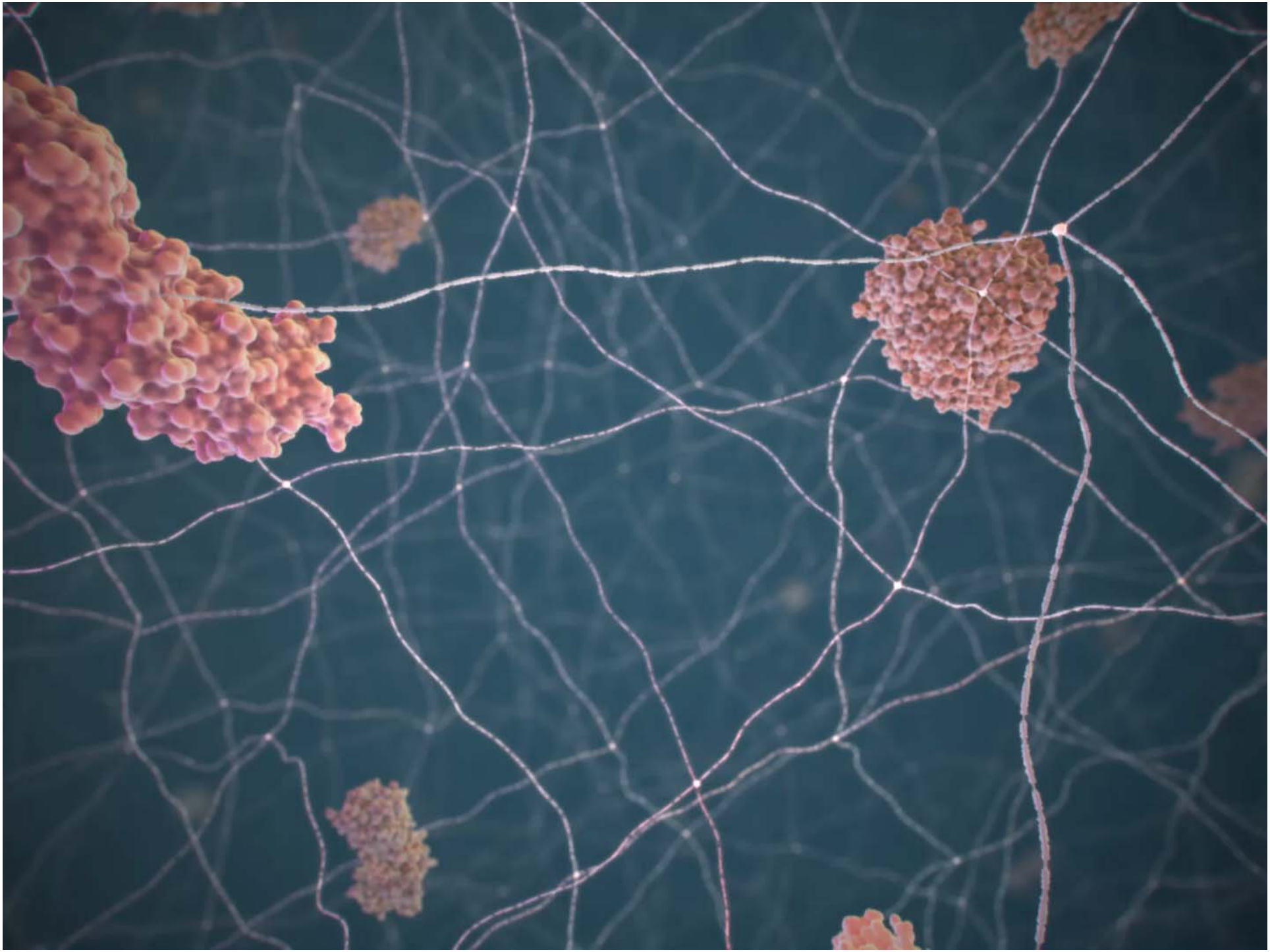
Commercialized by Expansion Technologies, Inc. (http://extbio.com); ESB is co-founder. ESB is an inventor on related patents.

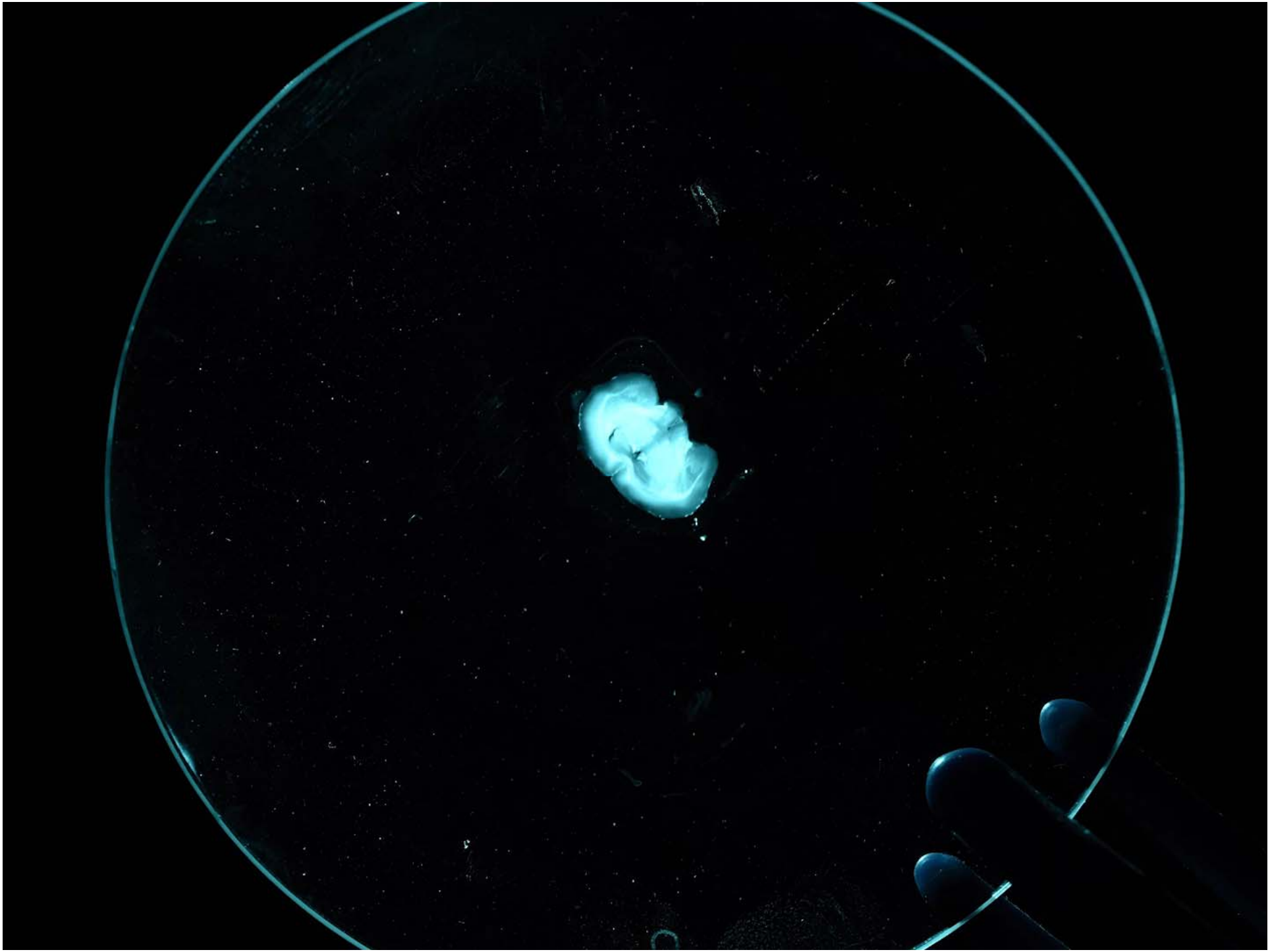


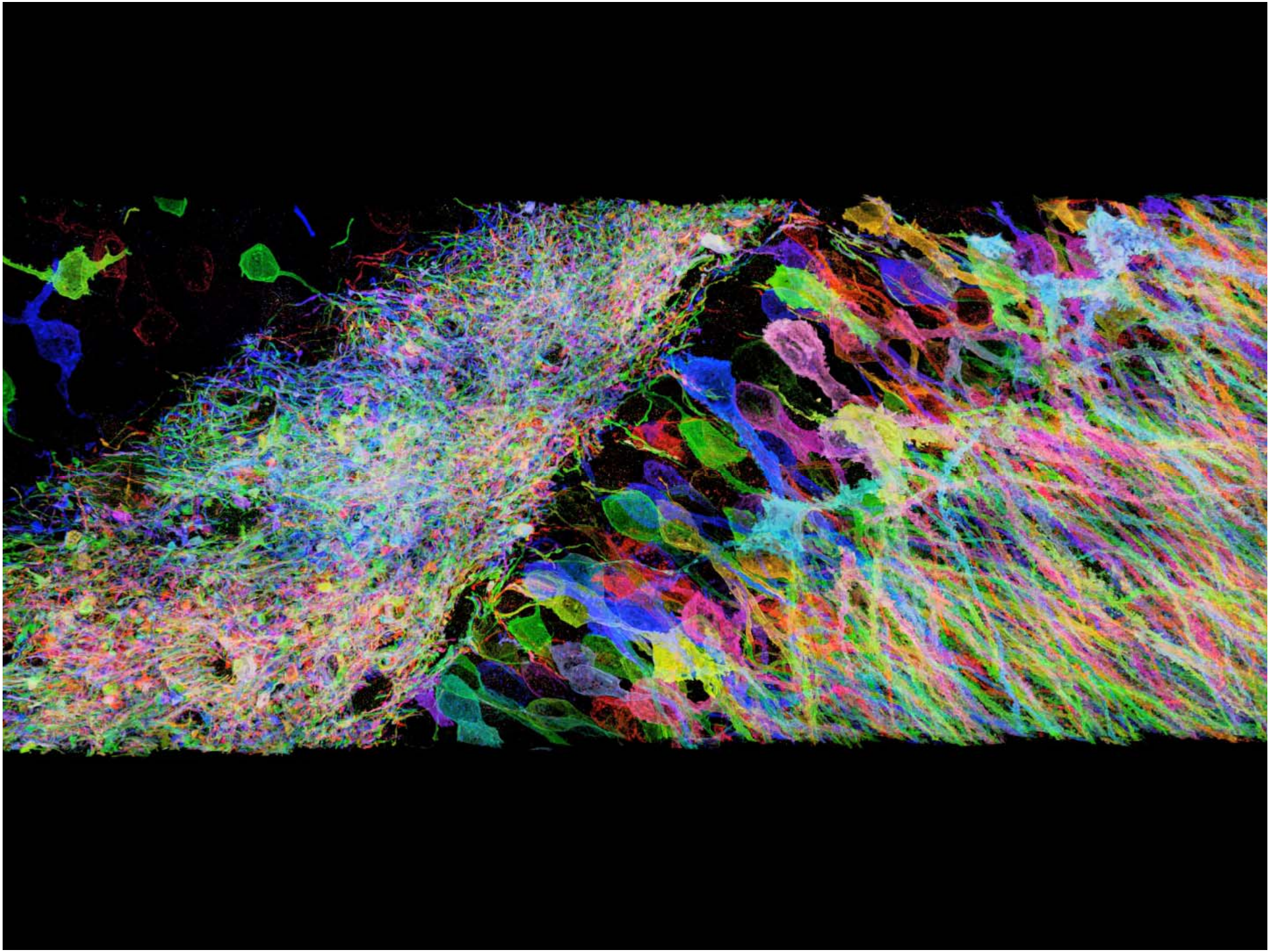


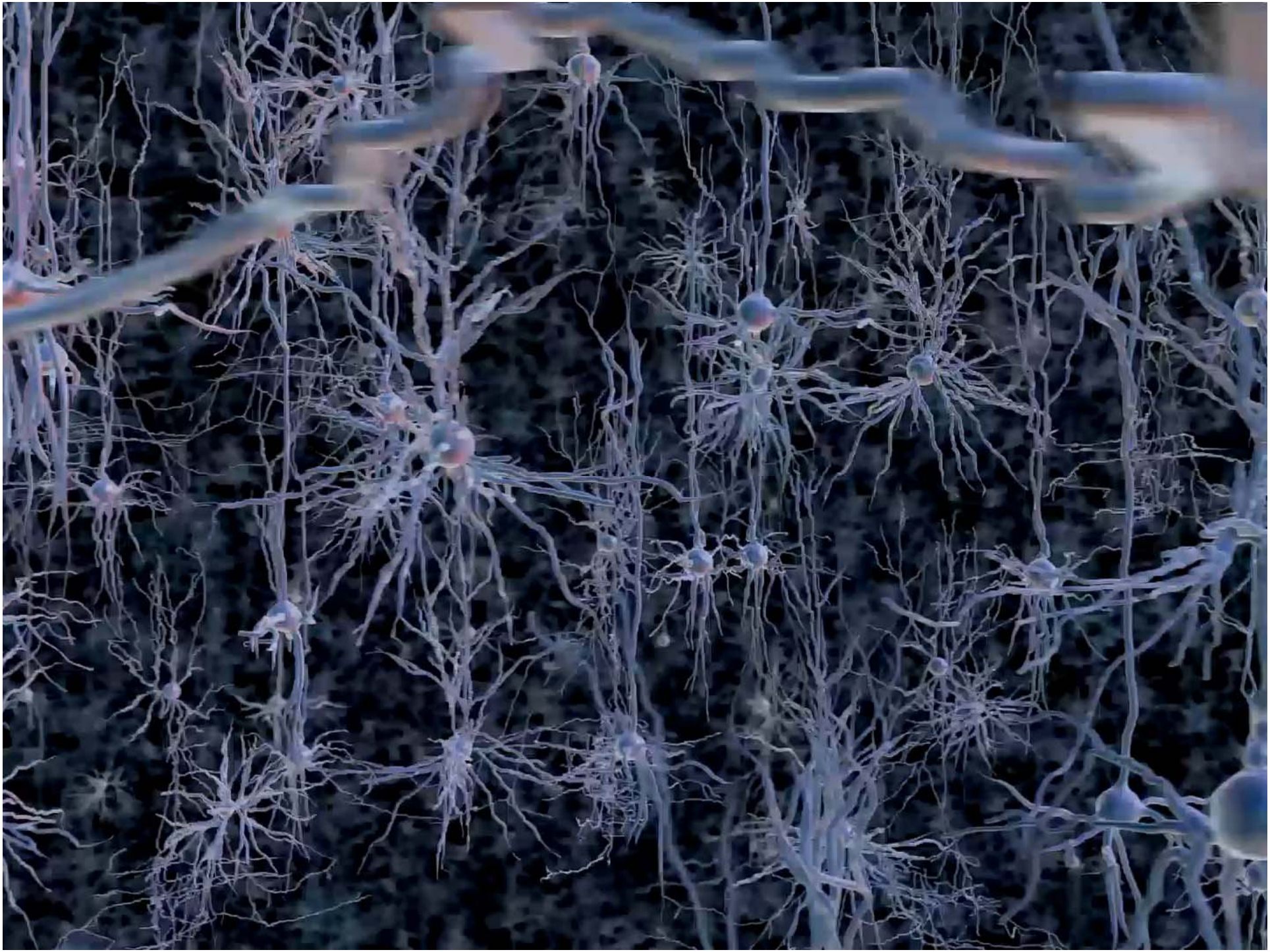


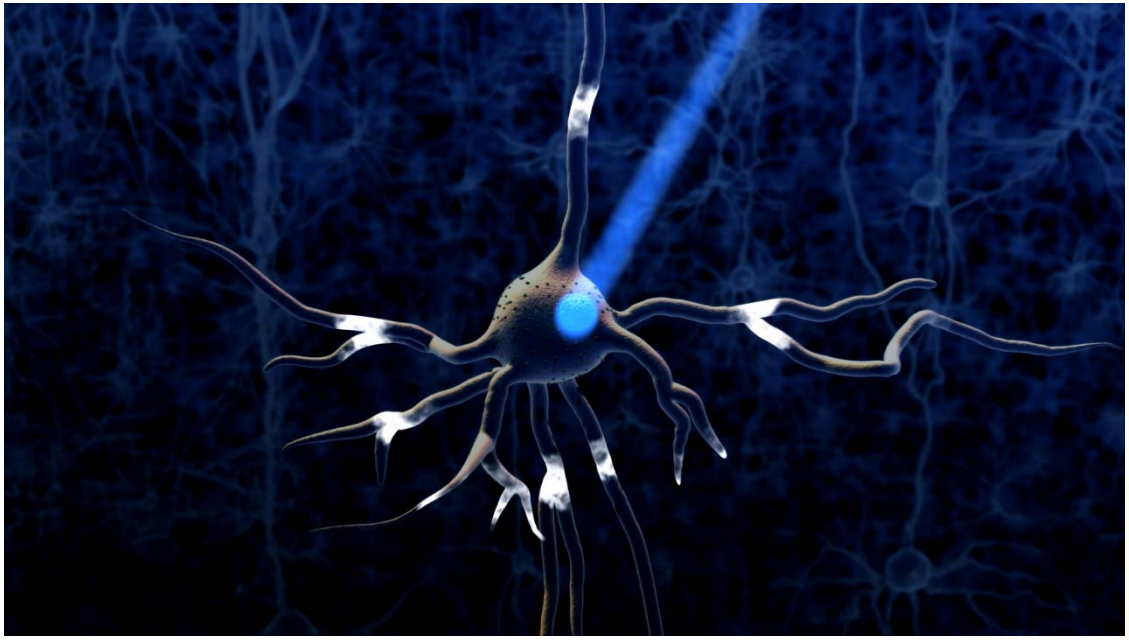


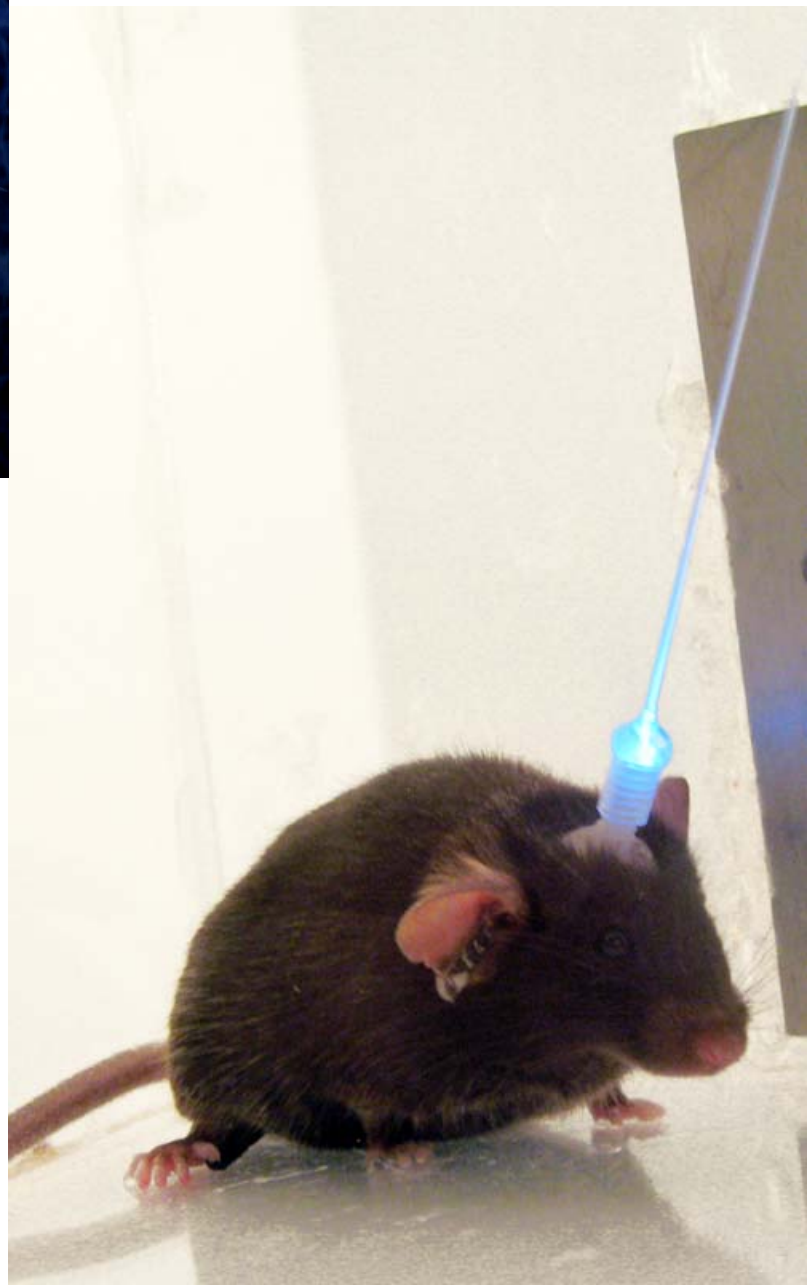


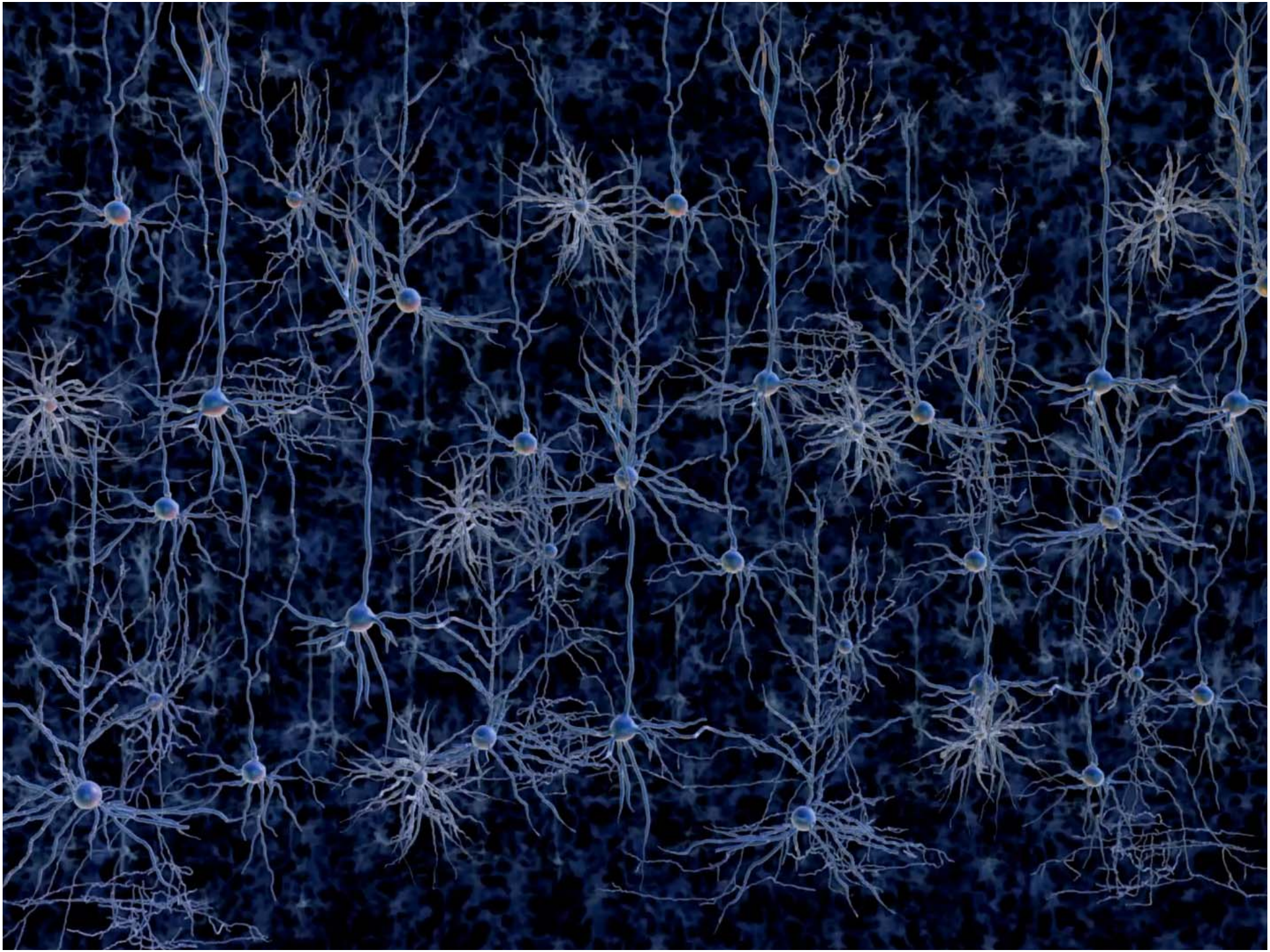




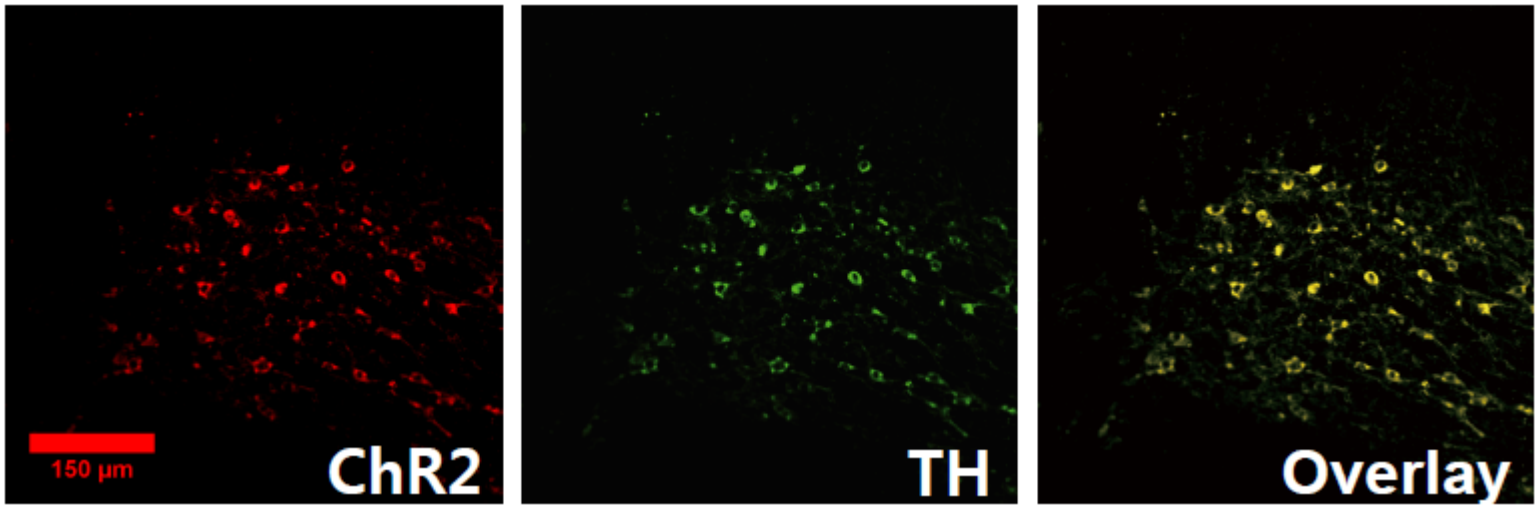






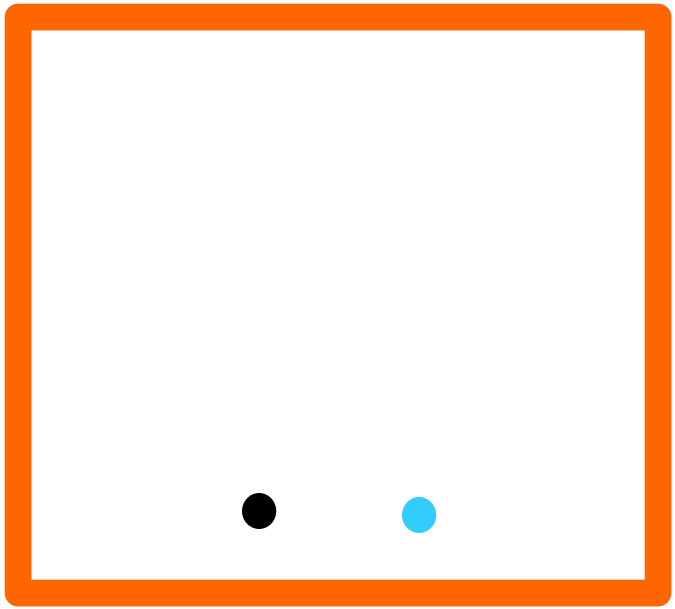


Making dopamine neurons sensitive to light



Kim et al. (2012) *PLoS One* 7(4):e33612

What do dopamine neurons do?



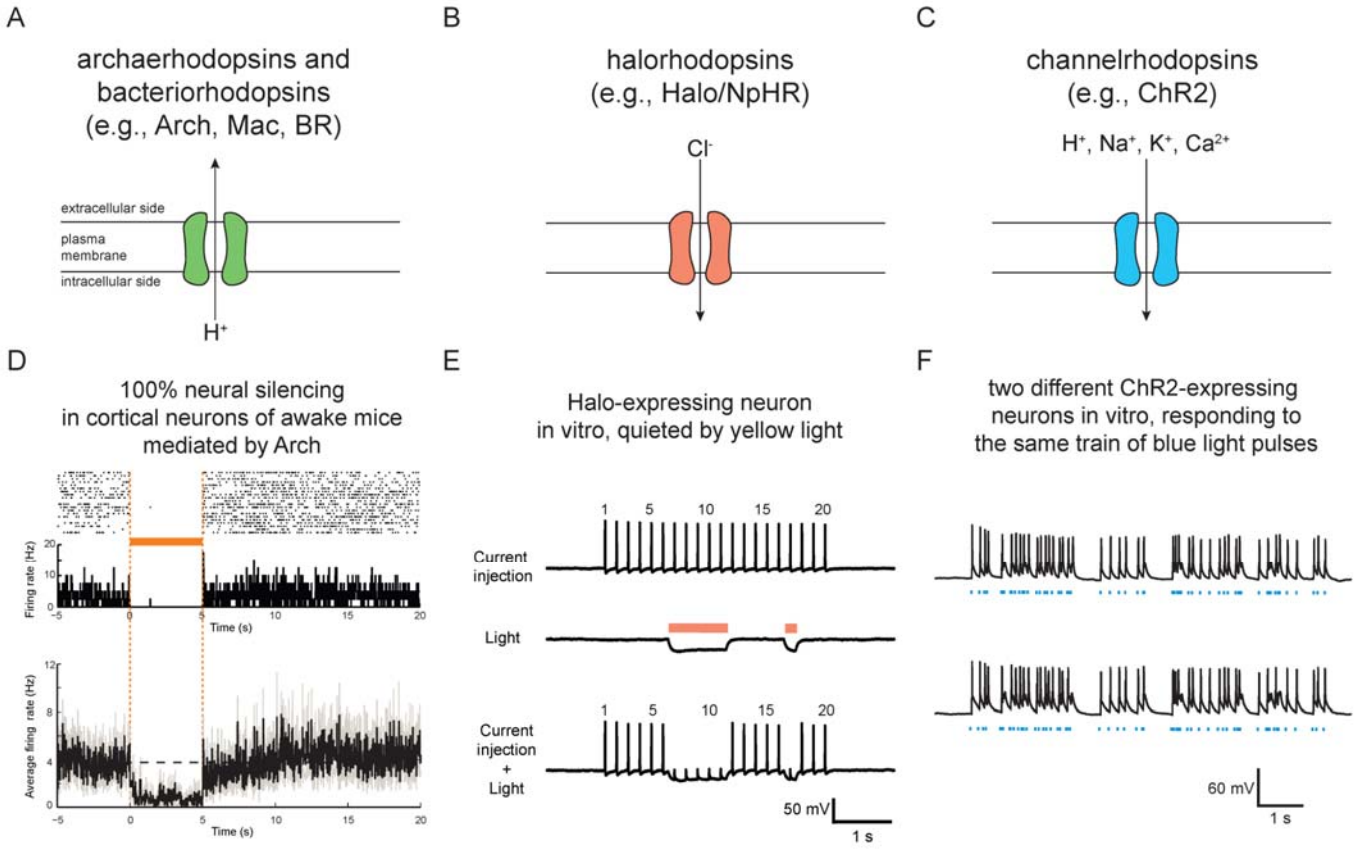
no light stimulation

light stimulation

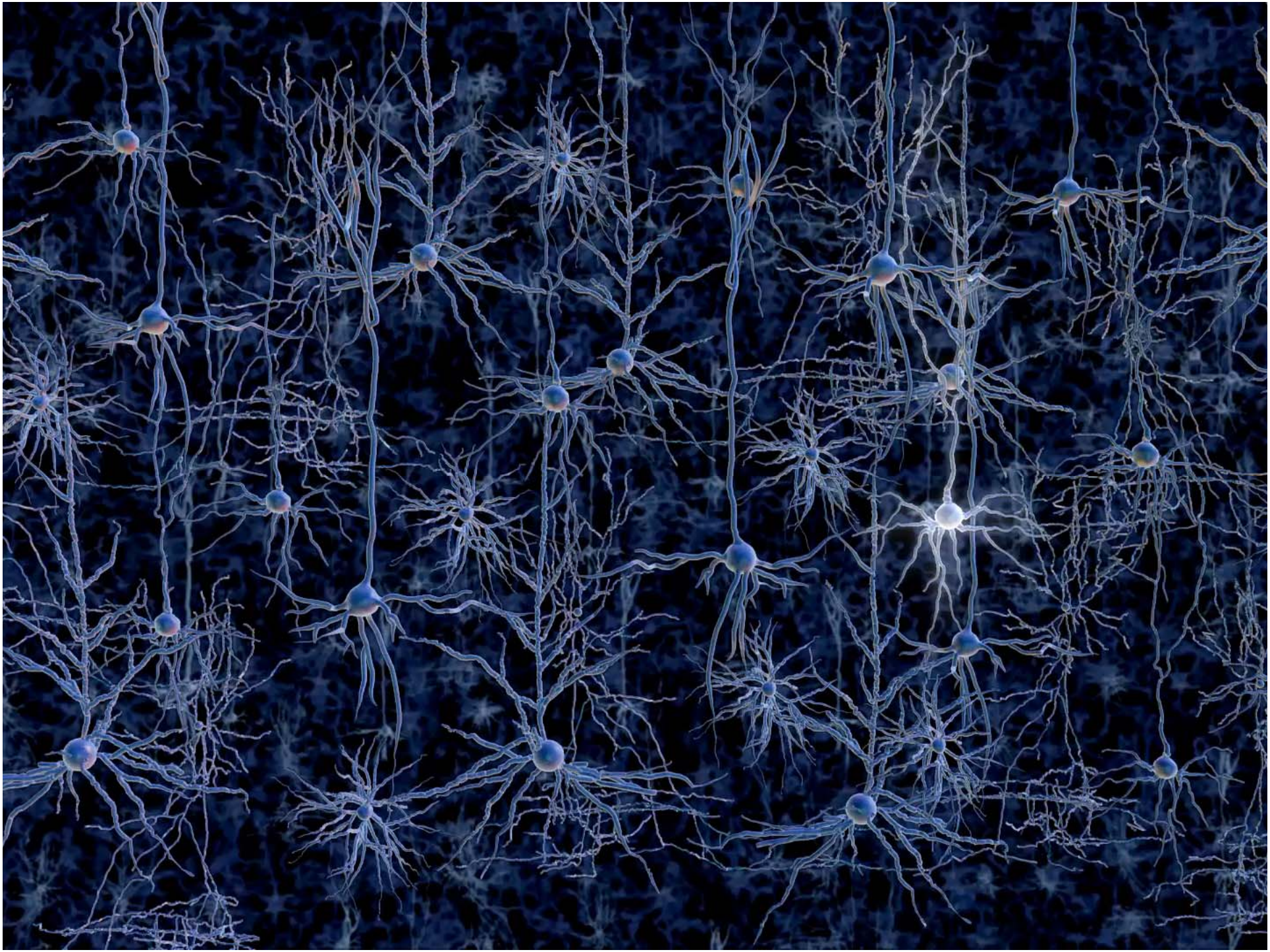
Kim et al. (2012) *PLoS One* 7(4):e33612

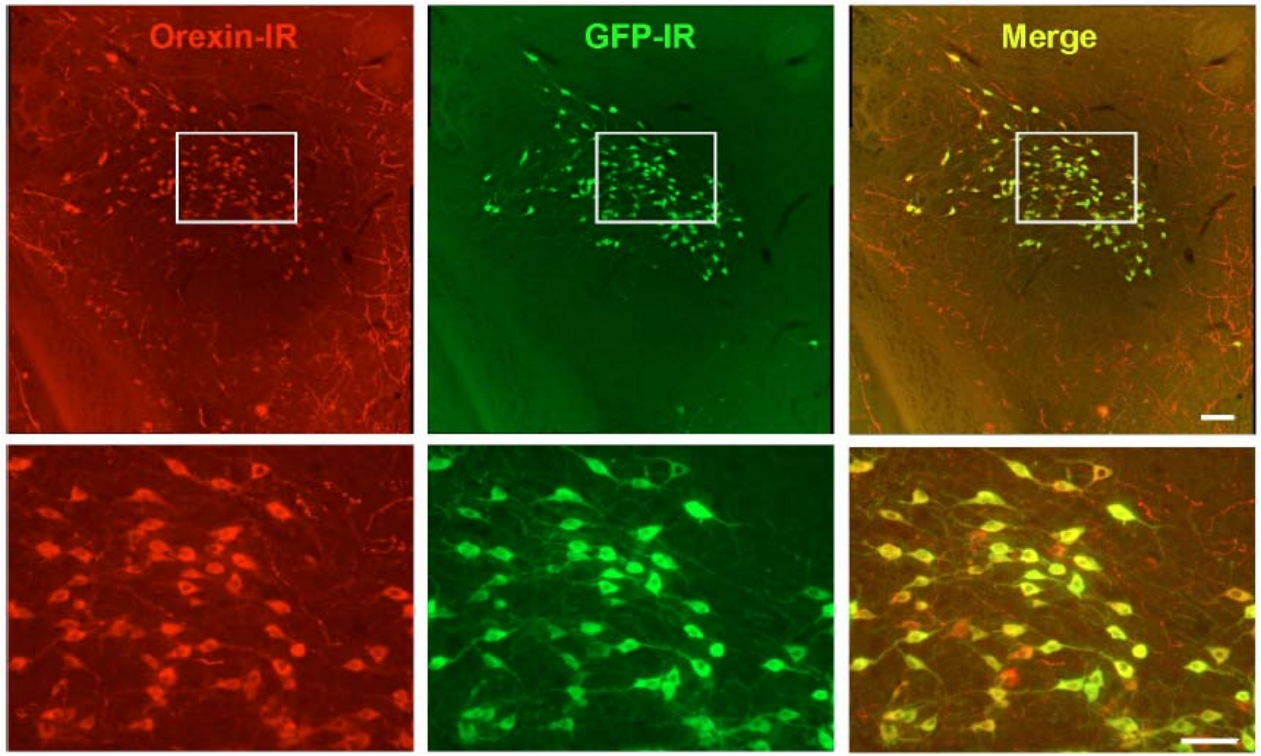
Kim et al. (2012) *PLoS One* 7(4):e33612

Three major optogenetic molecule classes

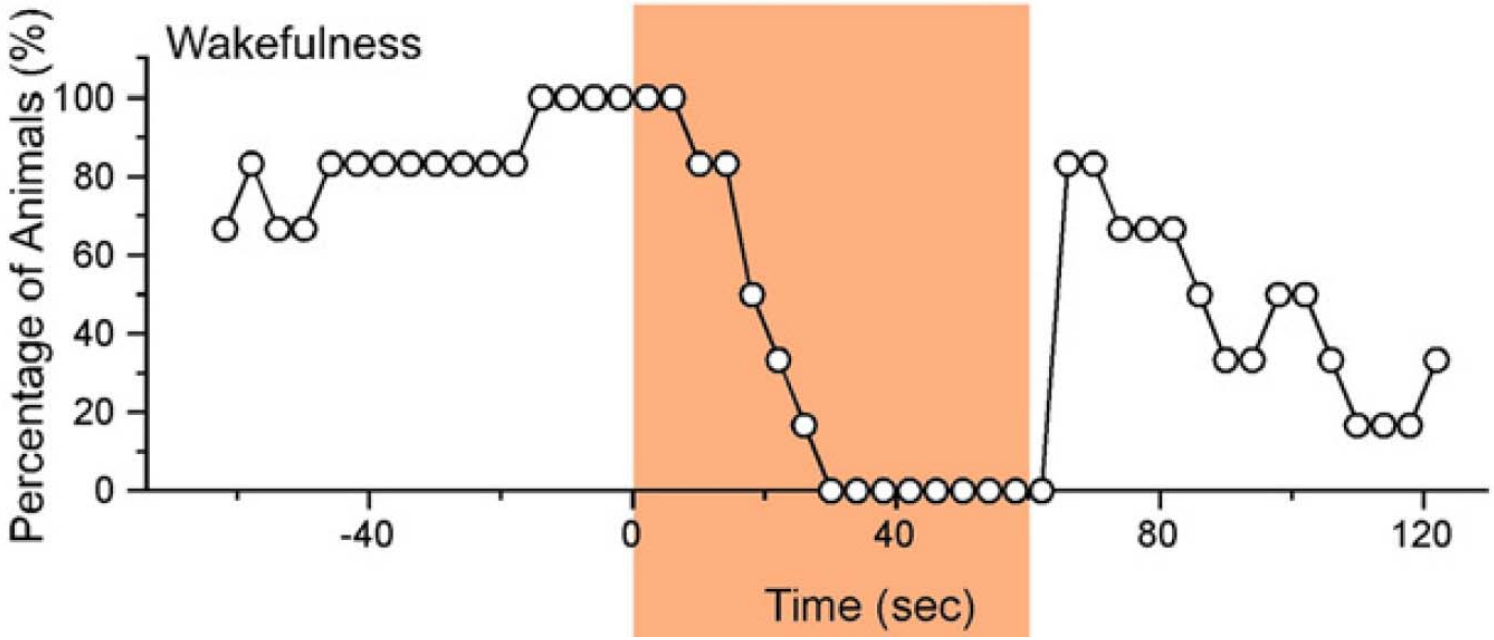


Boyden (2011) *Faculty of 1000 Biology Reports* 3:11.



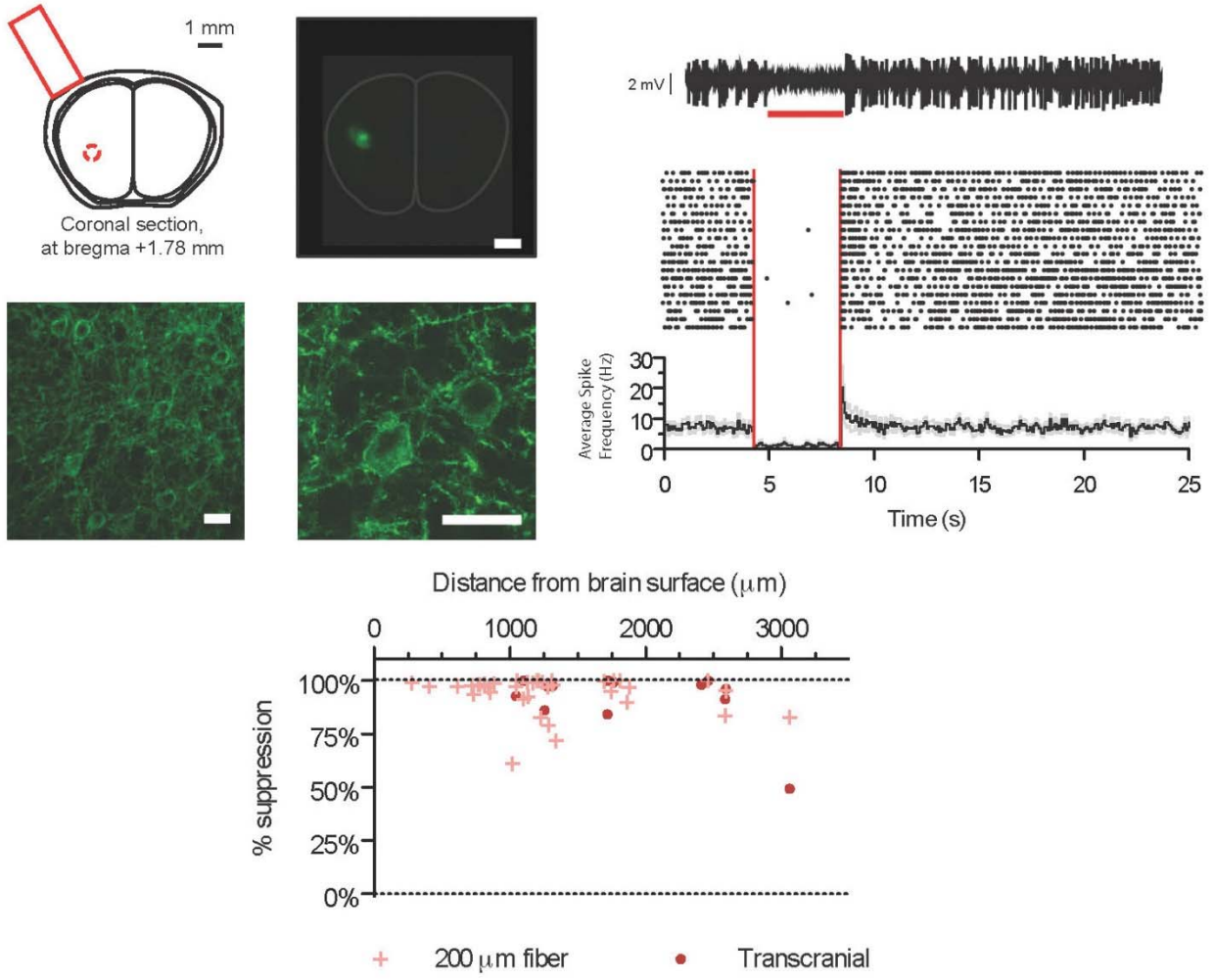


Tsunematsu et al. (2011) *Journal of Neuroscience* 31(29): 10529-10539.



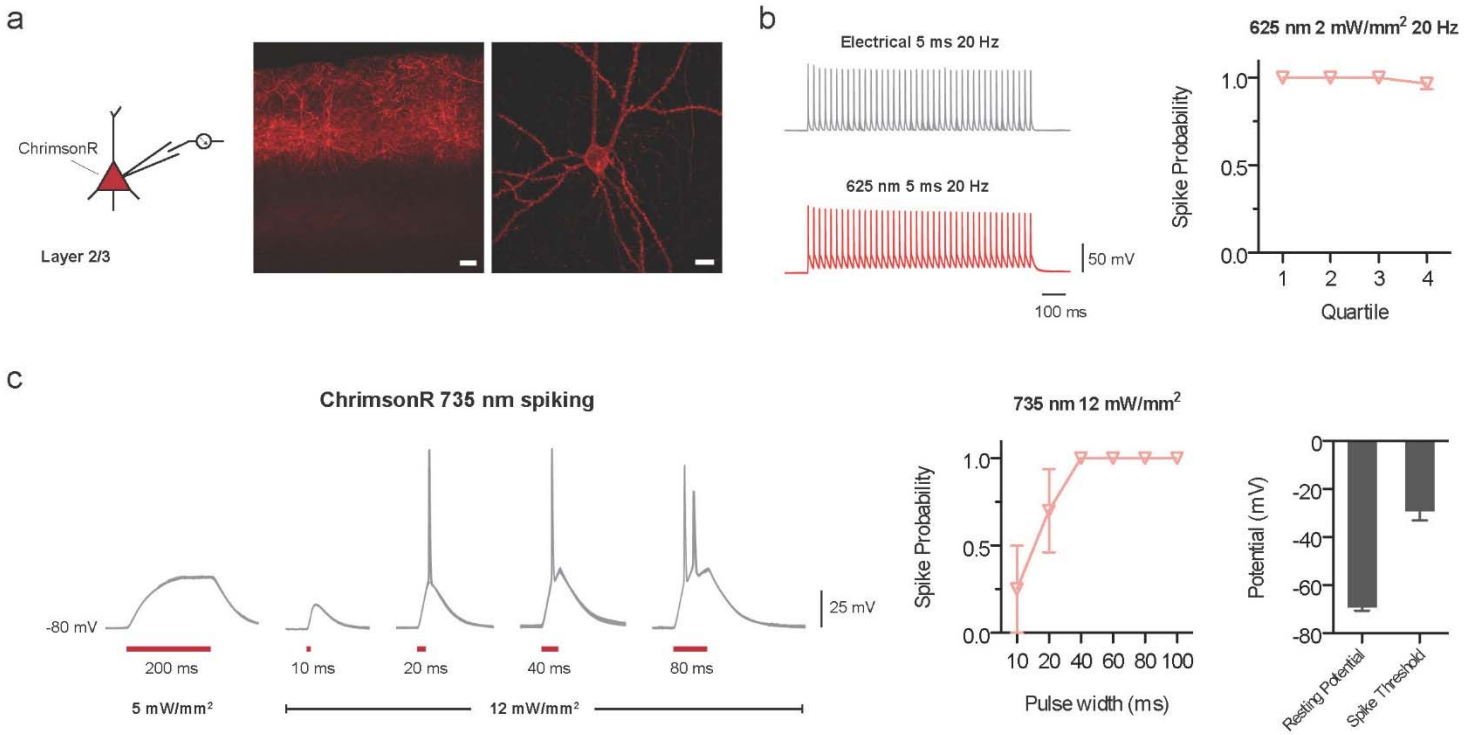
Tsunematsu et al. (2011) *Journal of Neuroscience* 31(29): 10529-10539.

Noninvasive optogenetic neural silencing: Jaws



Chuong et al. (2014) *Nature Neuroscience* 17:1123-1129.

Chrimson: near-infrared neural stimulation



Klapoetke et al. (2014) *Nature Methods* 11:338–346.

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Synthetic Neurobiology Group

http://syntheticneurobiology.org/

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Ticker tapes: George Church, Keith Tyo, Konrad Koerding

Transgenics: Hongkui Zeng

Conflict of Interest Statement

ESB is a co-founder of Eos Neuroscience, Cognito Therapeutics, and Expansion Technologies, on the science advisory board of PureTech Ventures, and compensated by or an equity holder in Constellation Diagnostics and Intellectual Ventures