

The Promise of Synthetic Cells

Marileen Dogterom

NWO Physics, April 4 2023, Basic Science for Sustainable Development

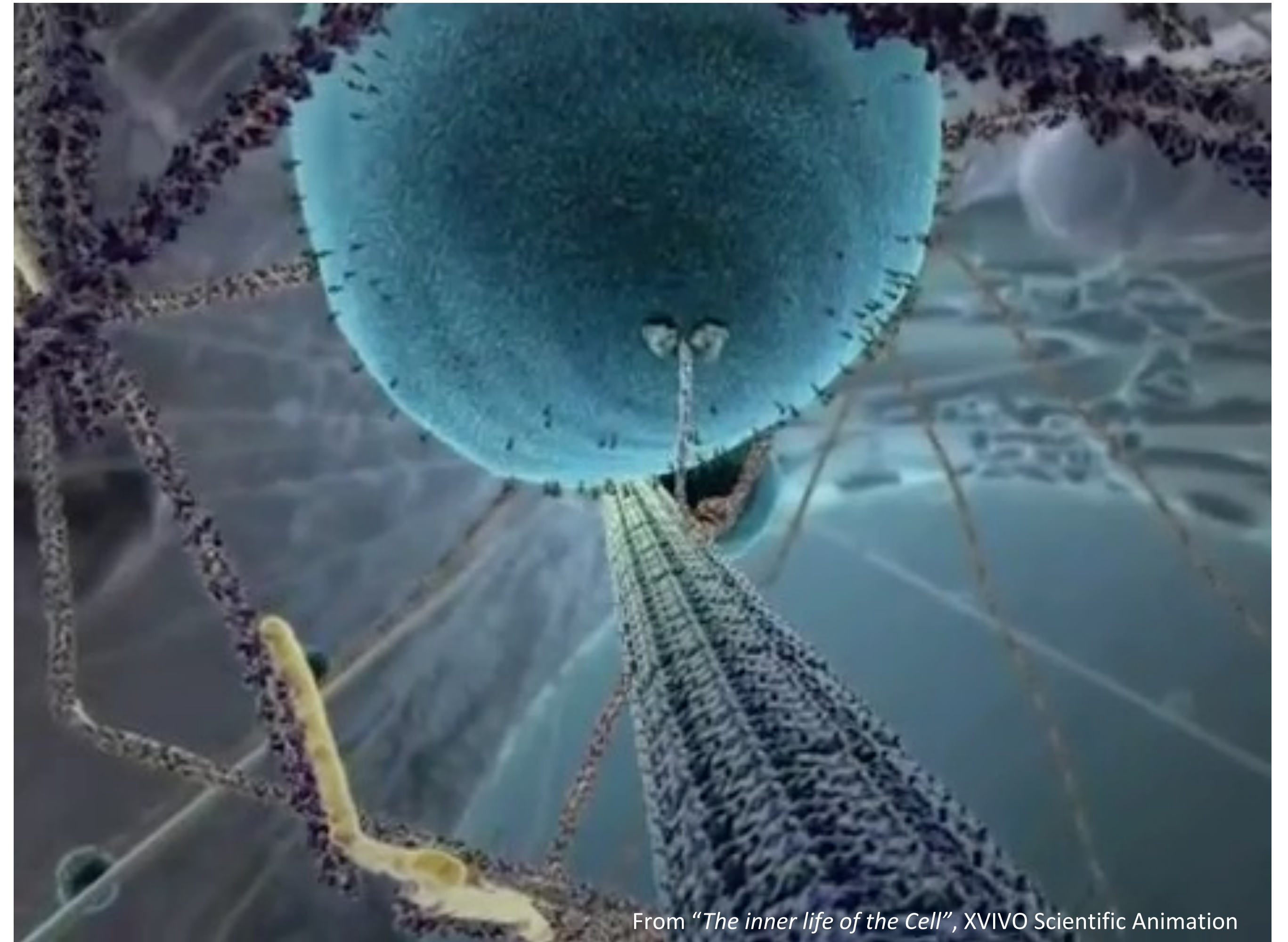


European Synthetic Cell Initiative

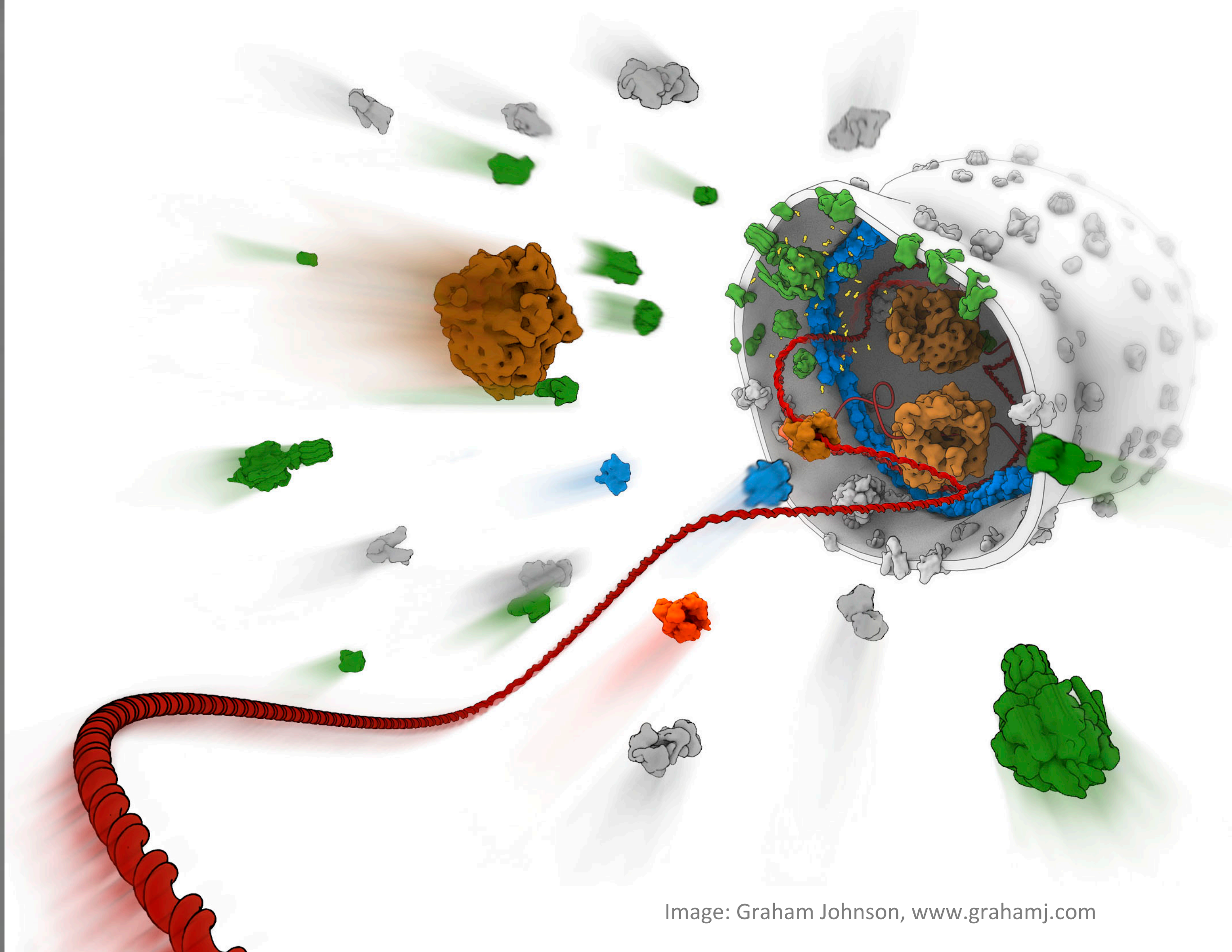
Nature is our next technology



The molecular building blocks of cells

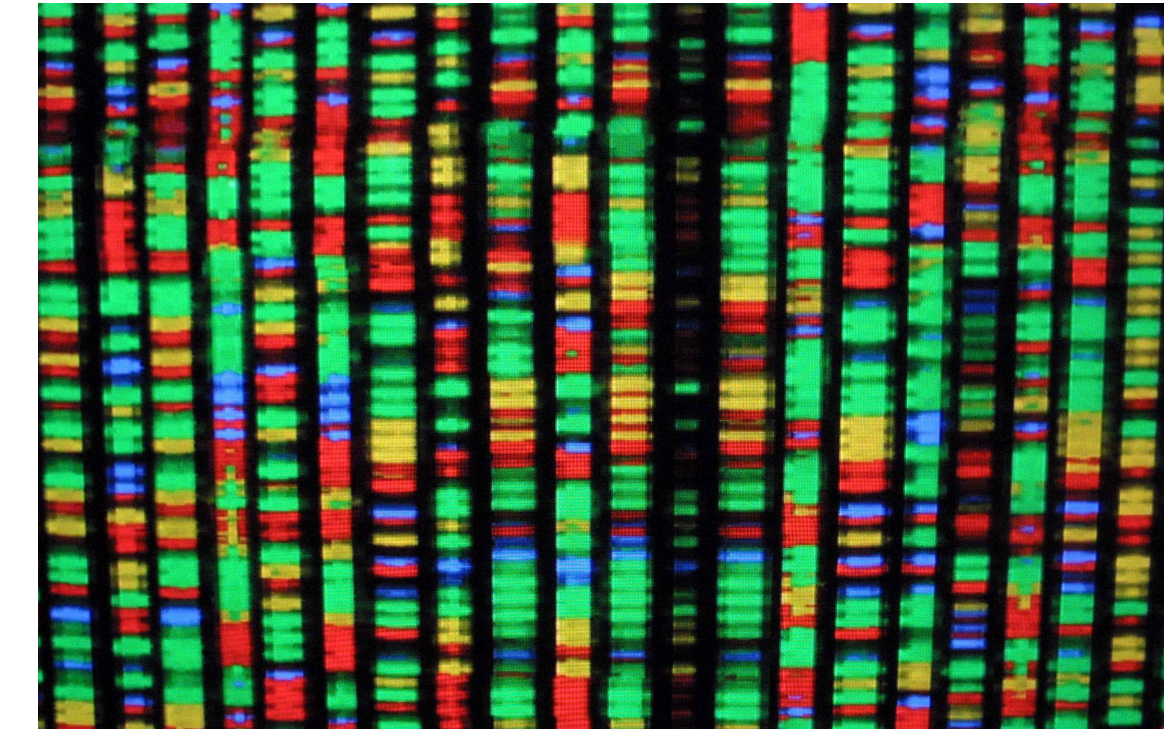


Building Synthetic Cells ?



Building a synthetic cell: a bottom-up, modular approach

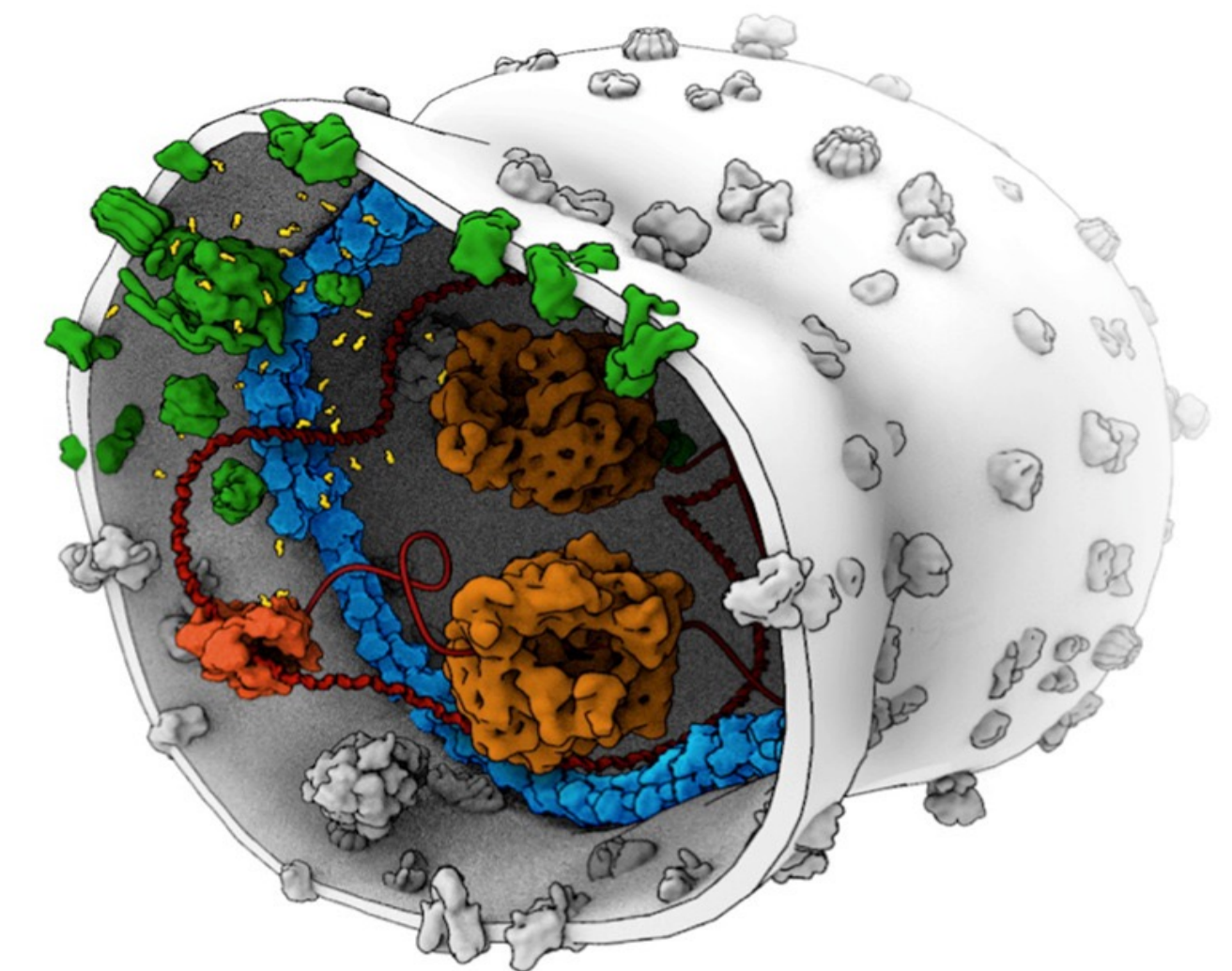
We know the molecular parts!



Genome sequence

BUT:

- How does life emerge from molecular interactions?
- Which molecular components are minimally required?
- What functions are minimally necessary for life?



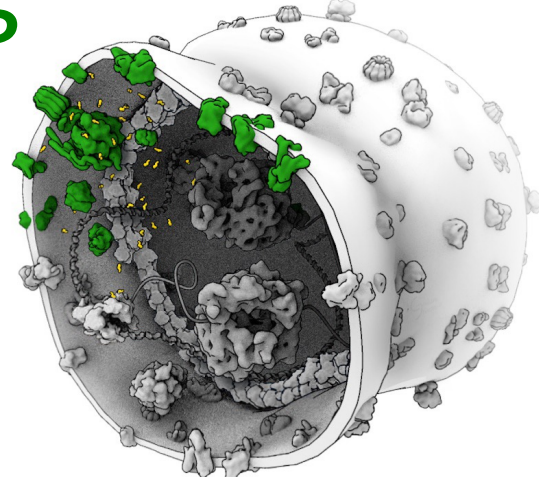
Cell fueling

DNA Processing

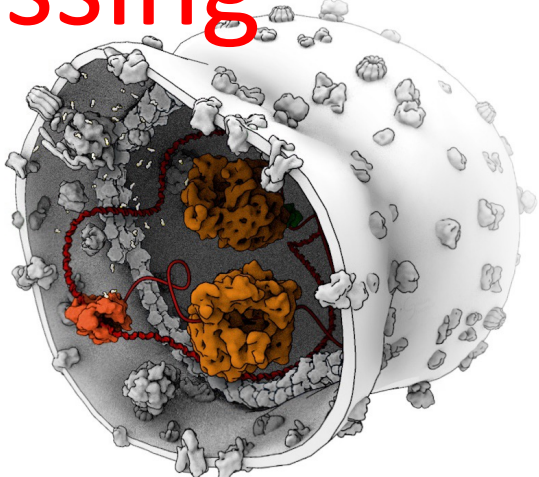
Cell division

Building a synthetic cell: a collaborative effort

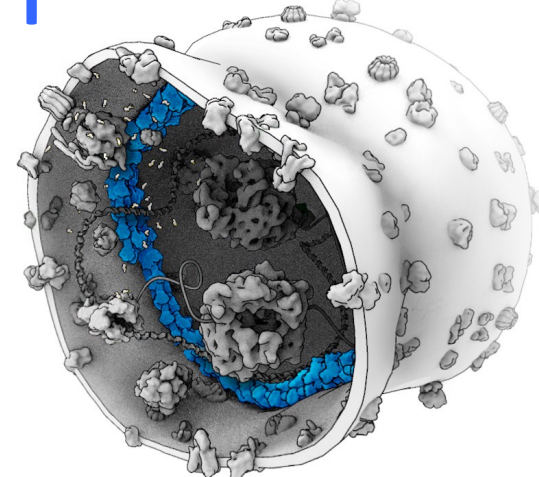
Fueling



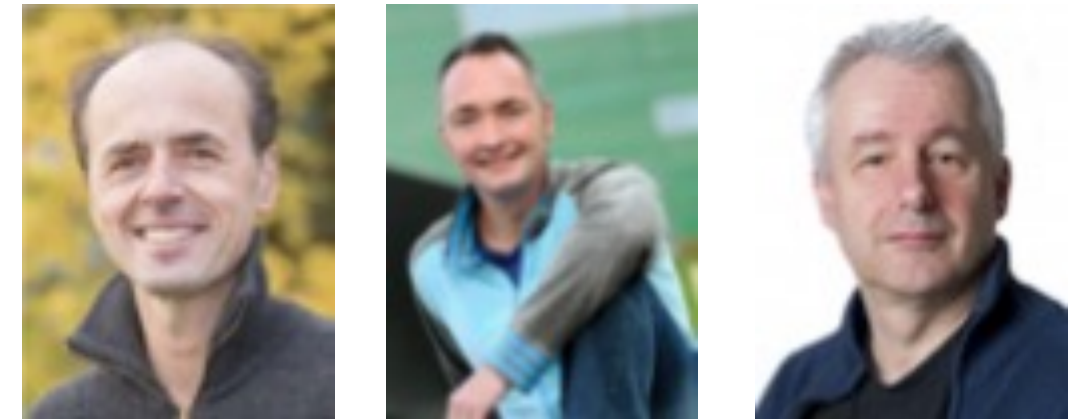
DNA processing



Division



Spatio-temporal integration of basic modules

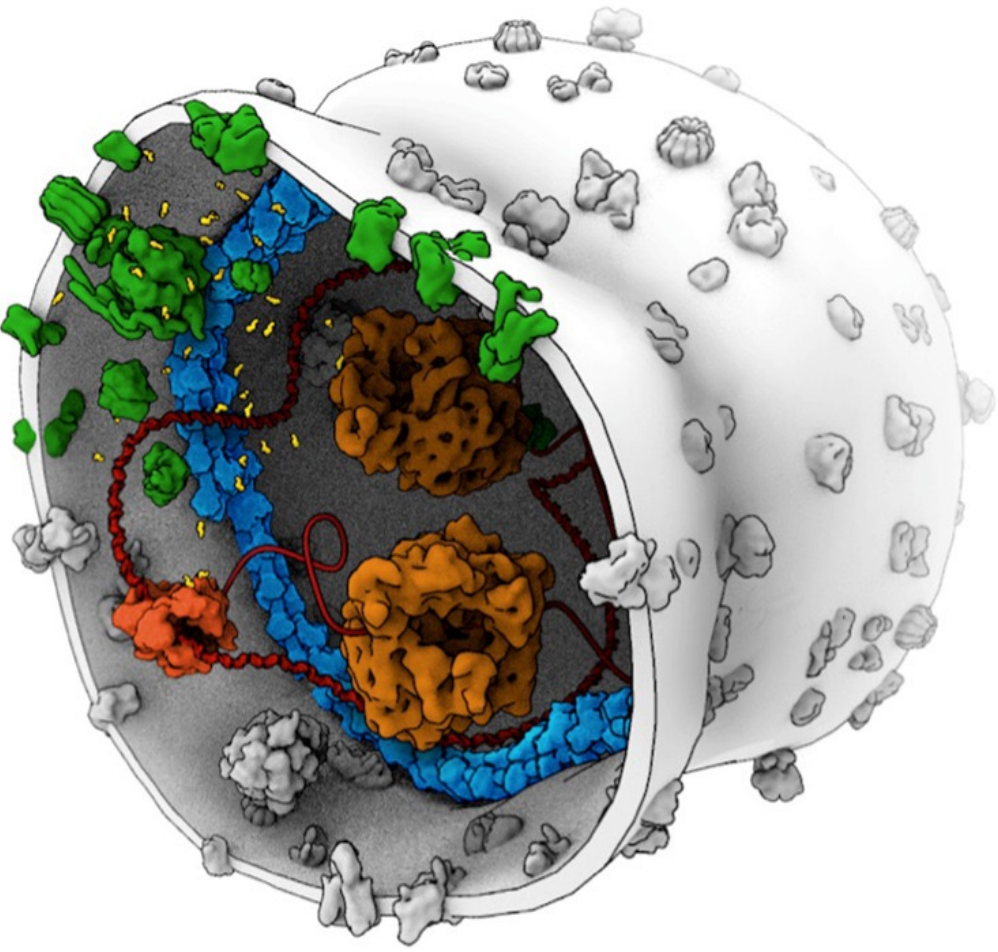


Multi-scale modeling

Whole genome optimization



Philosophy and Ethics



Our Long Term Vision

Synthetic Cell Products

Circular economy



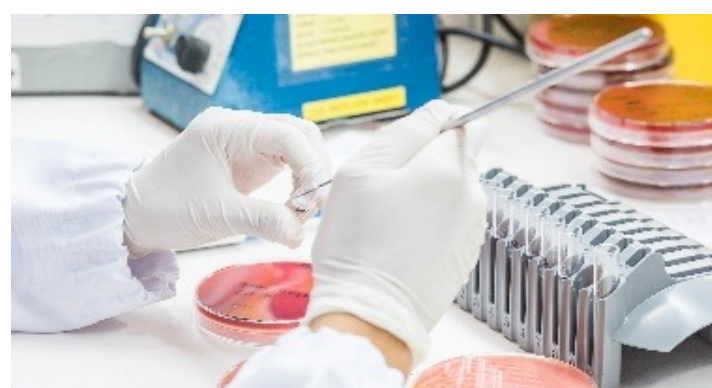
- Recyclable biomaterials
- Zero waste production methods
- Synthetic cells for production of biofuels and other compounds

High-tech materials



- Smart biosensors
- Self-healing responsive materials
- Sustainable substitutes for animal source food

Medicine



- Biomarker discovery
- Targeted personal medicine
- Regenerative medicine

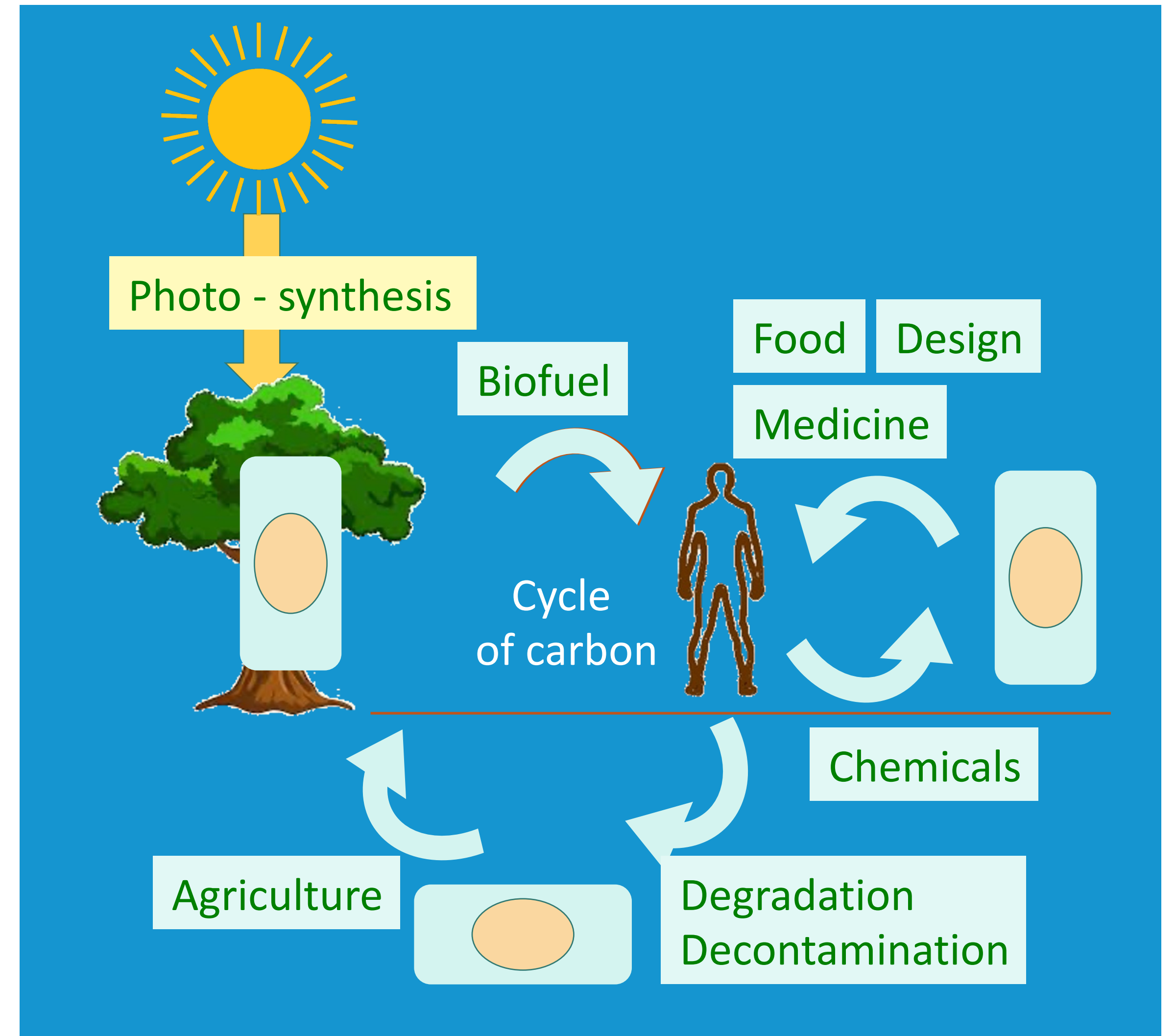


Image by CEA, France

Our Long Term Vision

Synthetic Cell Products

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- Recyclable biomaterials
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- Targeted personal medicine
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“nature is our next technology”

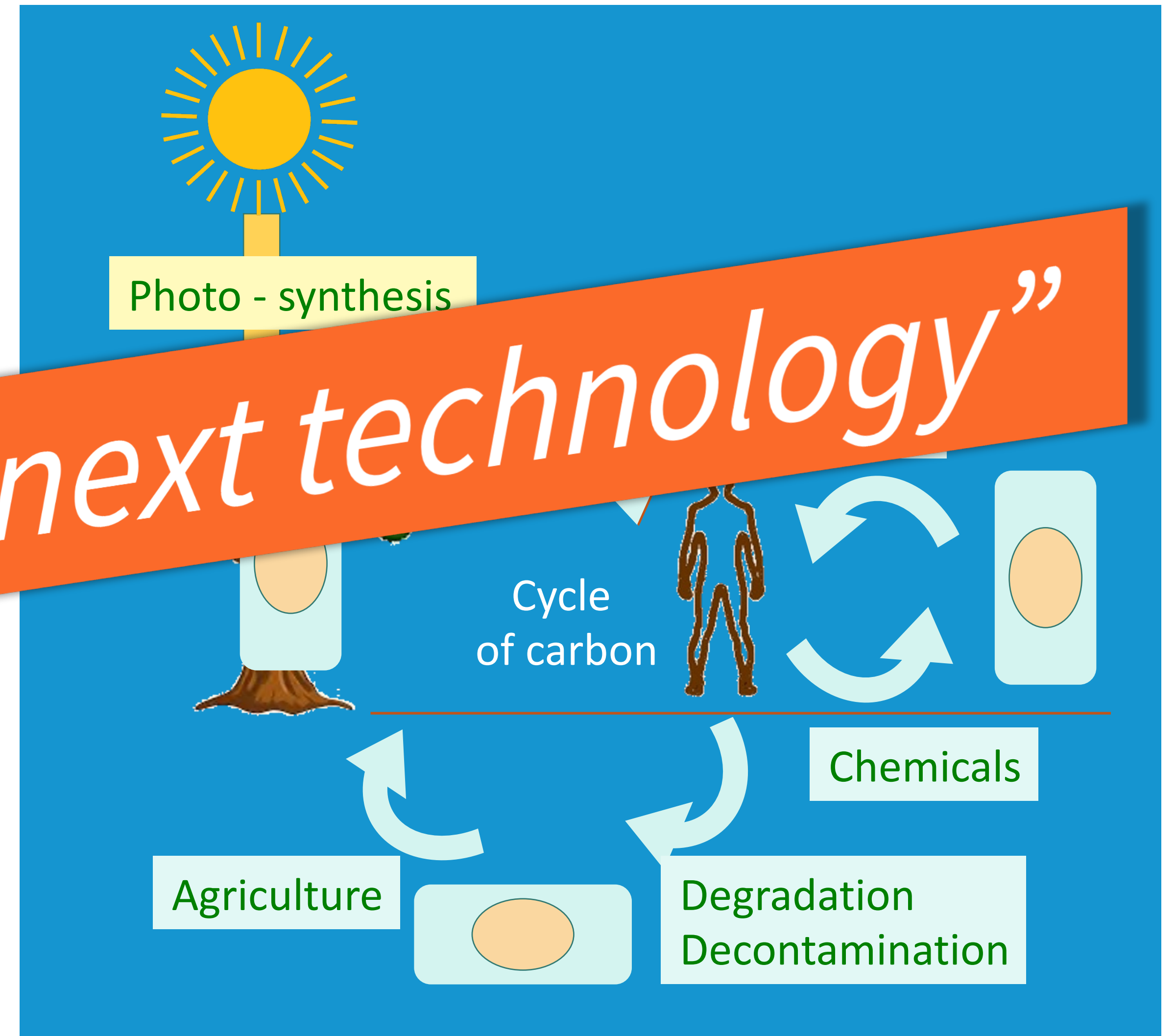
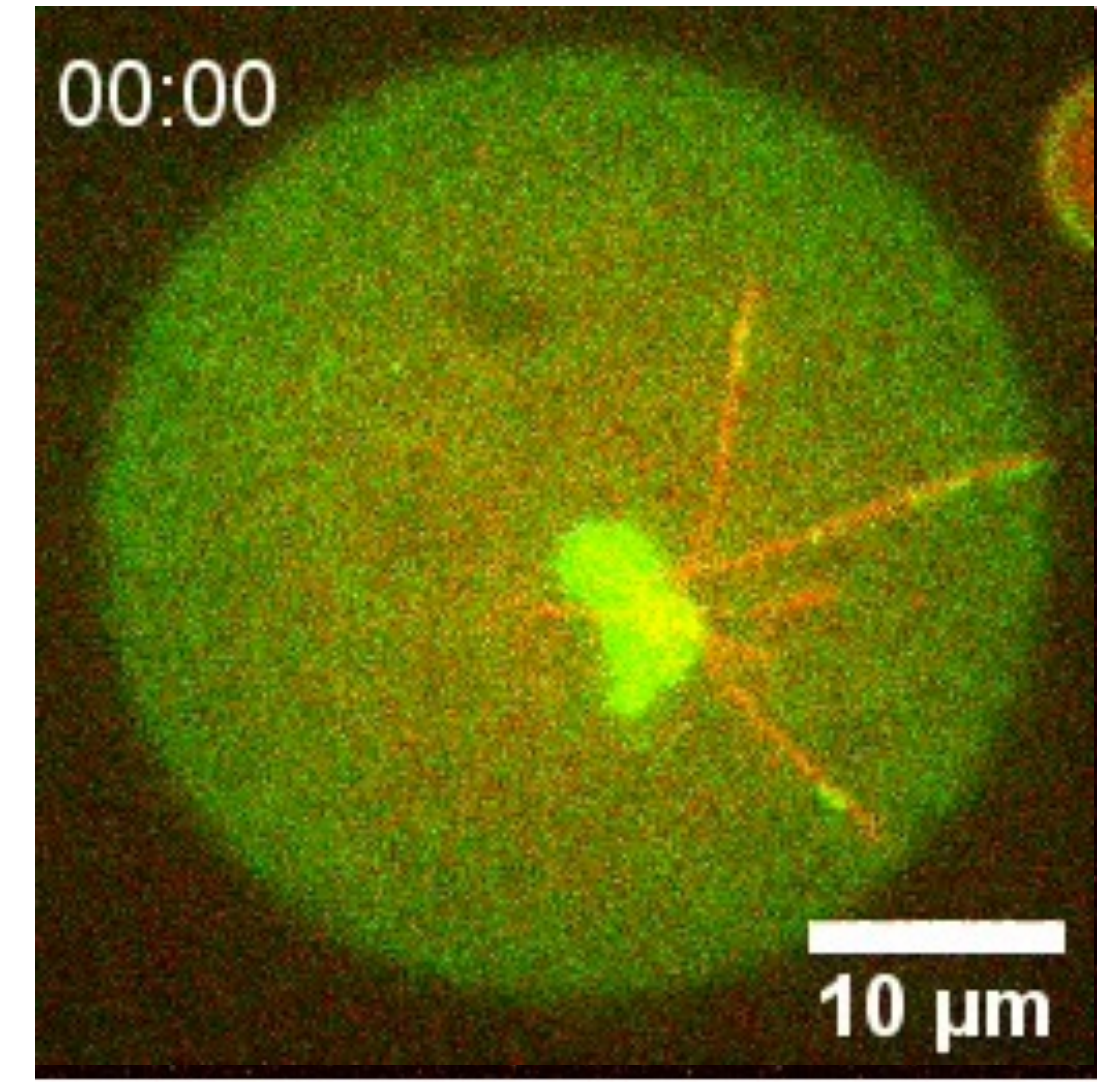
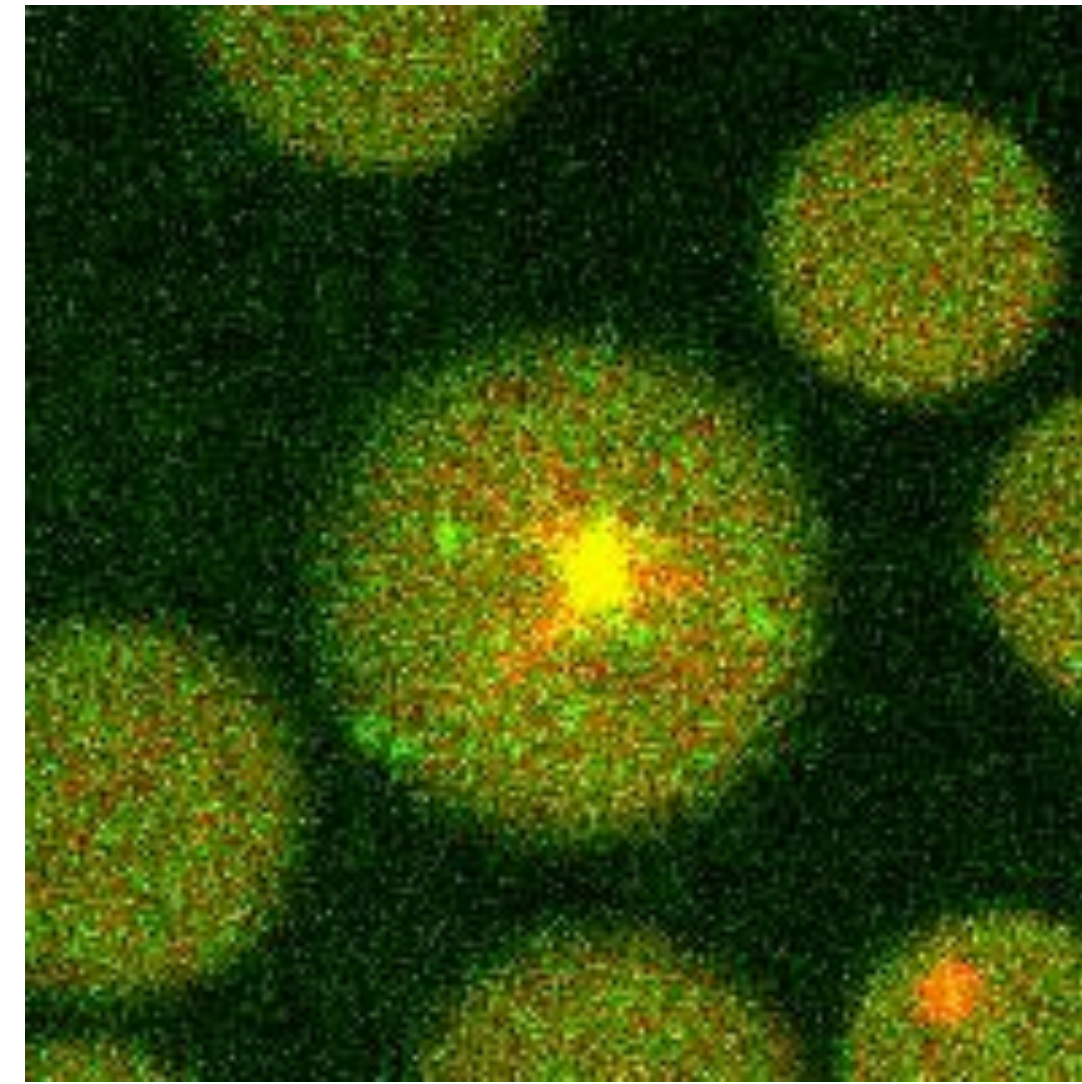
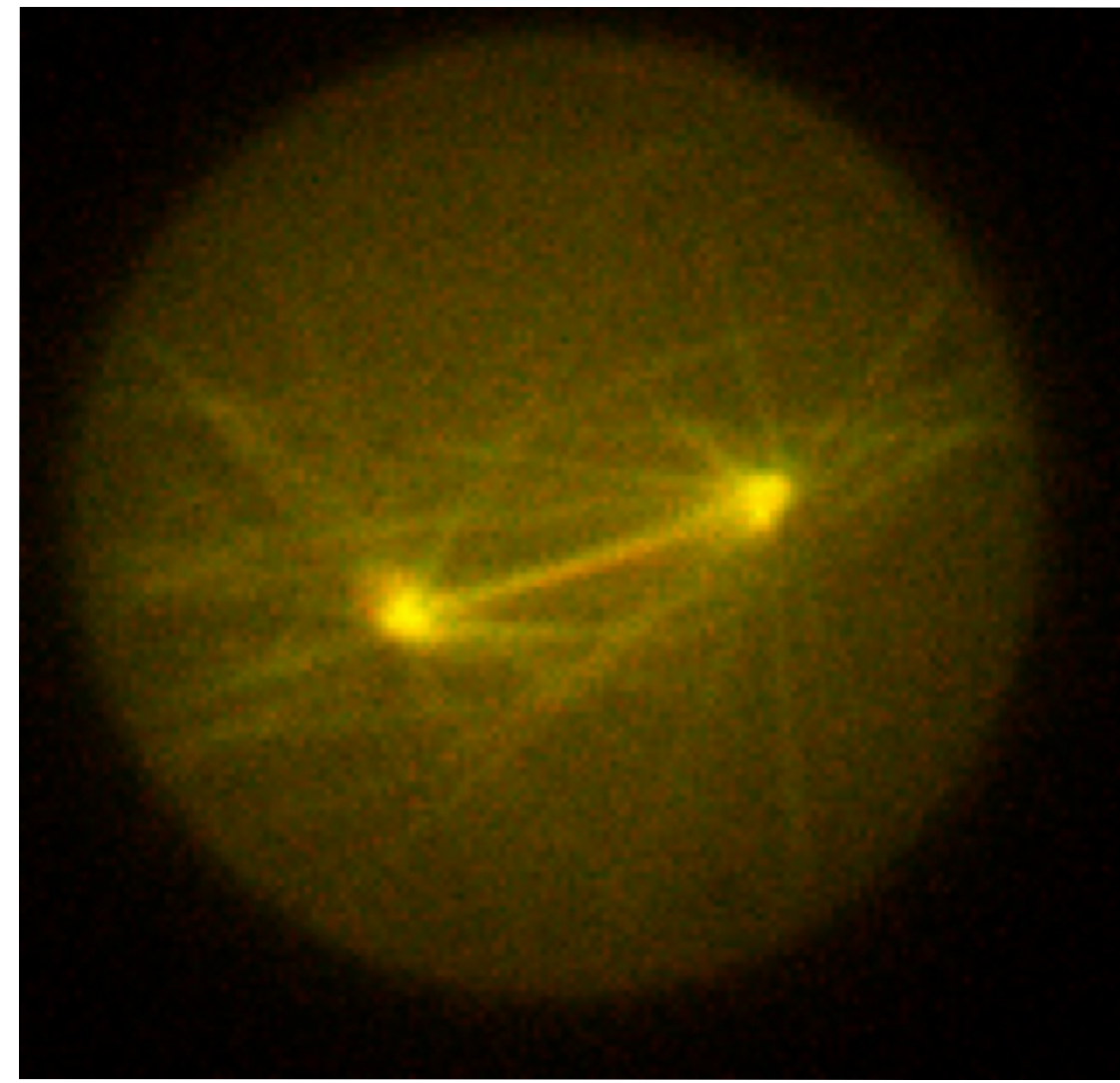
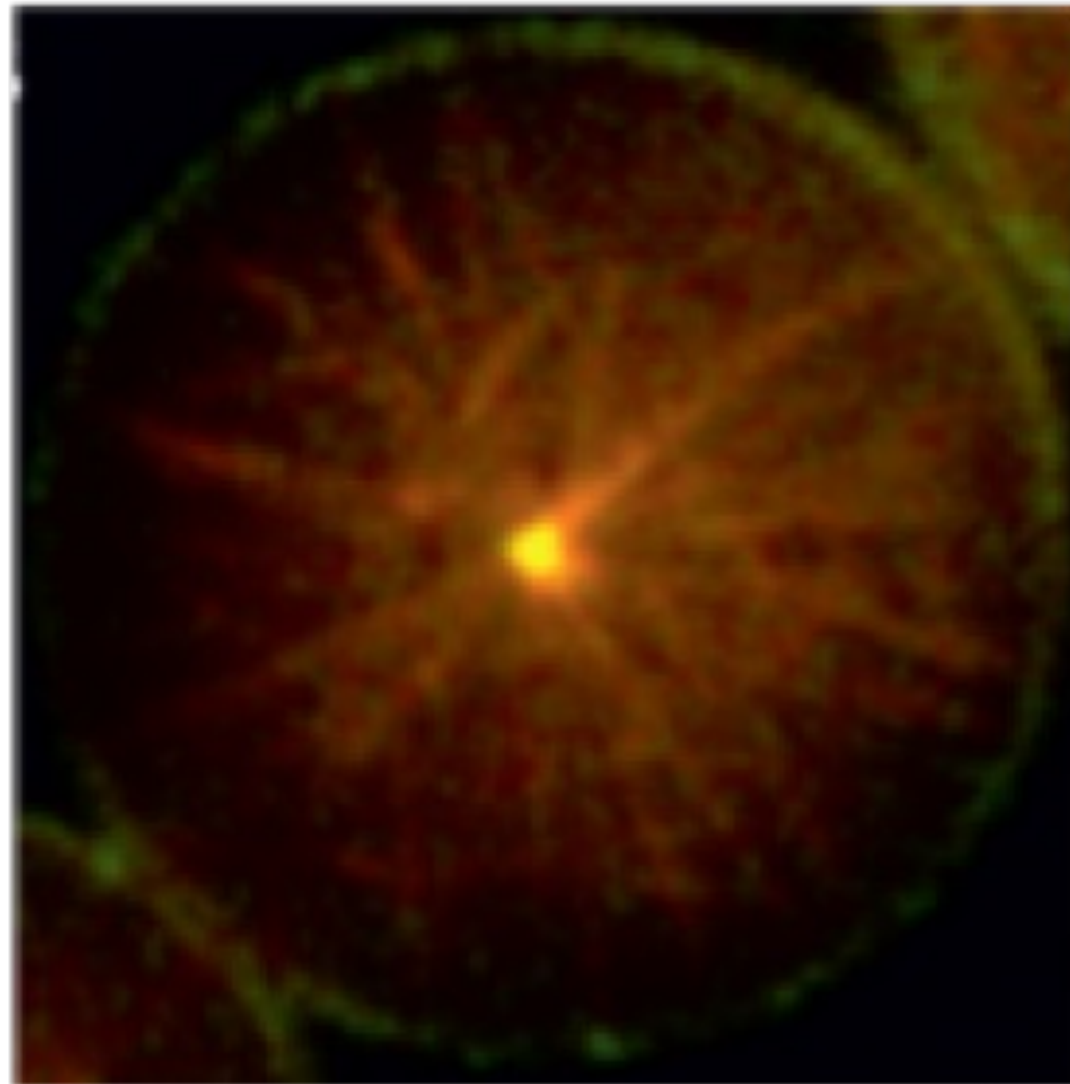
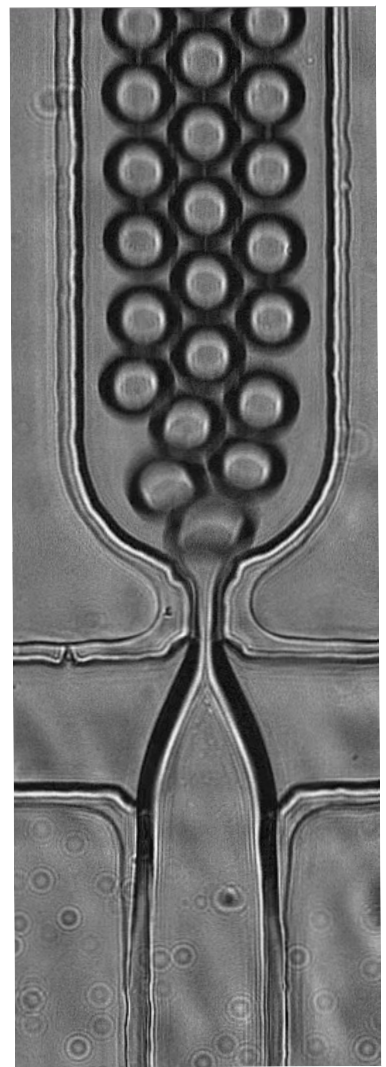


Image by CEA

Reconstituting Cytoskeletal Systems in Artificial Cells



Reza Amini
Yash Yawale
Ali Nick Maleki
Nemo Andrea
Sinda Khanfir
Beatriz Orozco Monroy

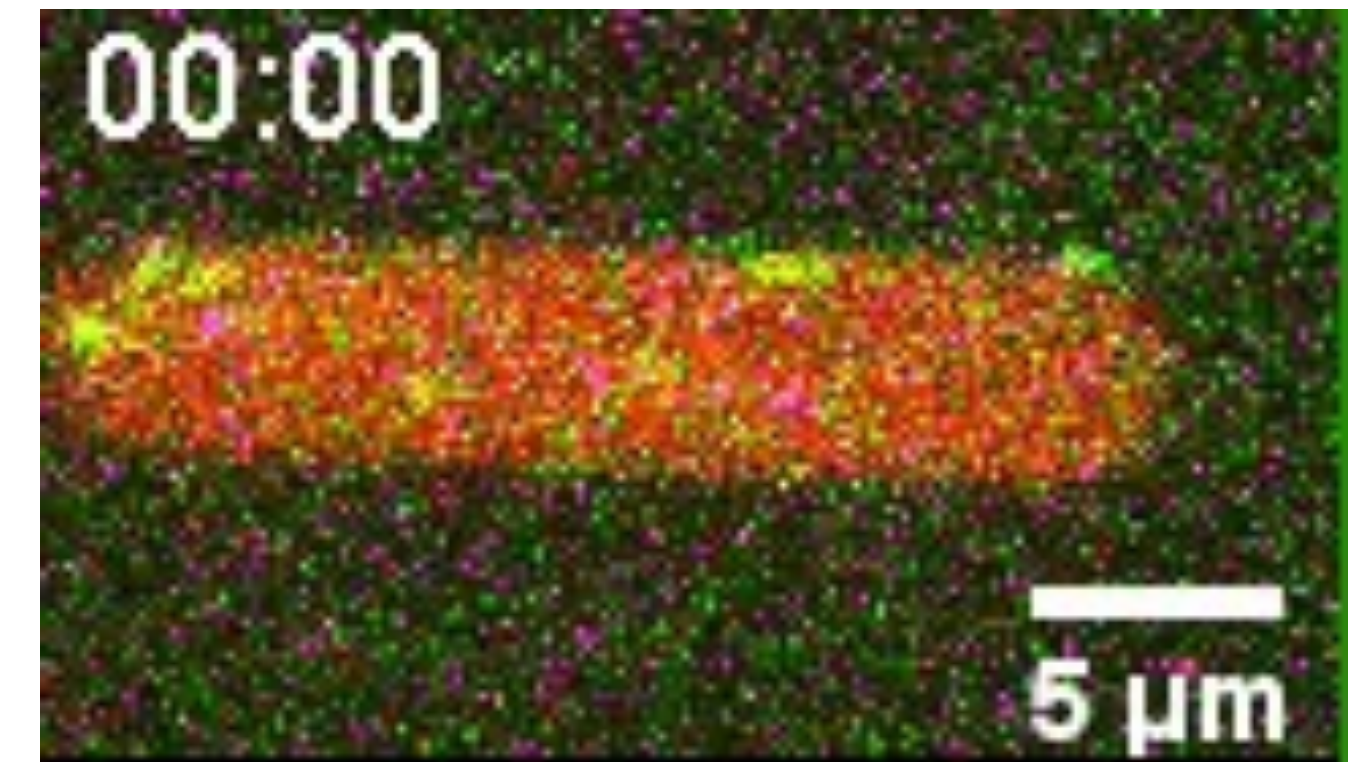
Irina Bareja

Roland Dries
Esengul Yildirim
Eli v/d Sluis
Ashmiani van den Berg

BaSyC
www.basyc.nl

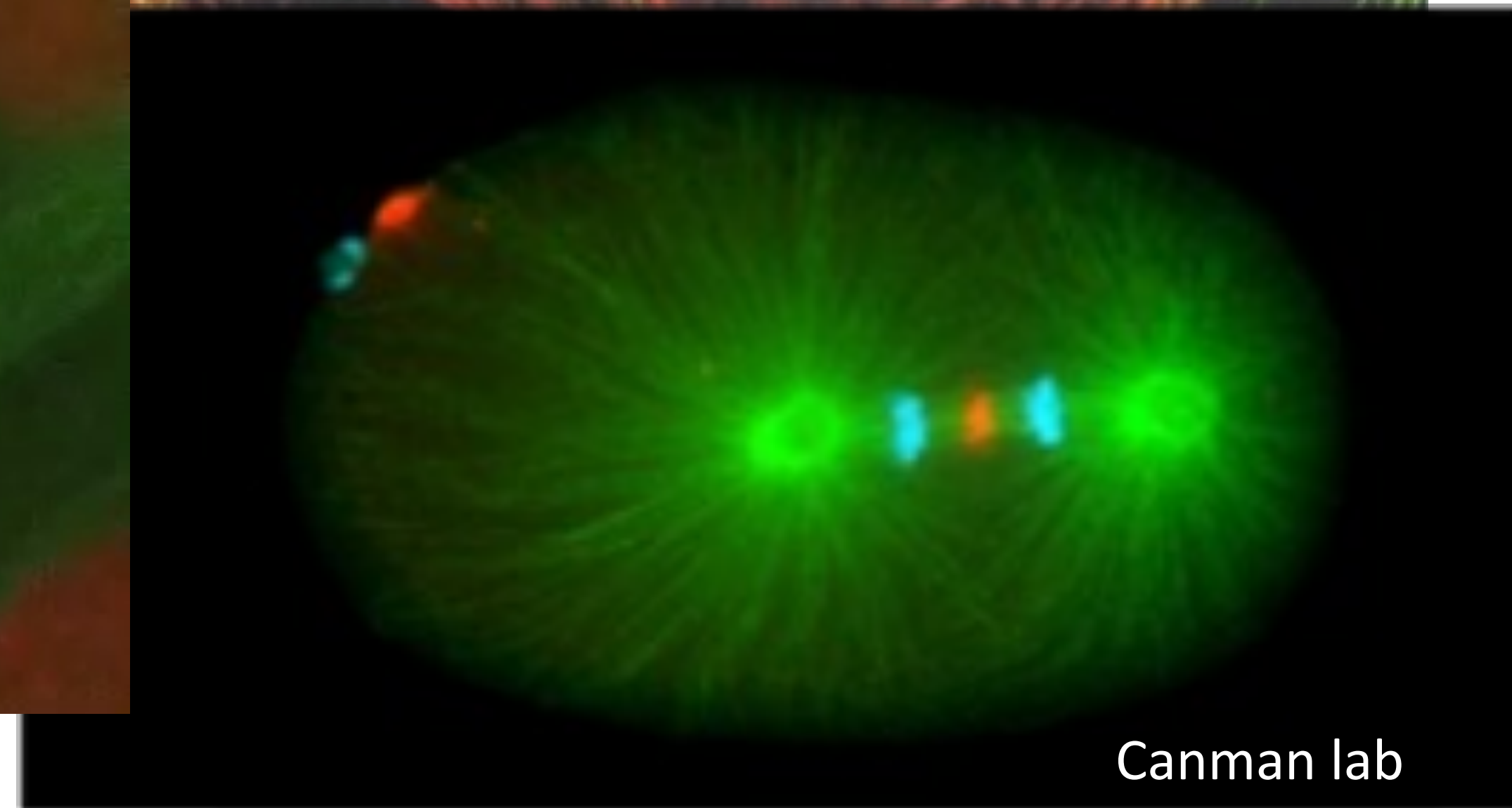
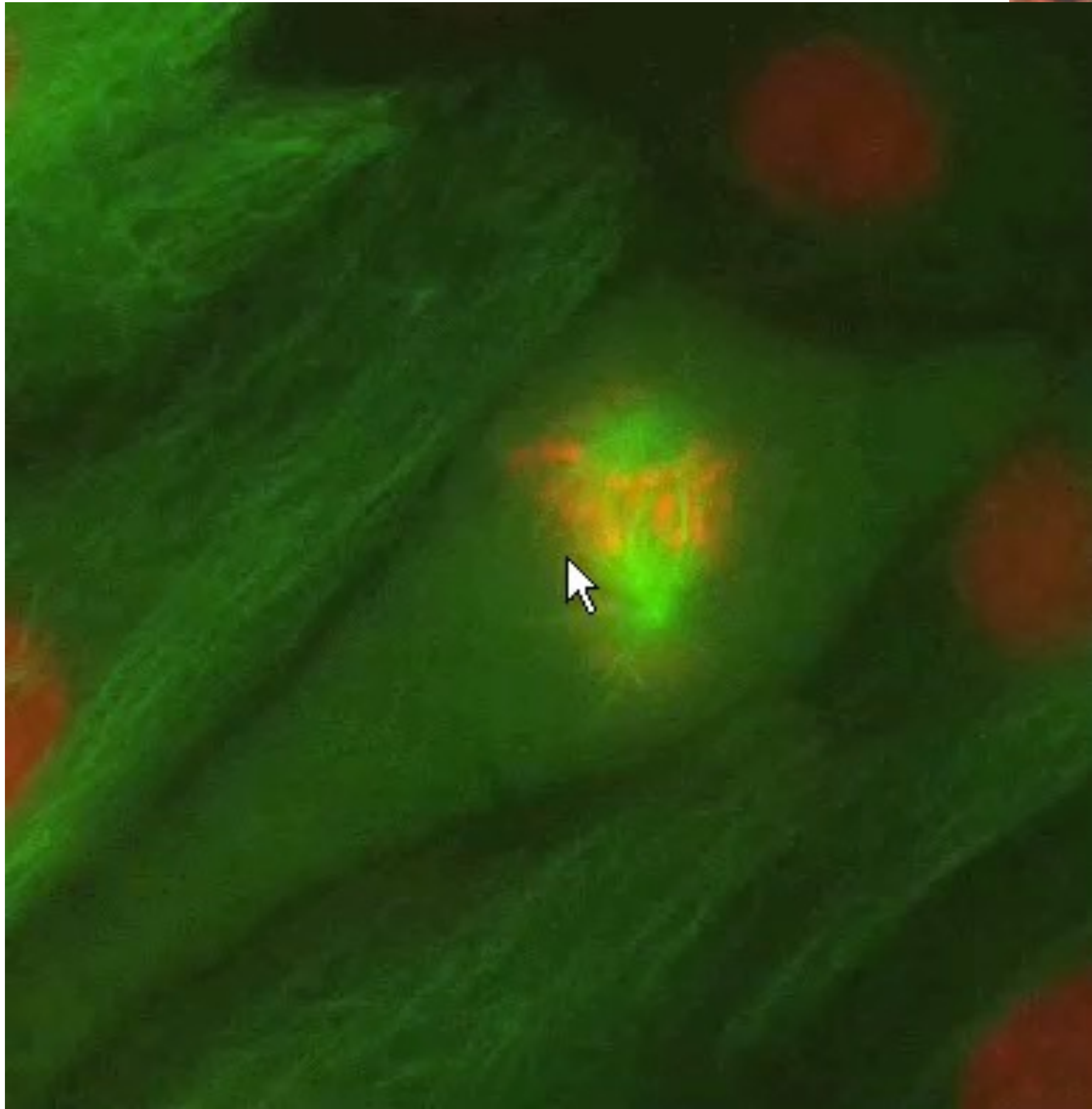
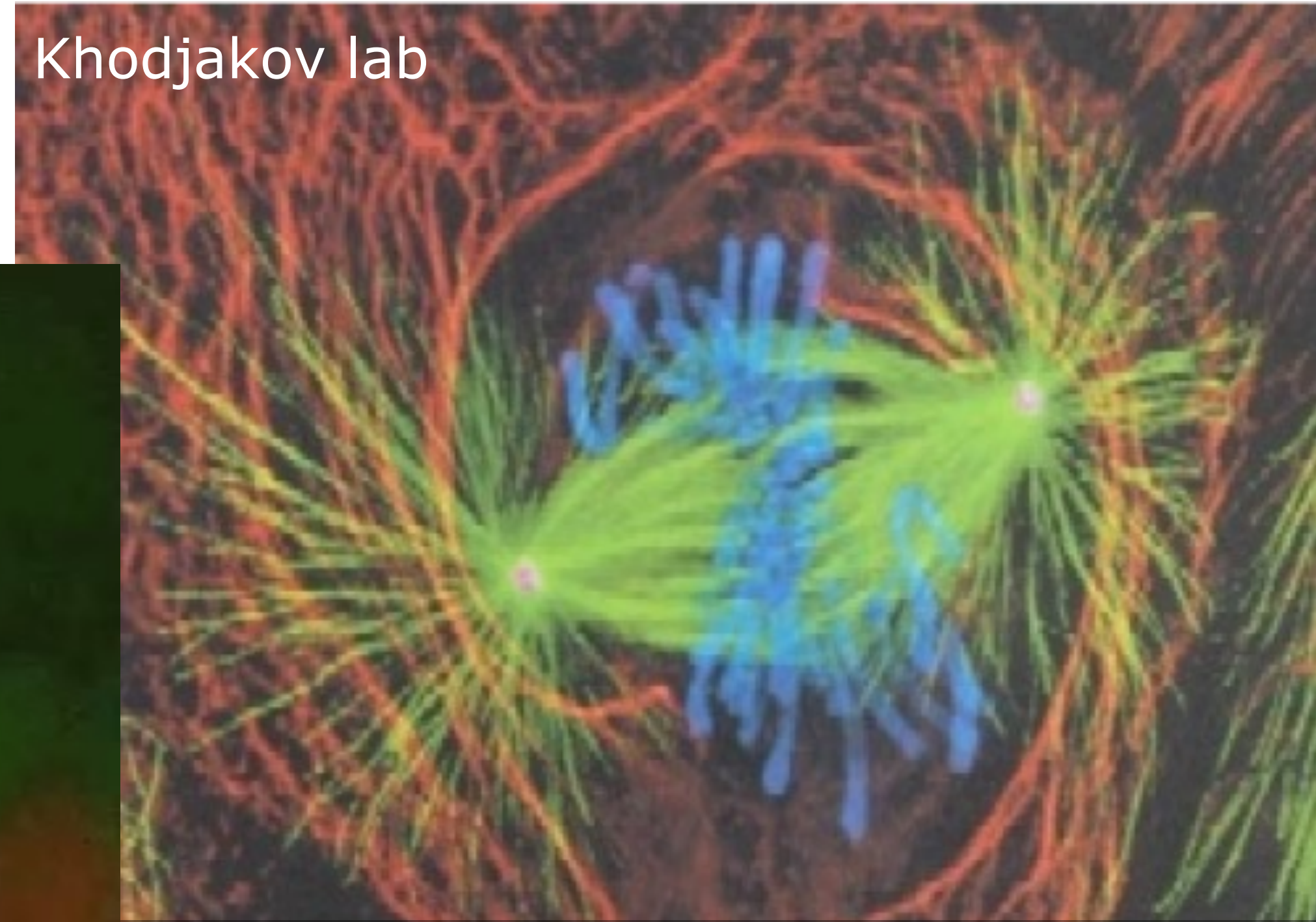
SC
www.syntheticcell.eu

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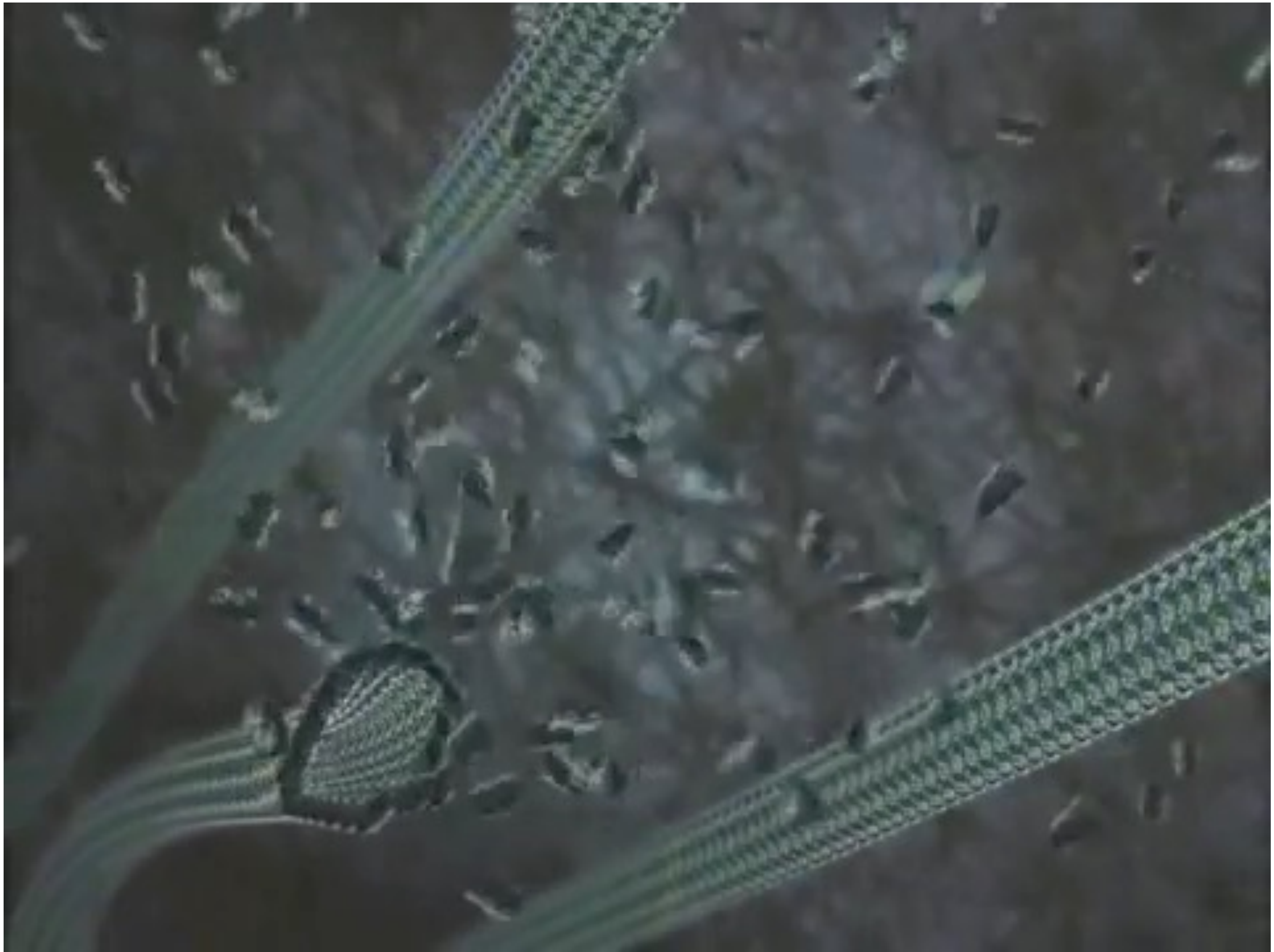


Dividing cells

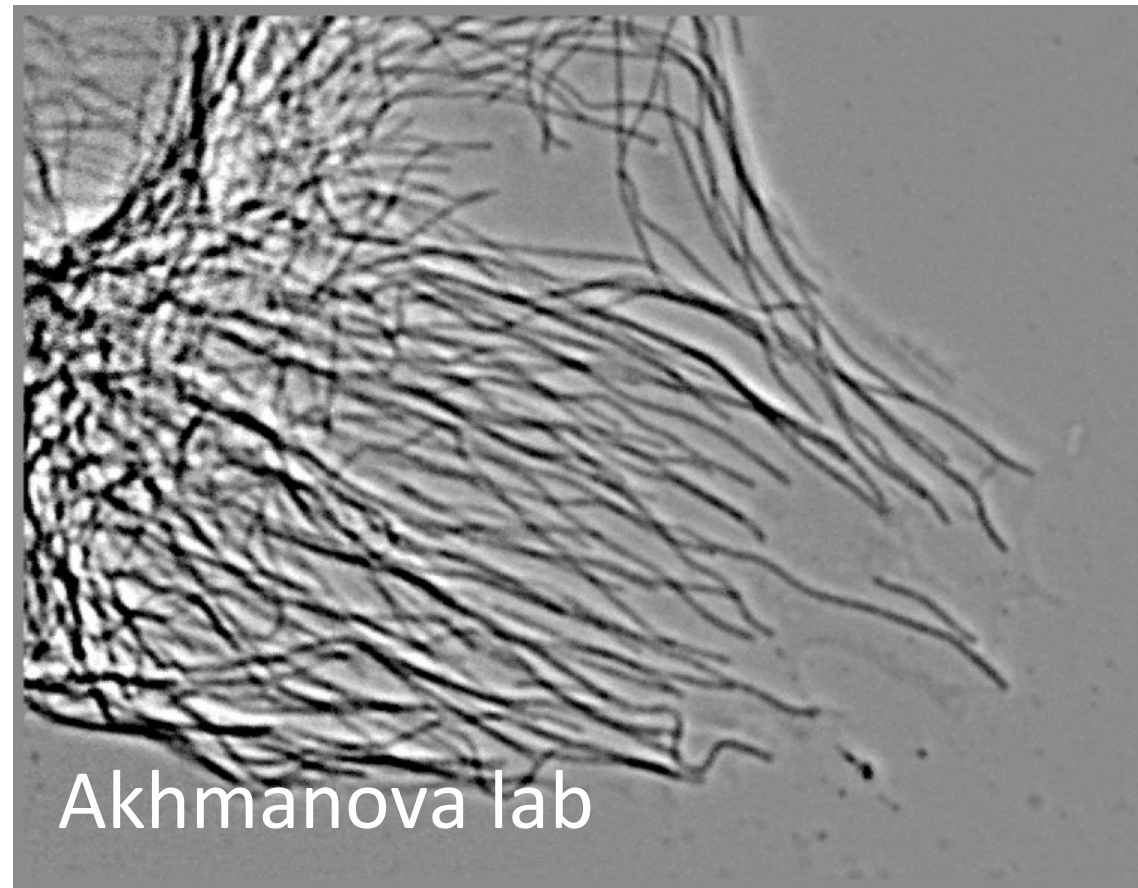
Khodjakov lab



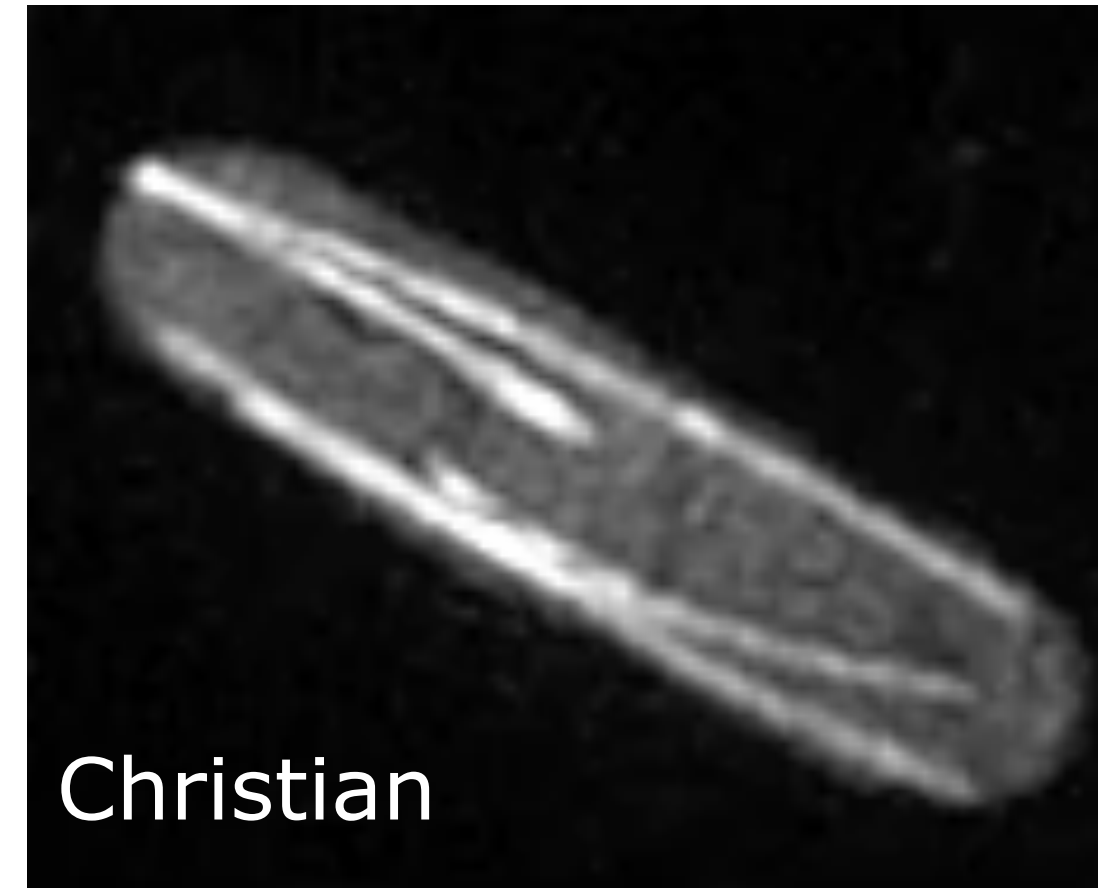
Canman lab



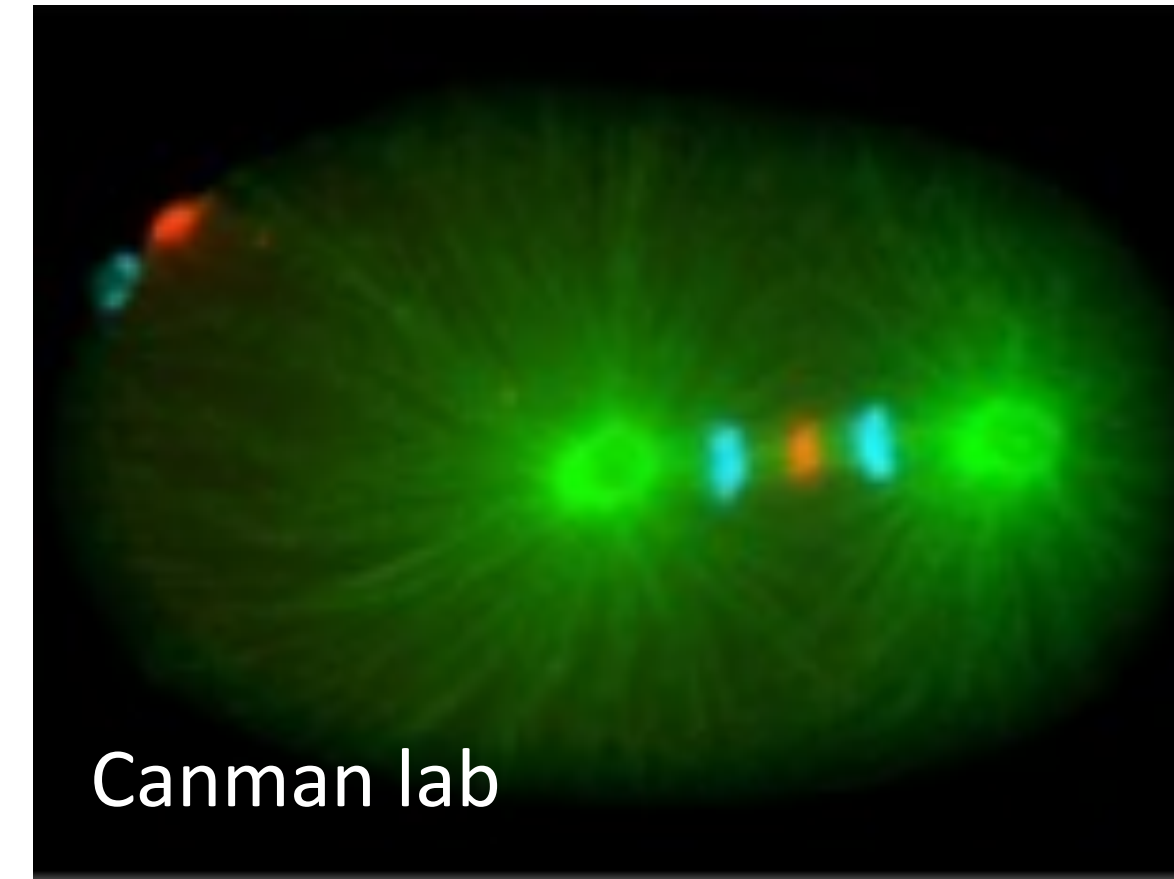
Building functional microtubule complexity in vitro



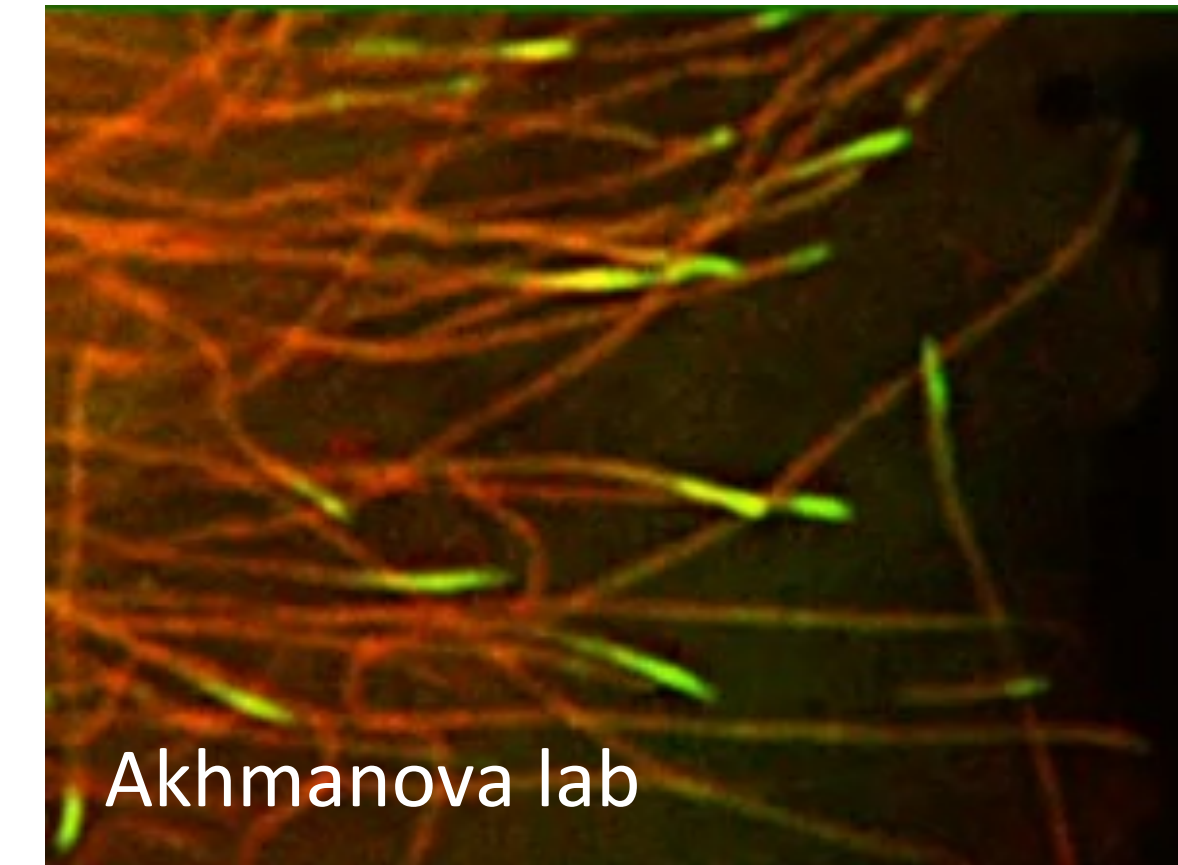
Dynamics



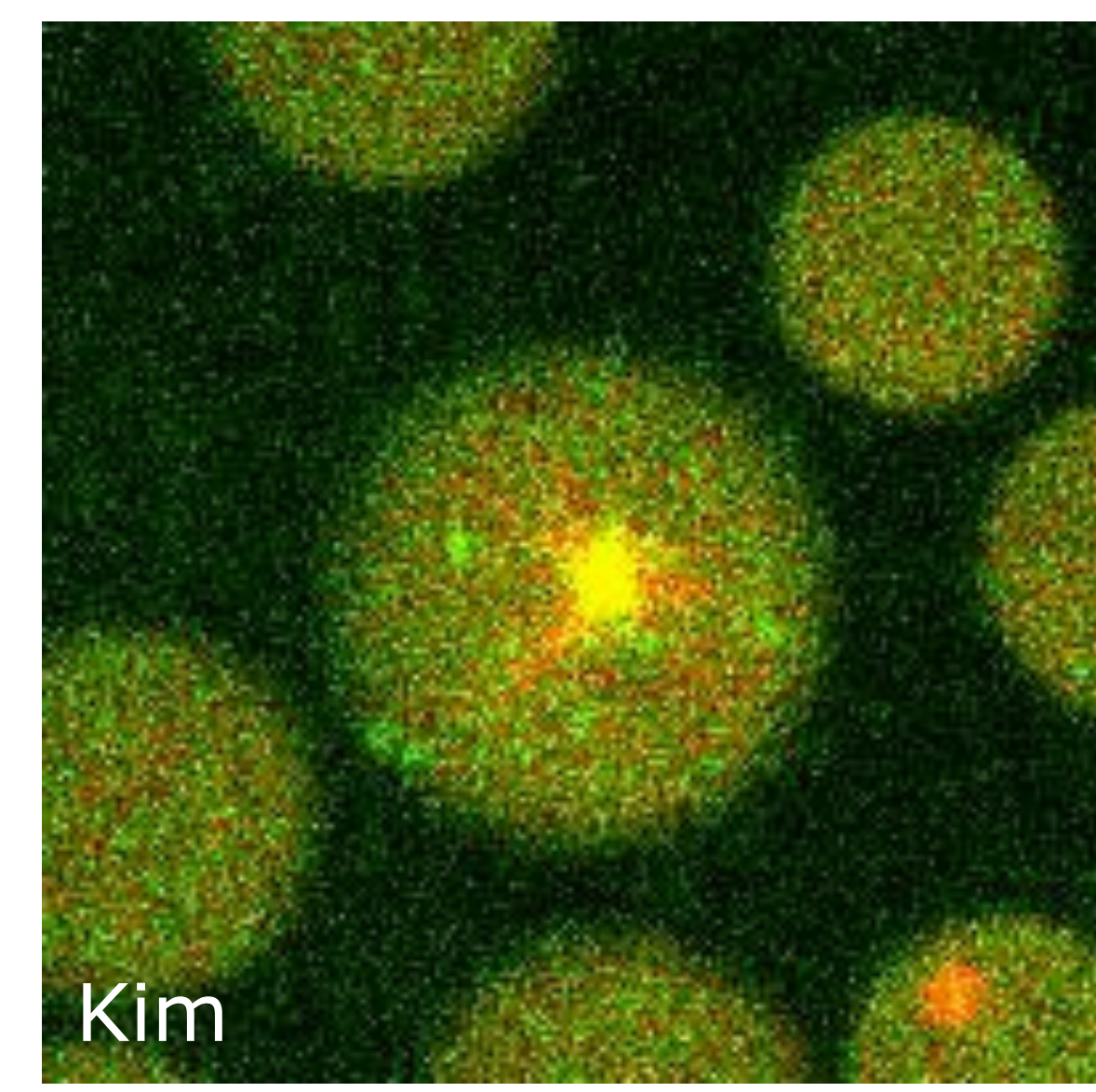
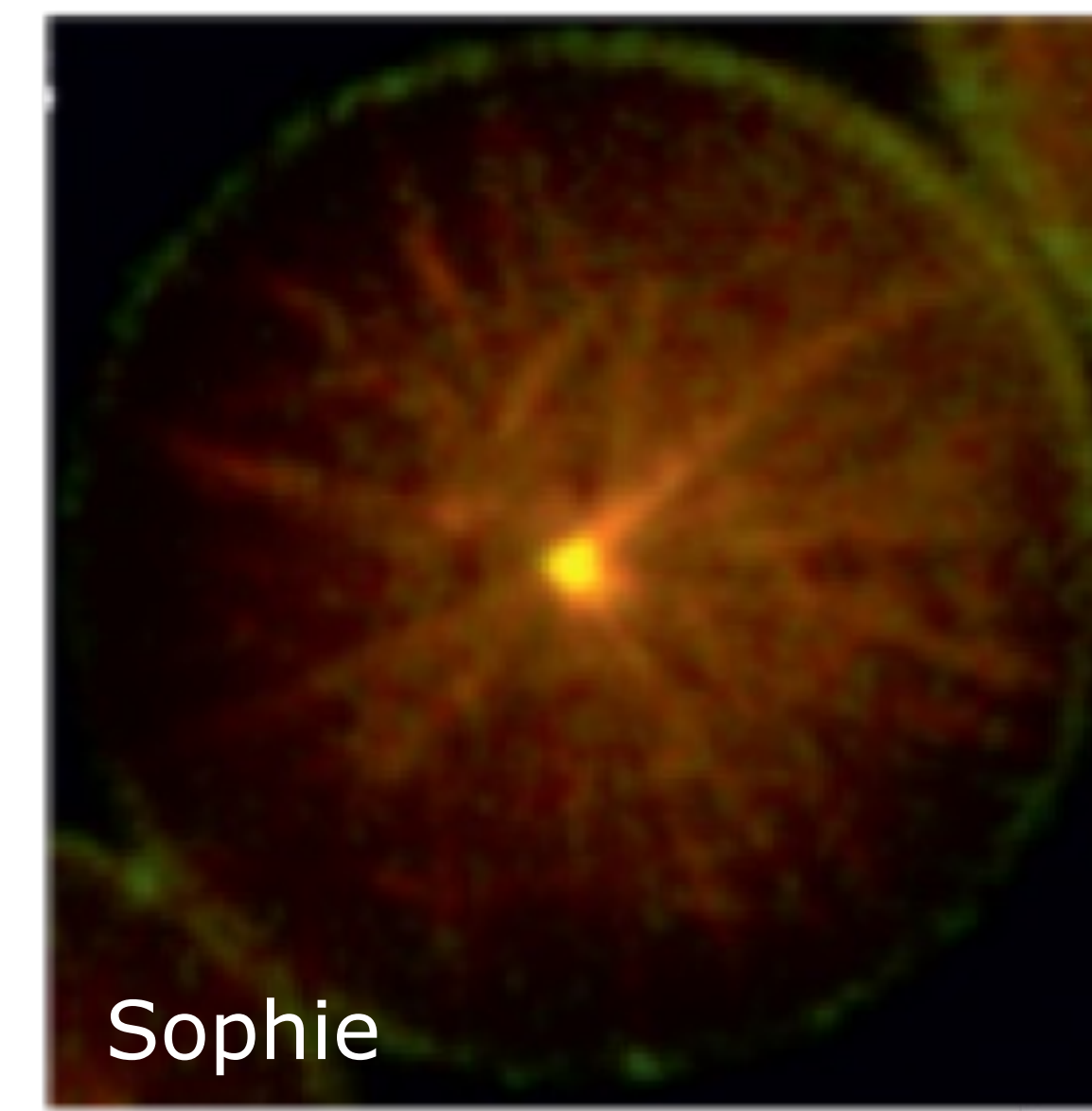
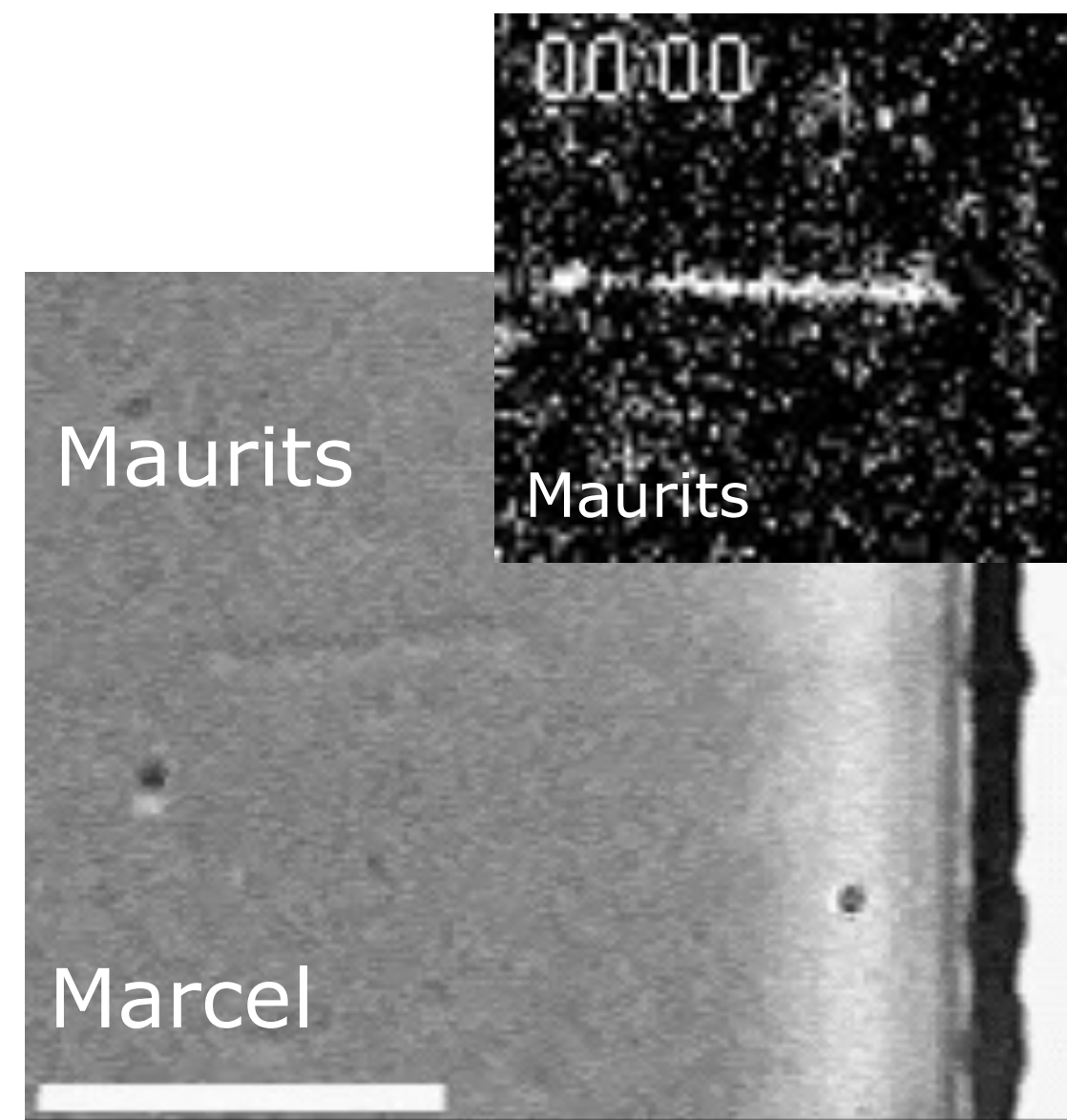
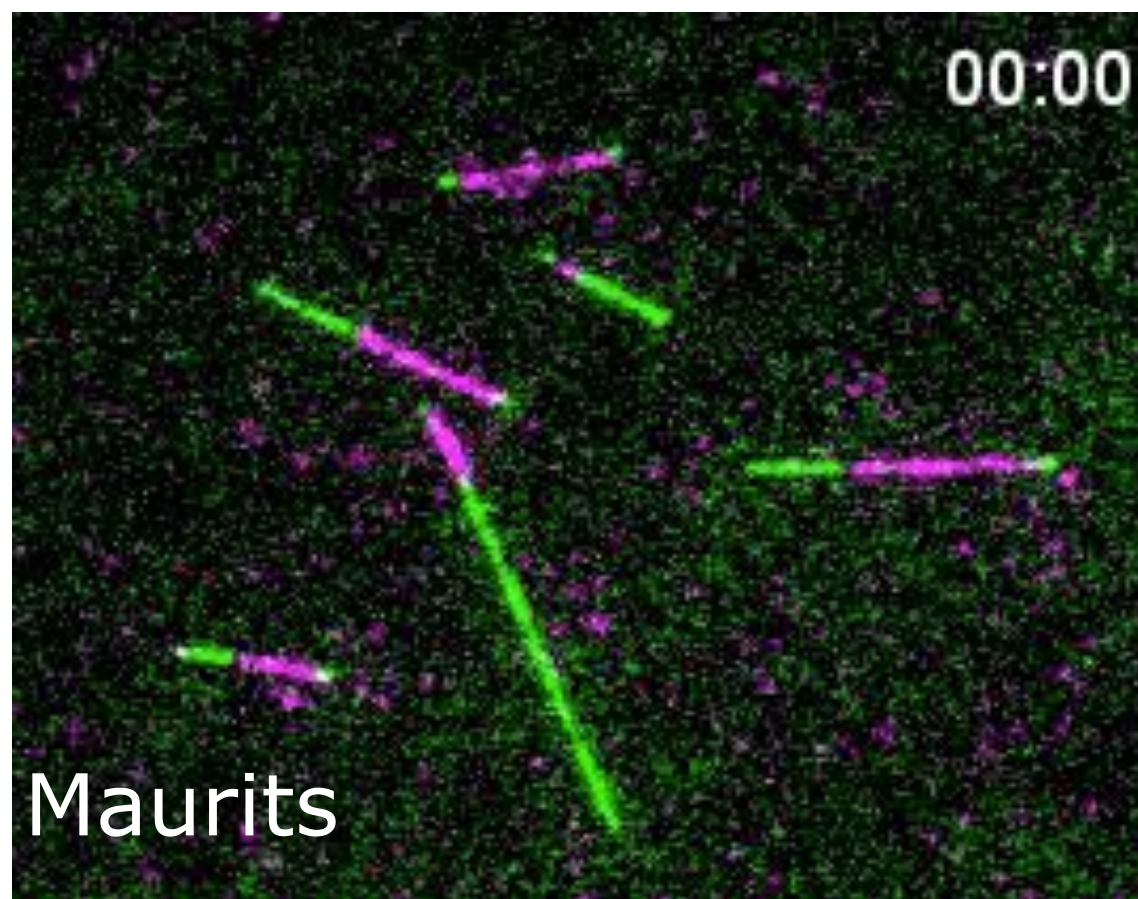
Forces



Positioning

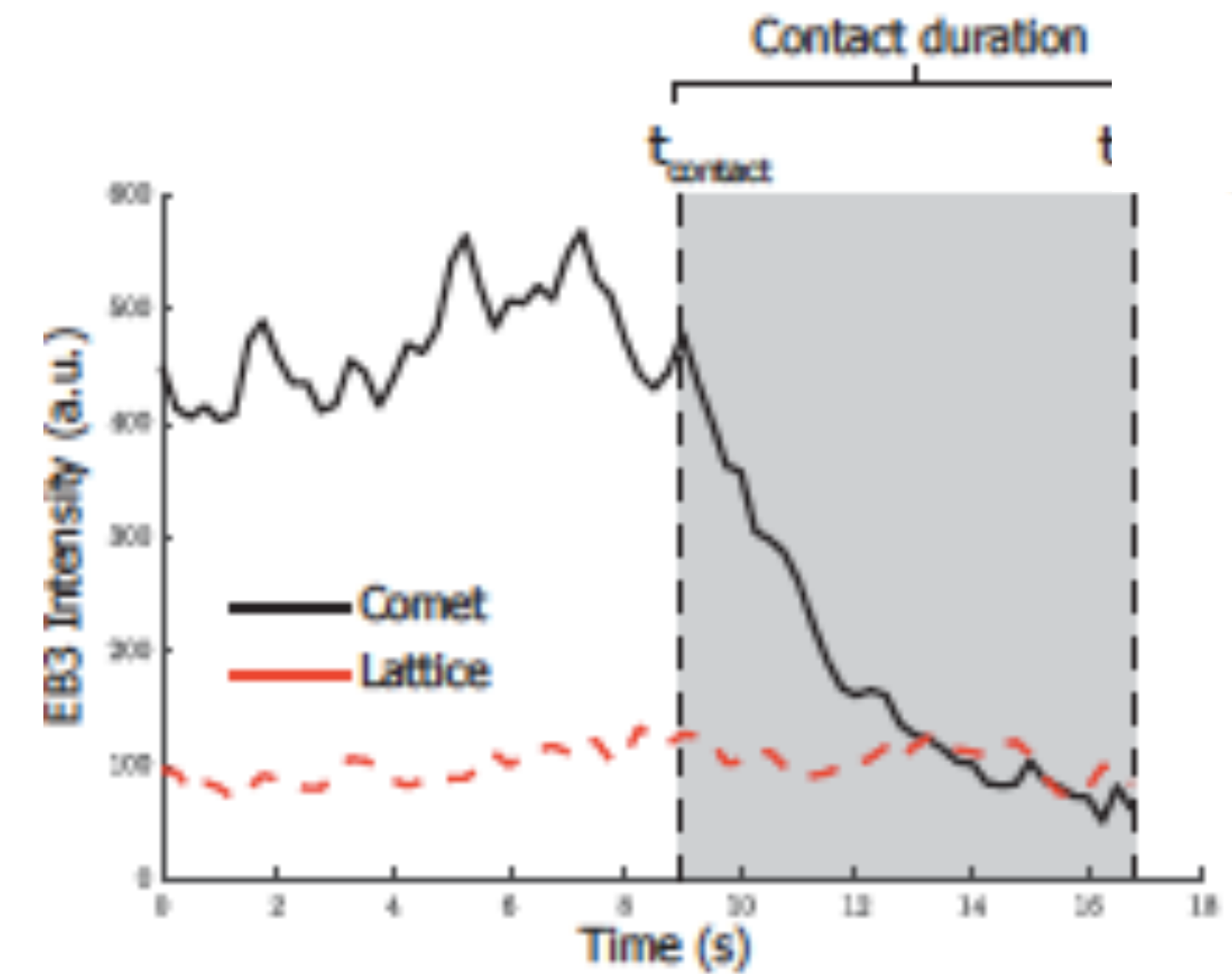
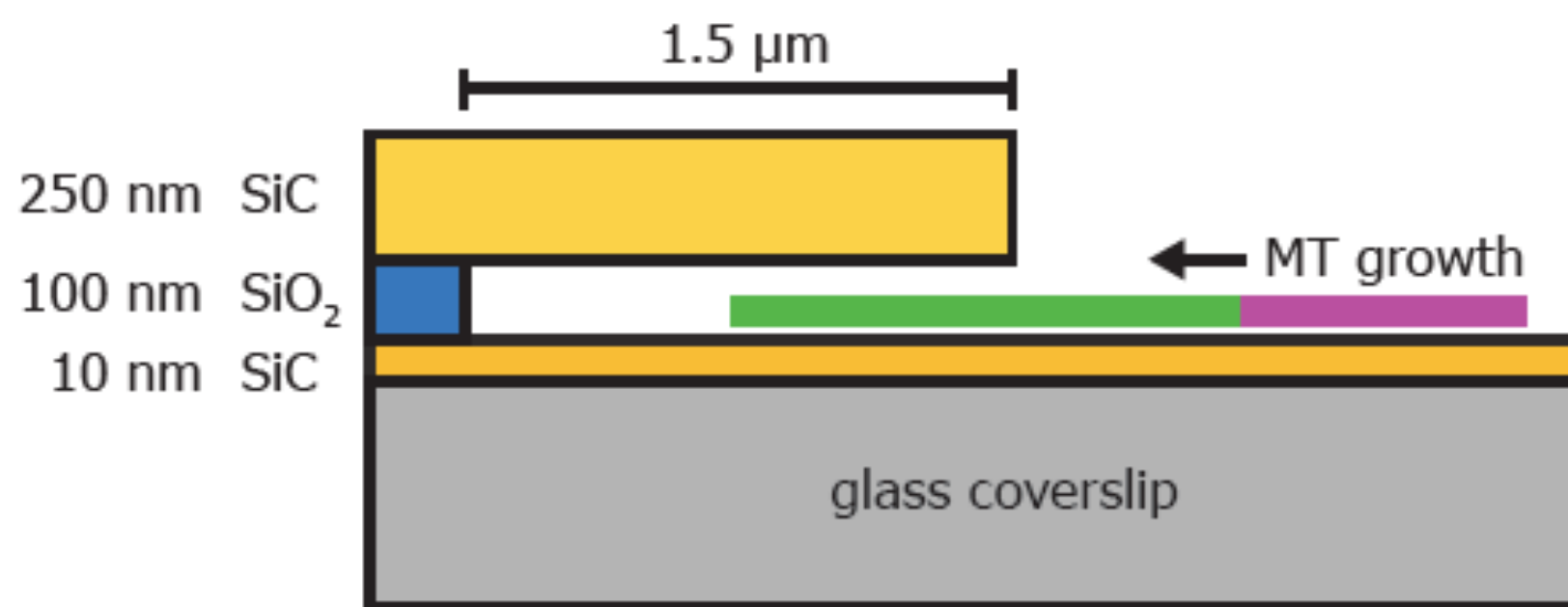
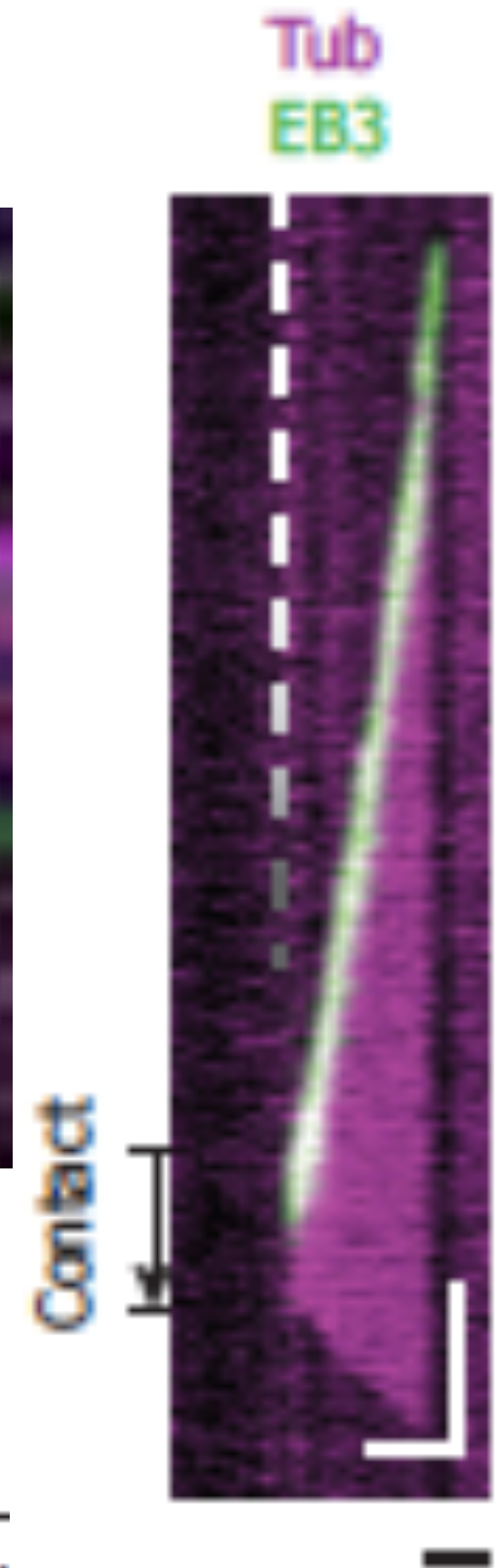
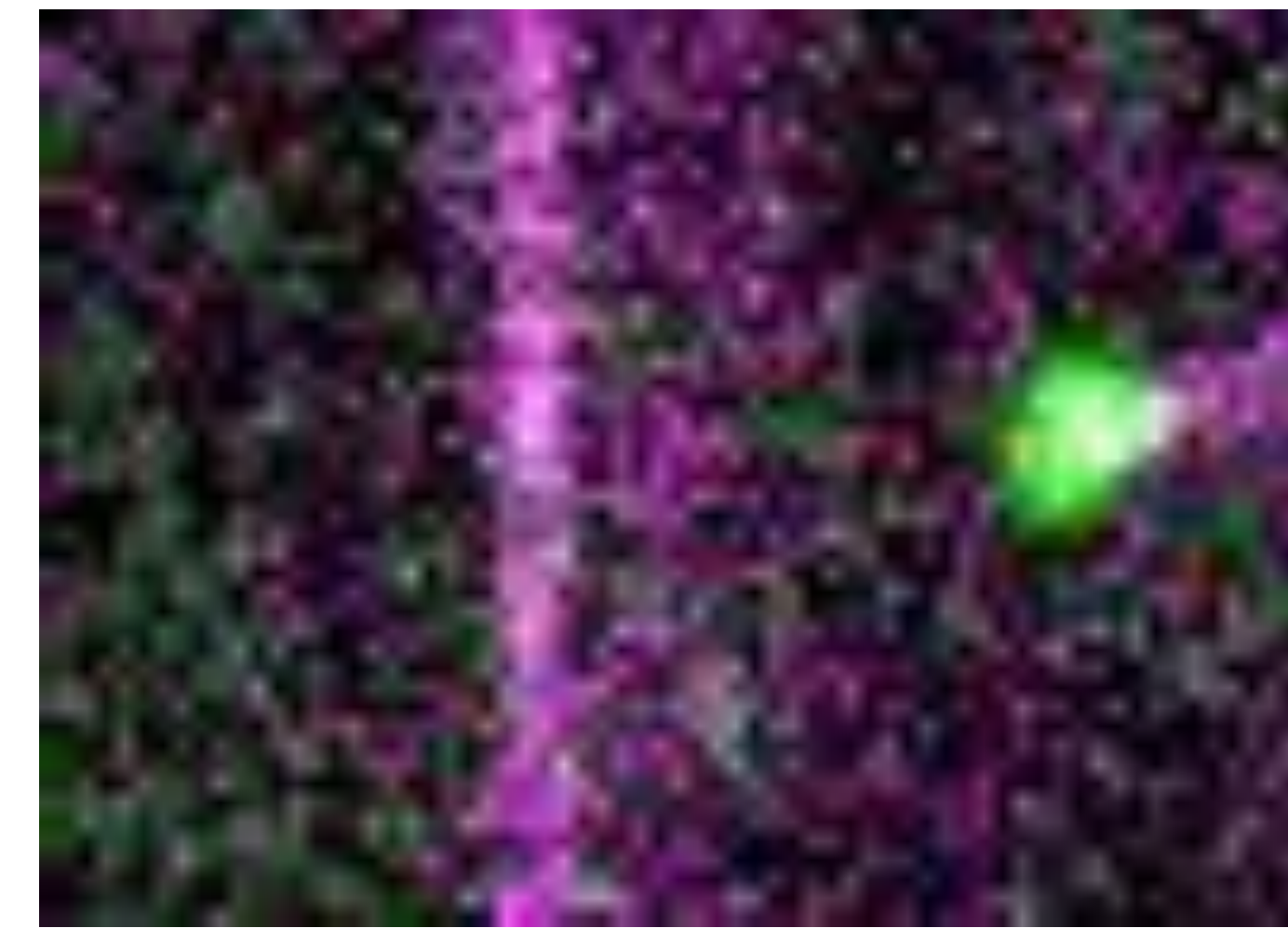
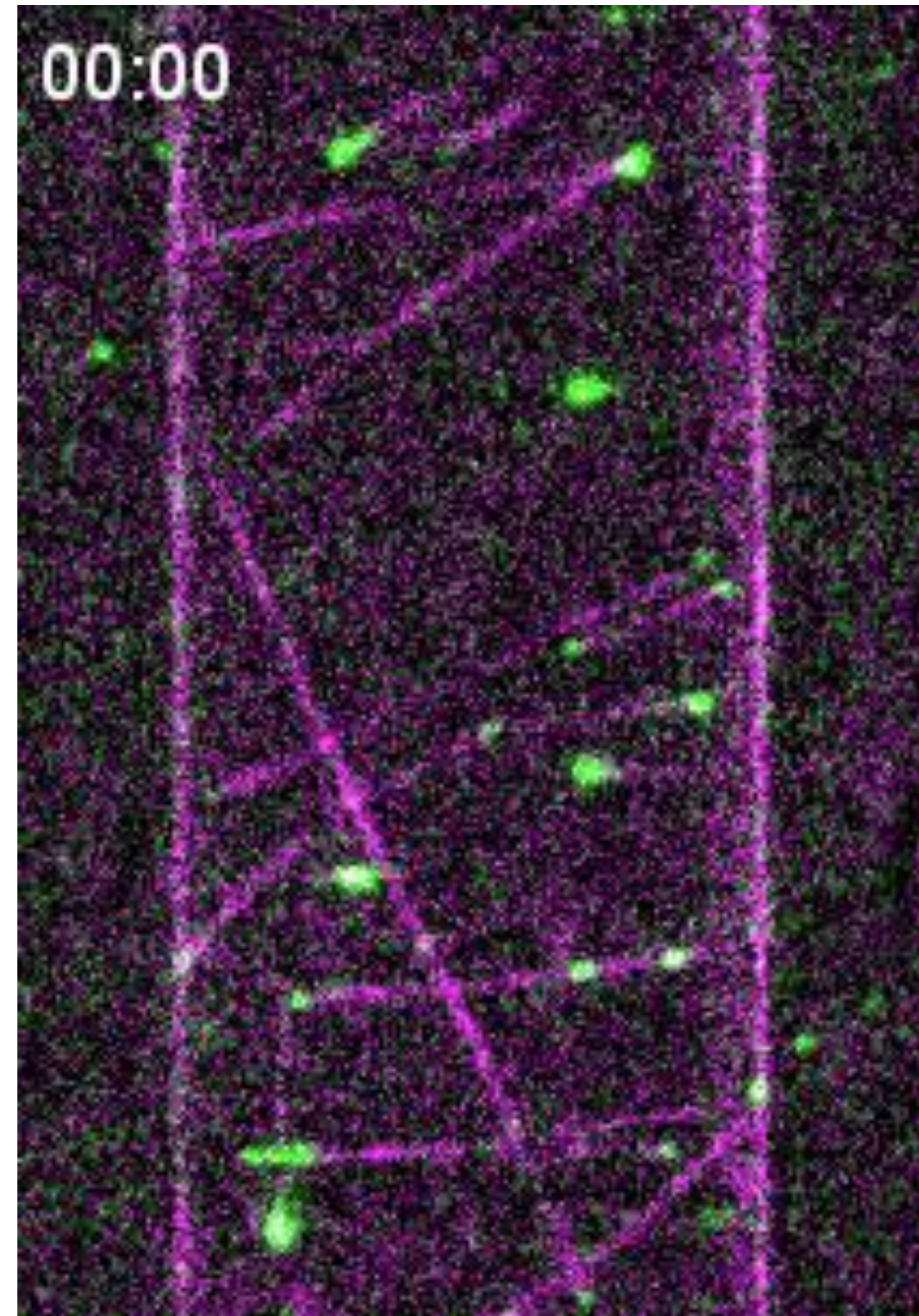
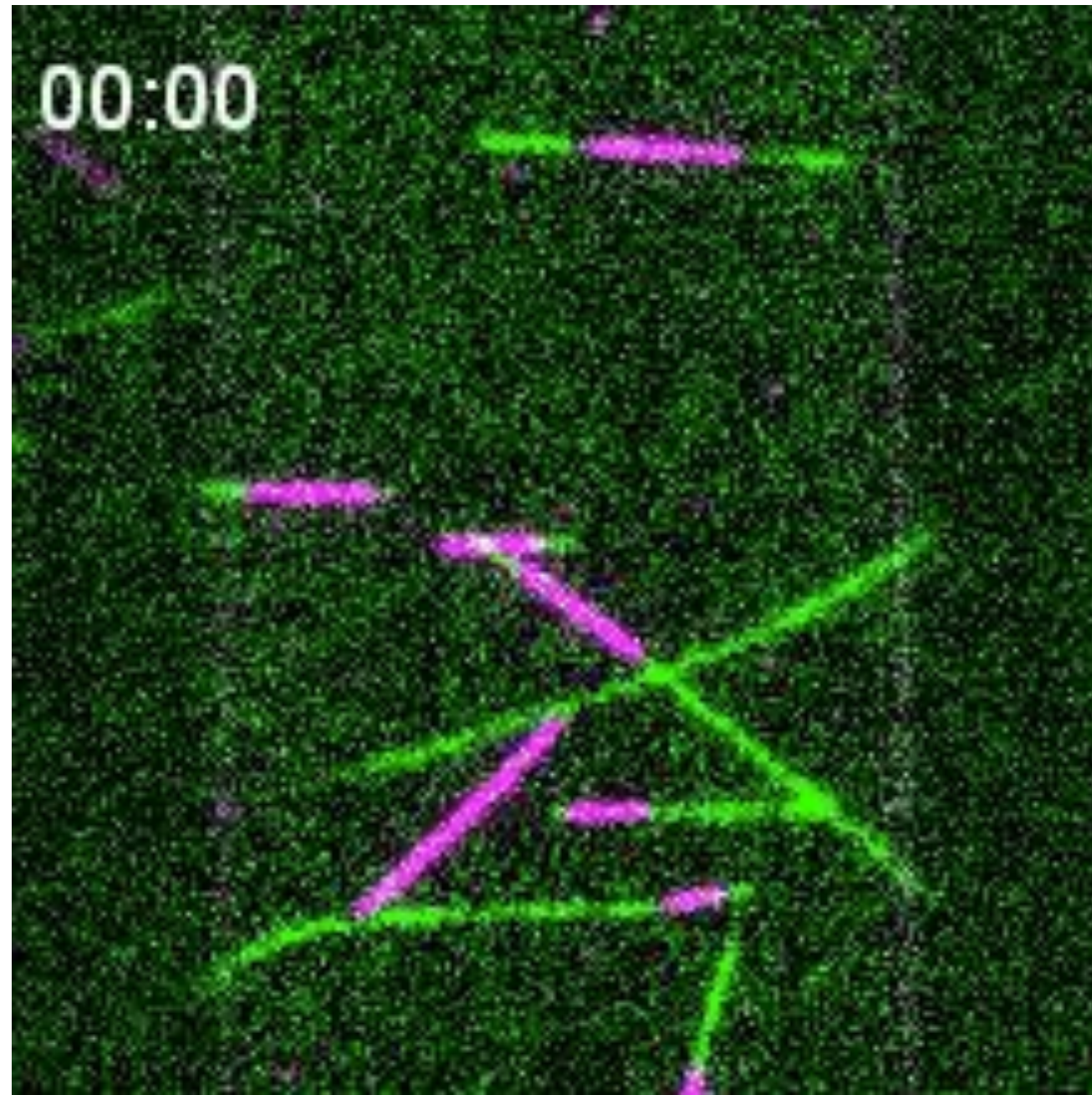


Control



Dogterom & Yurke, Science 1997, Janson et al, JCB 2003; Kerssemakers et al, Nature 2006; Bieling et al, Nature 2007; Laan et al, Cell 2012; Preciado L. Et al, Nat Comm 2014, Dogterom & Koenderink, Nature Rev MCB 2018

Combining forces and molecular control



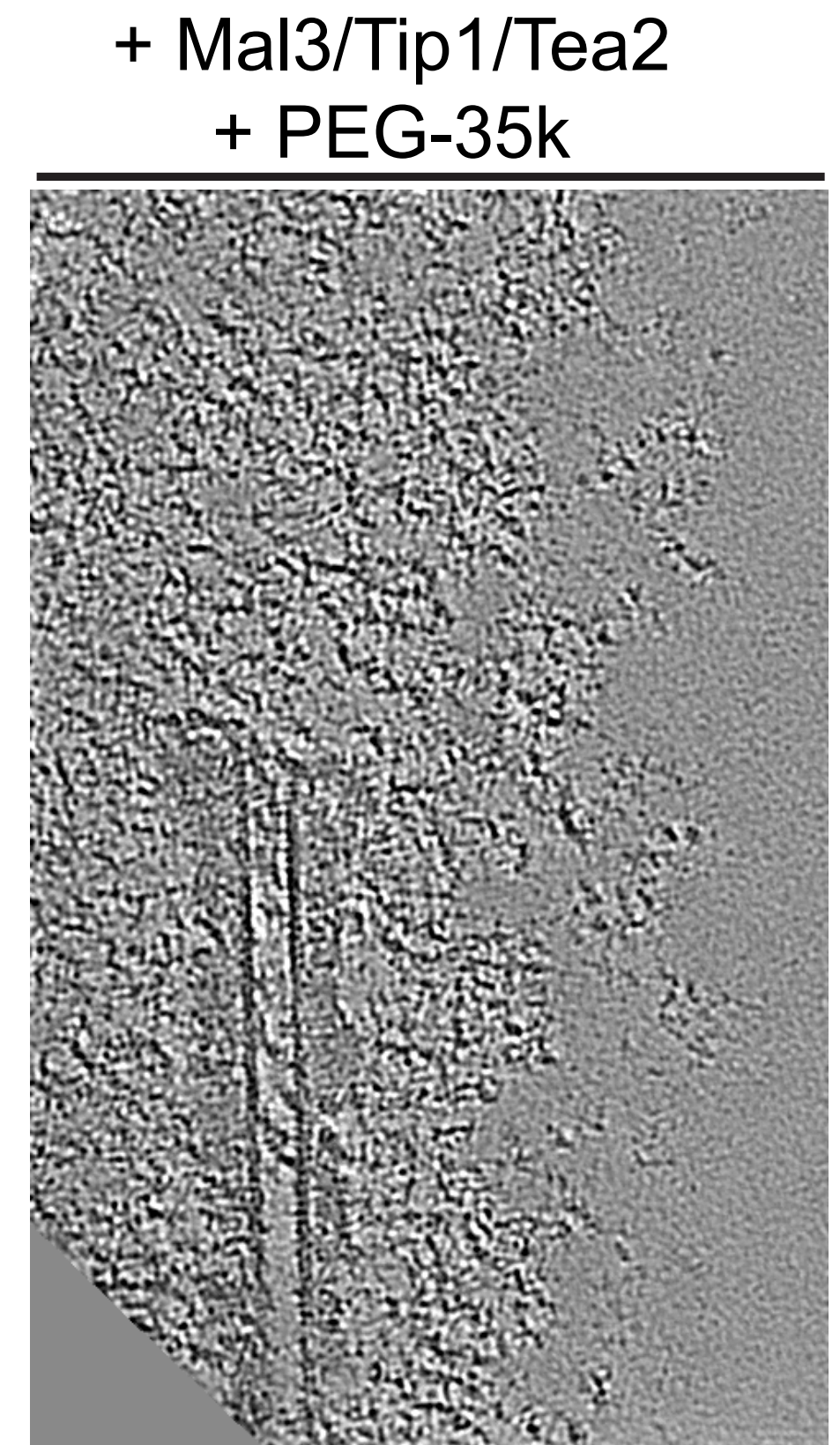
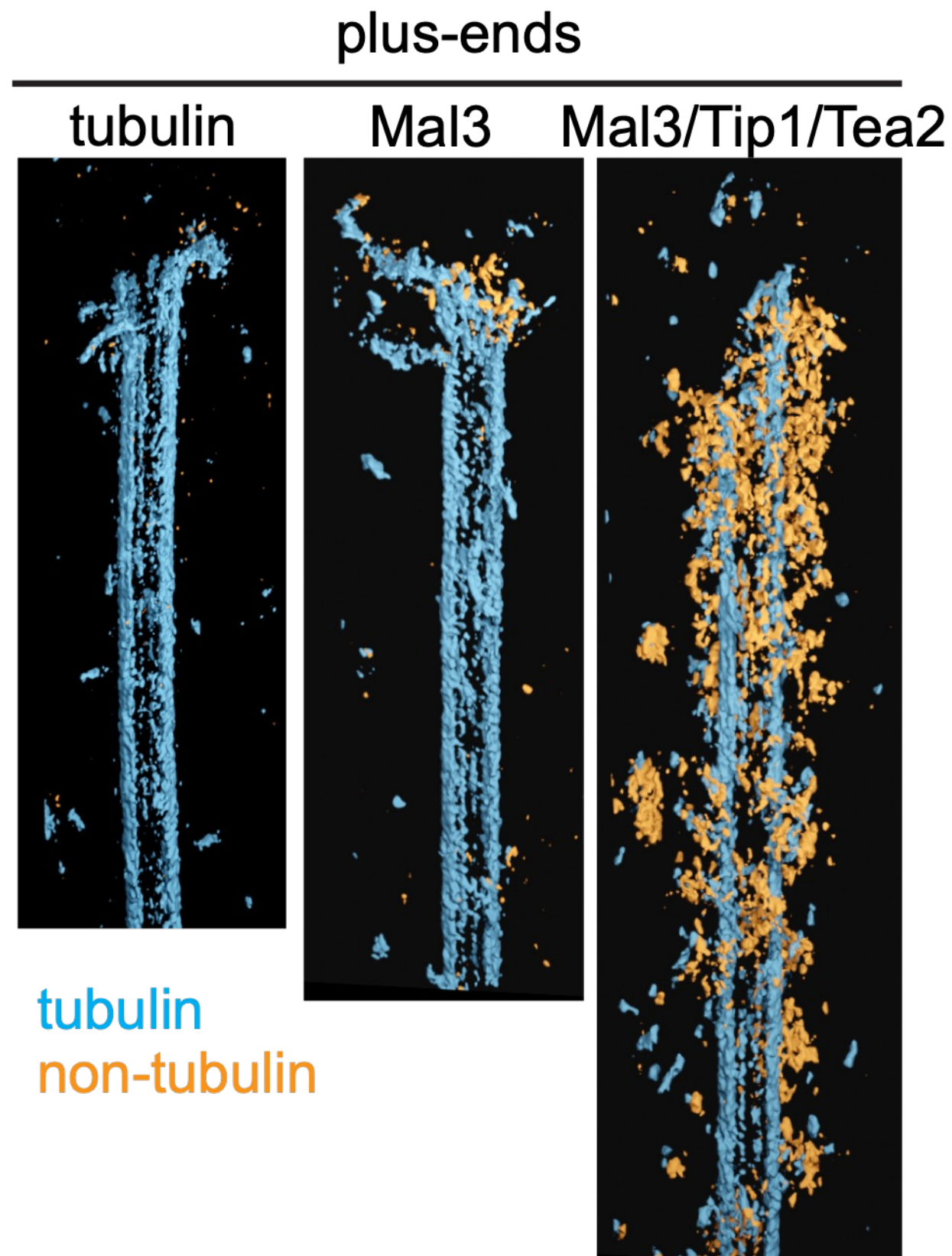
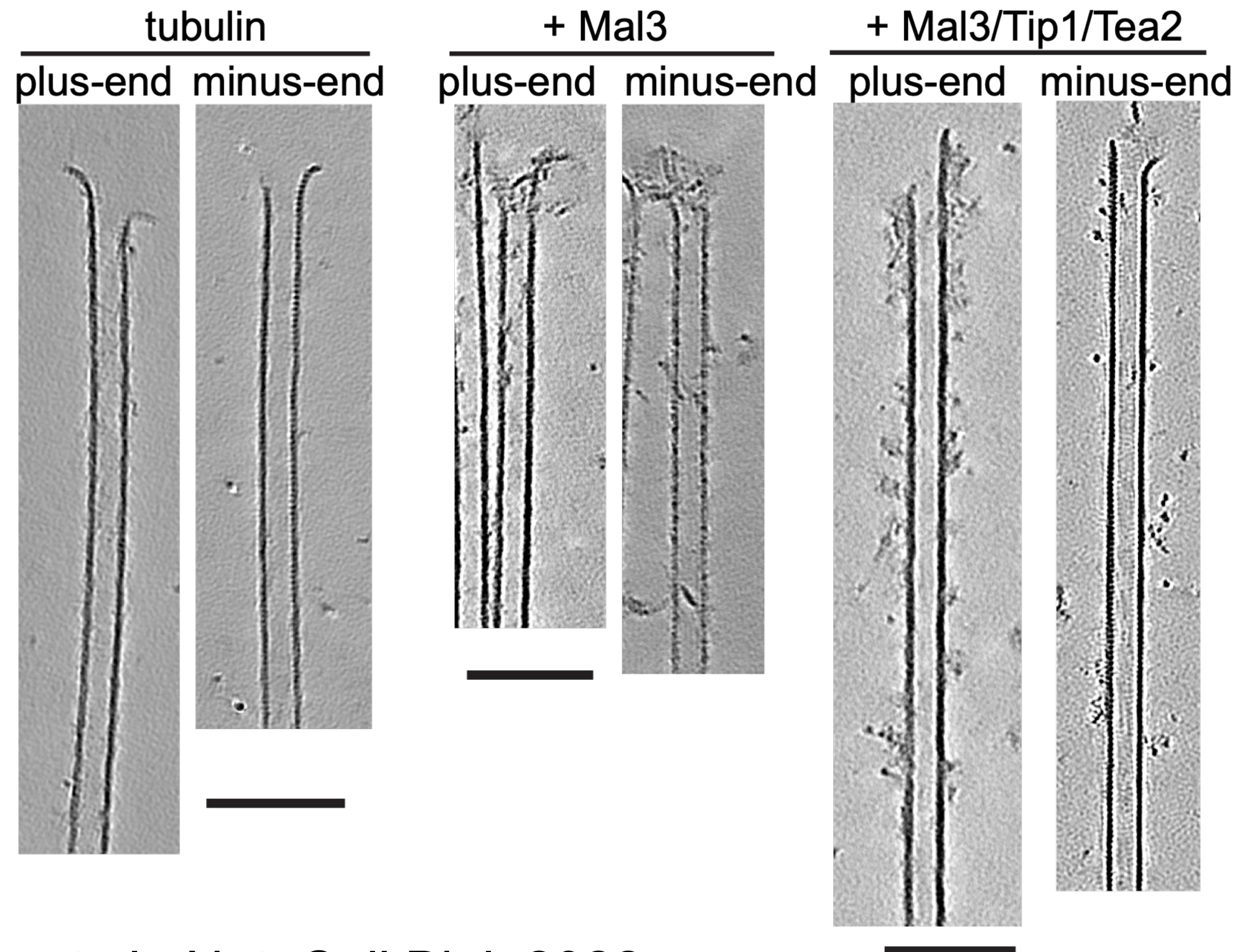
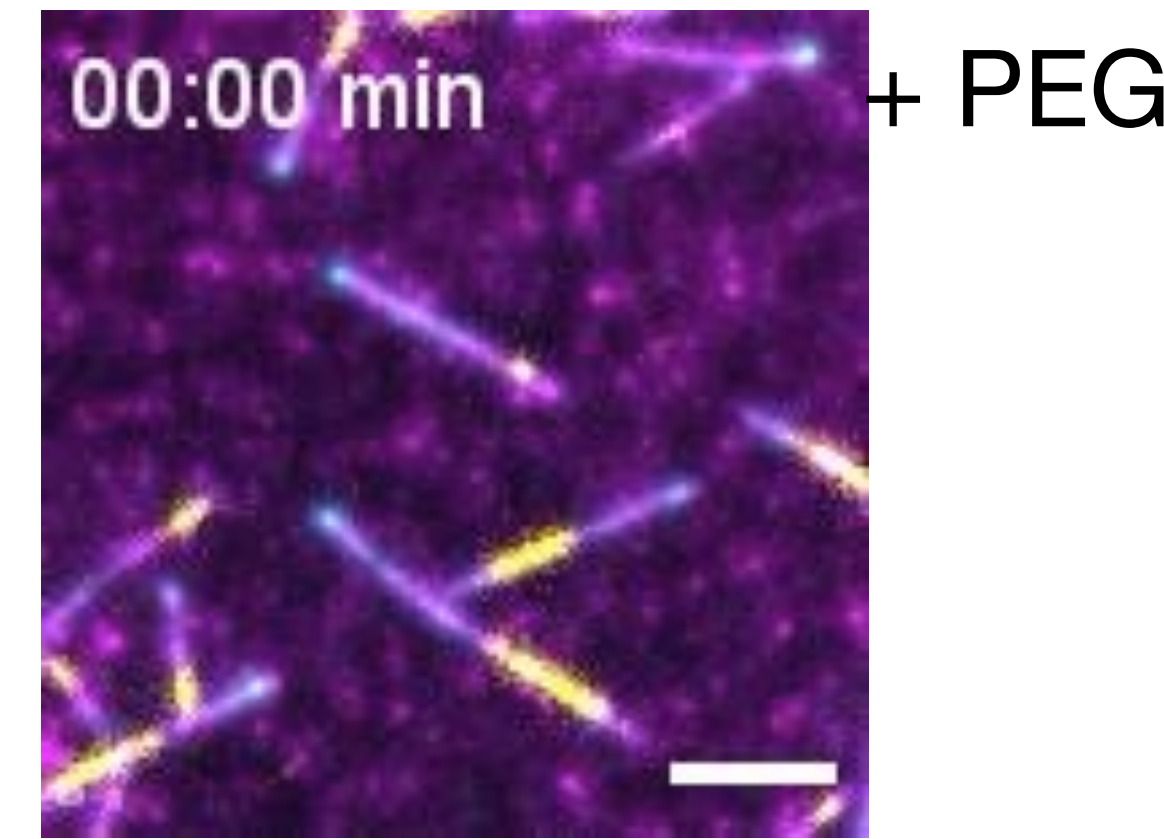
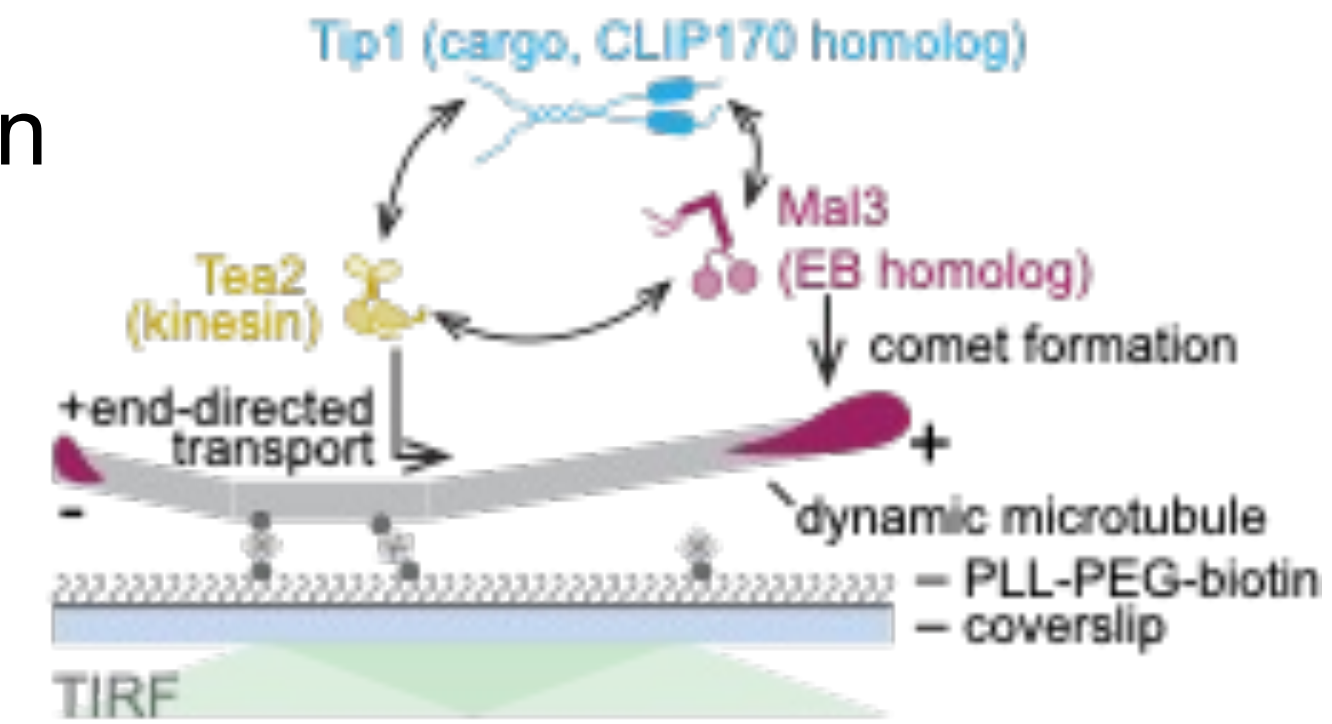
Architecture of MT-binding complexes ?

Bieling et al., Nature 2007

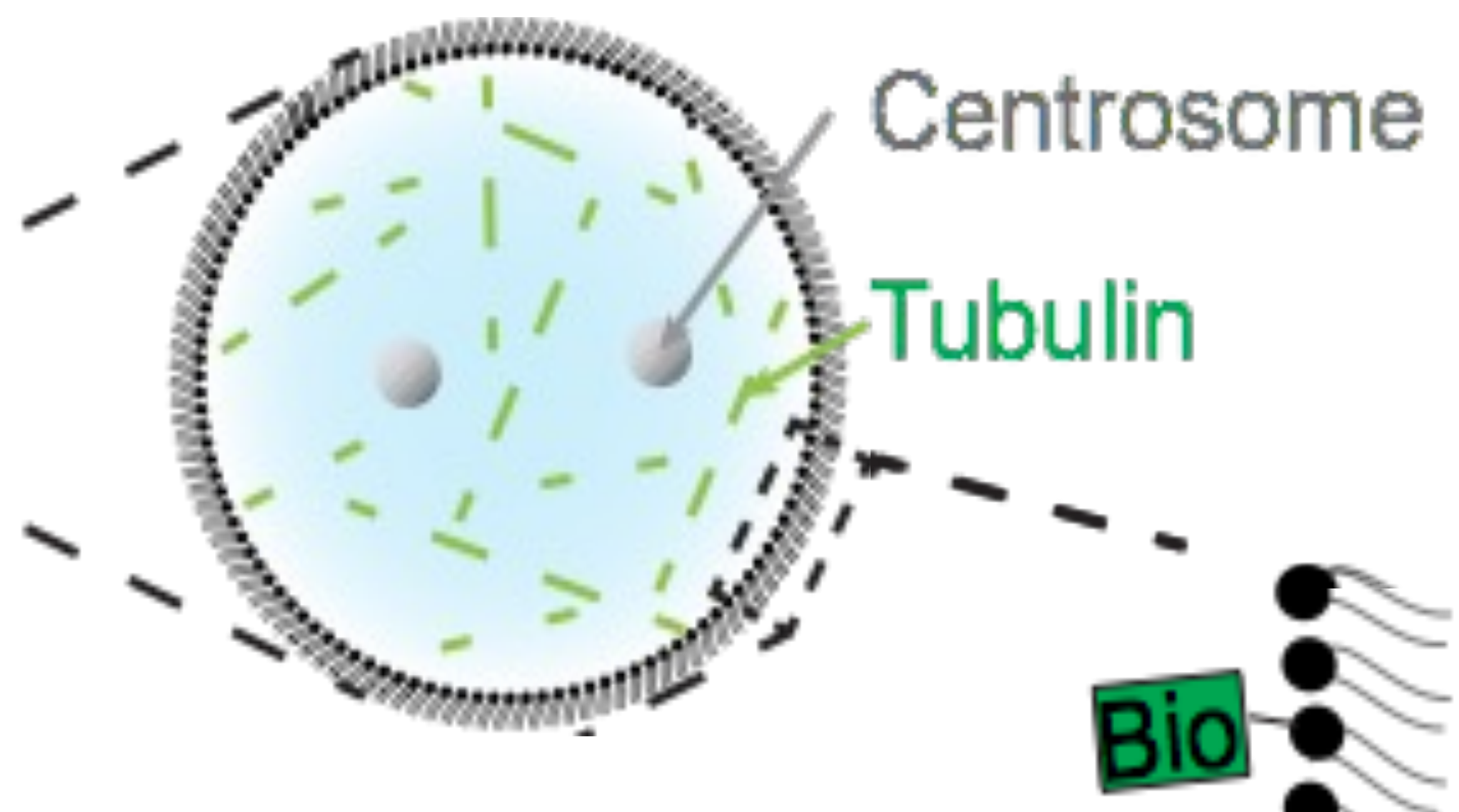
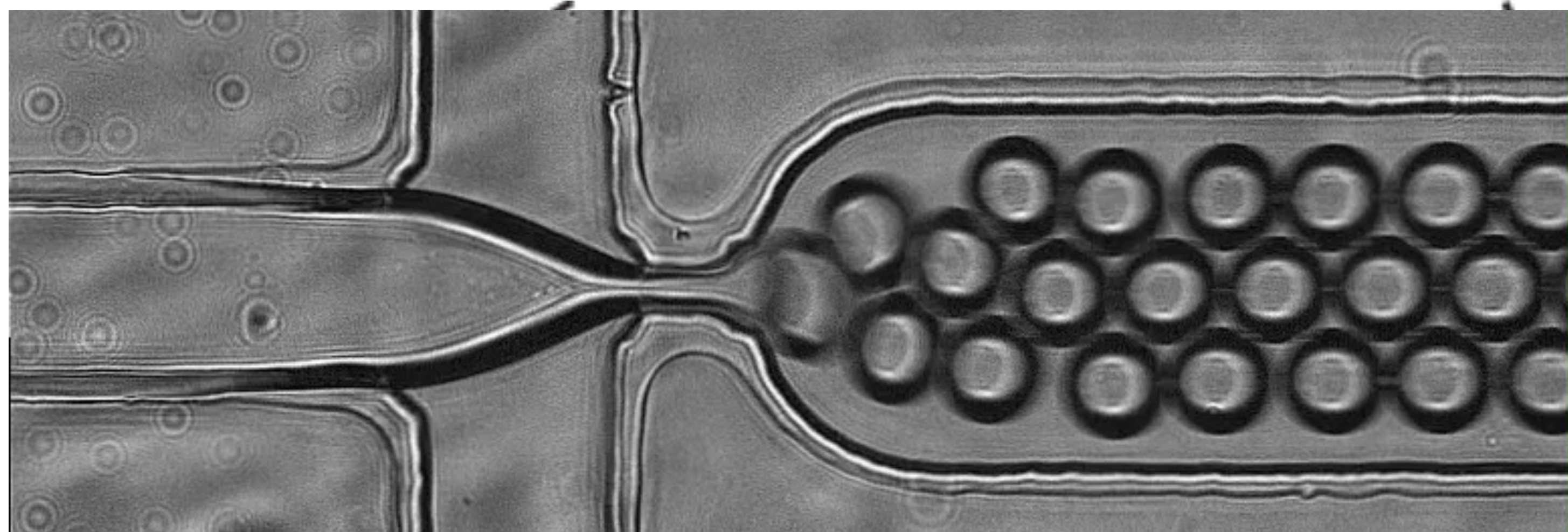
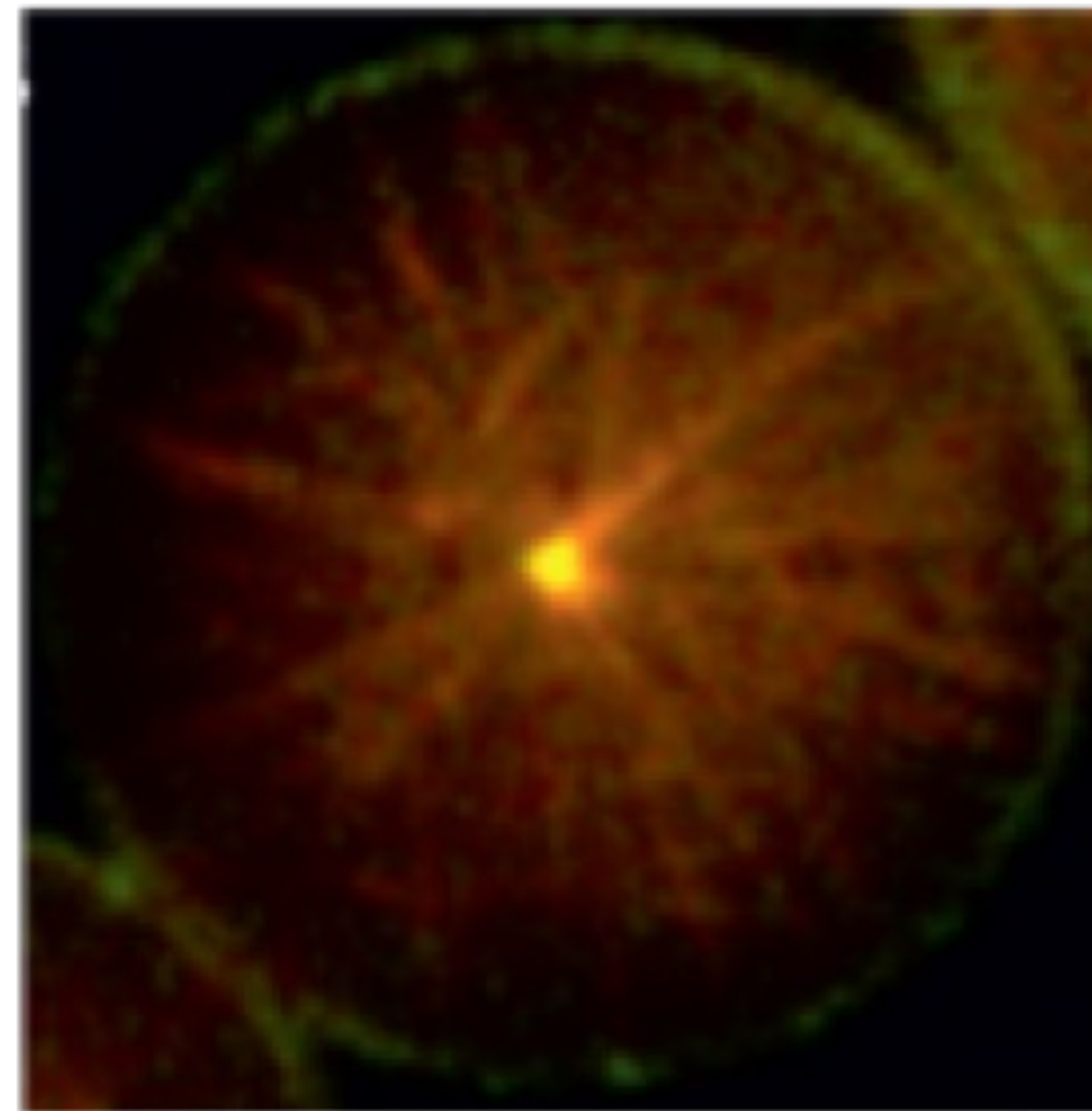
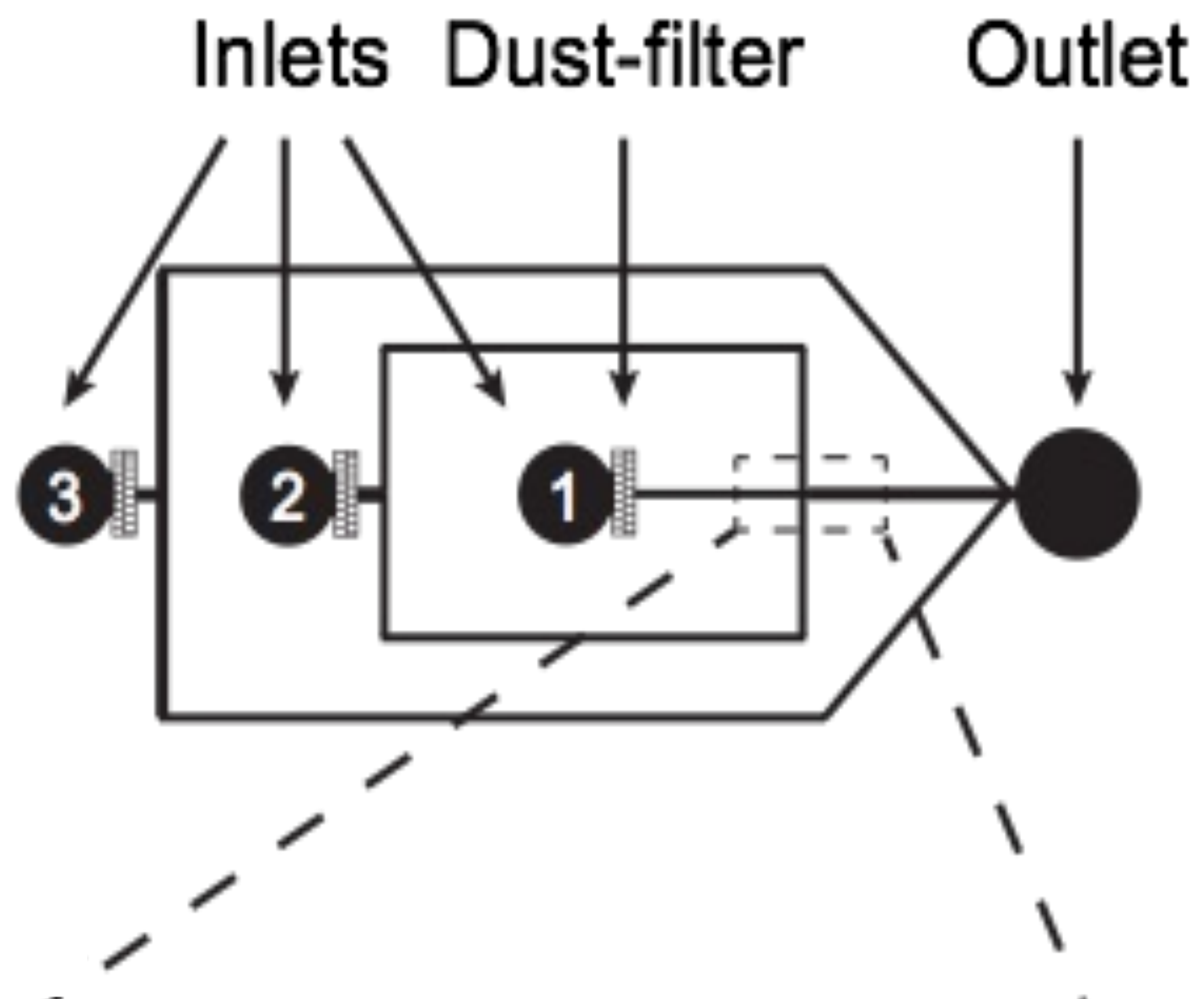
Vladimir Volkov



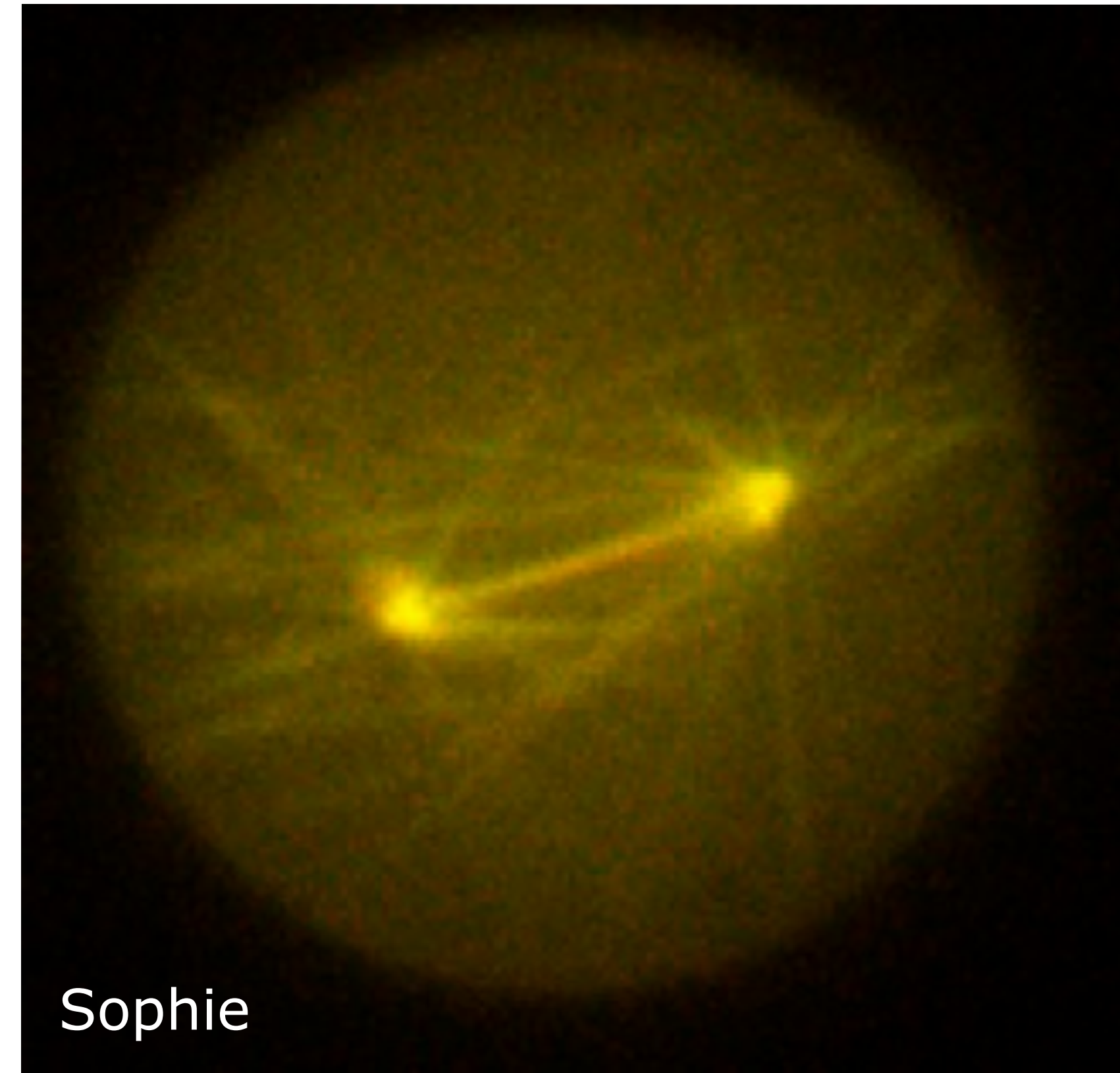
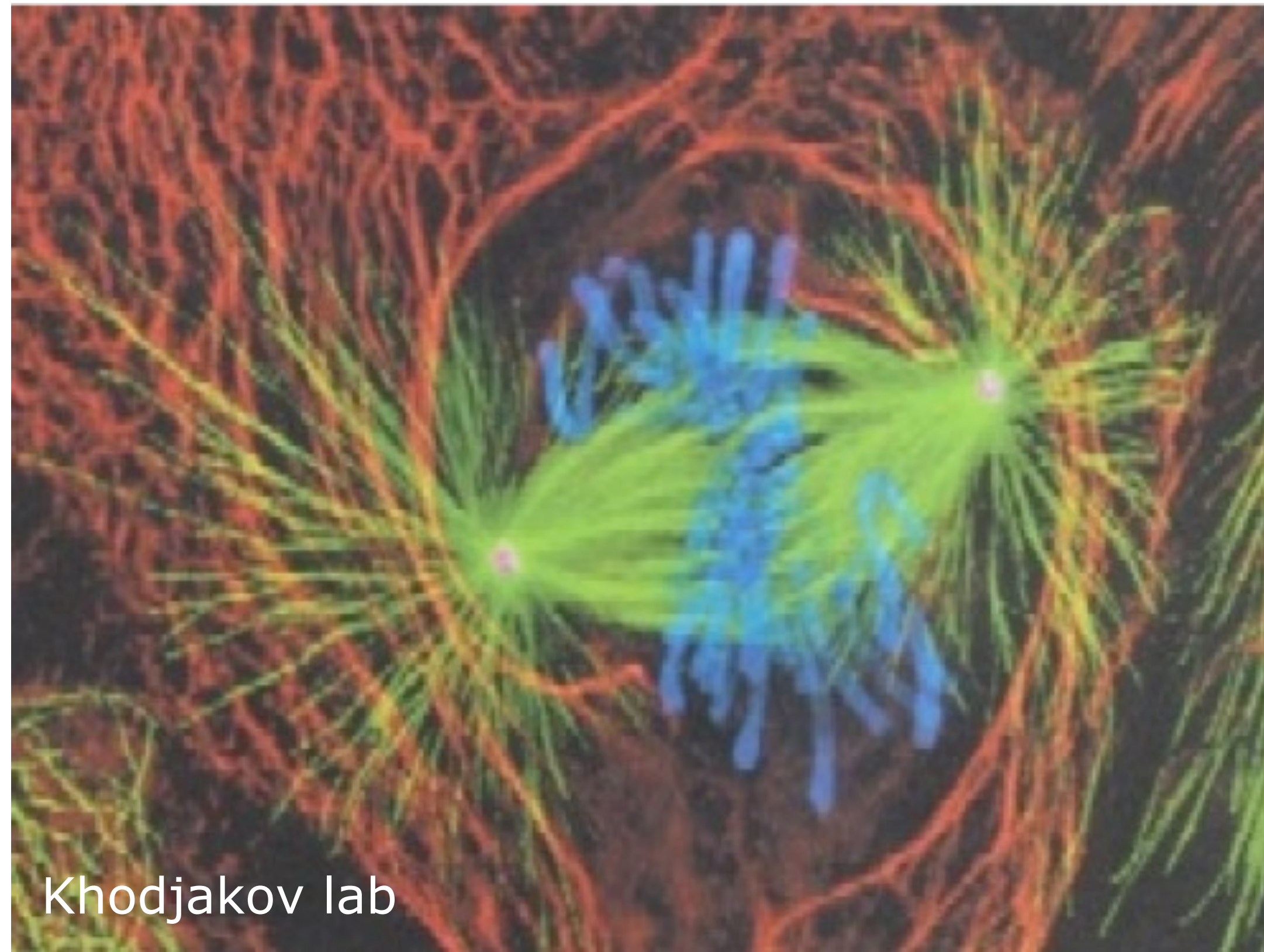
Louis Reese Renu Maan



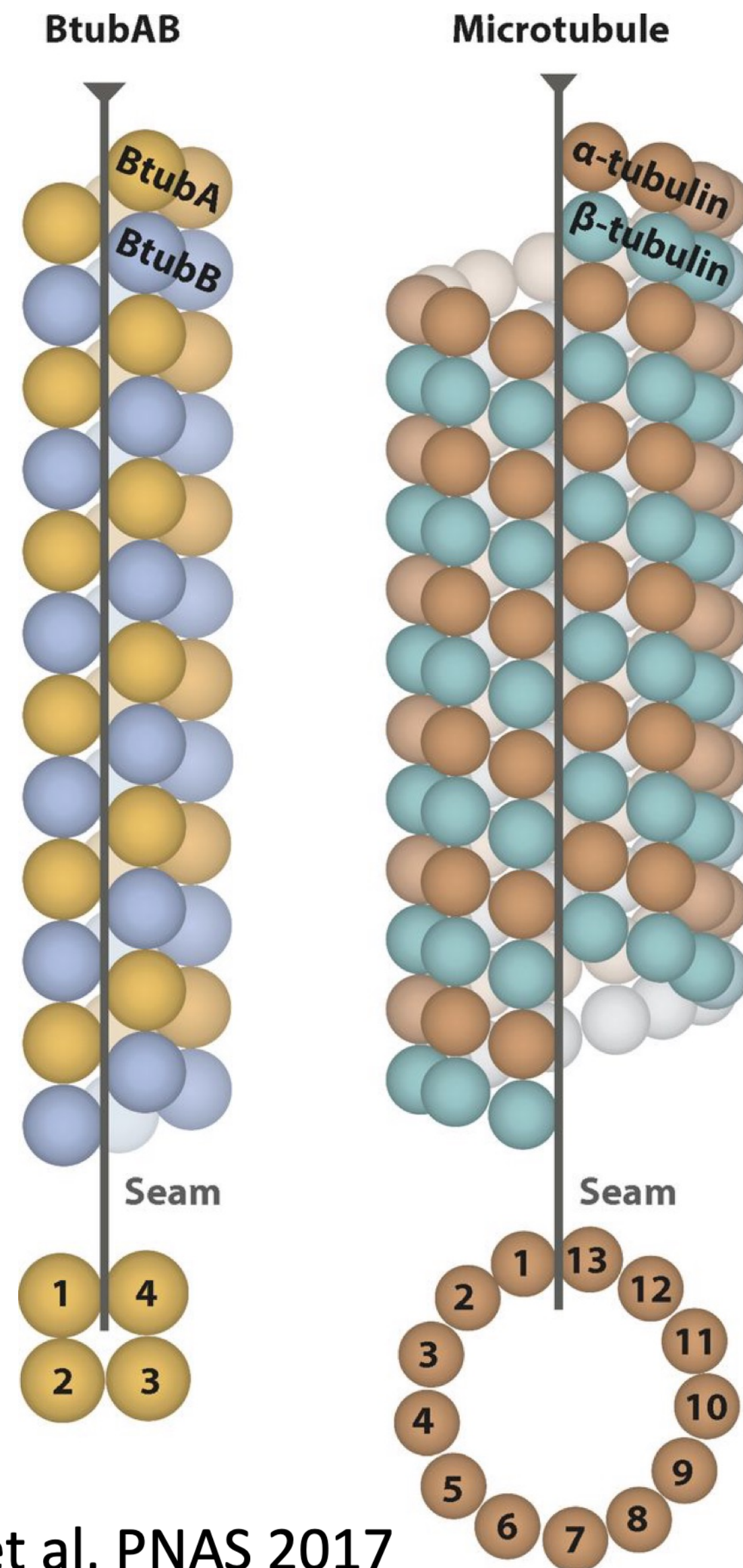
Maan et al., Nat. Cell Biol. 2022



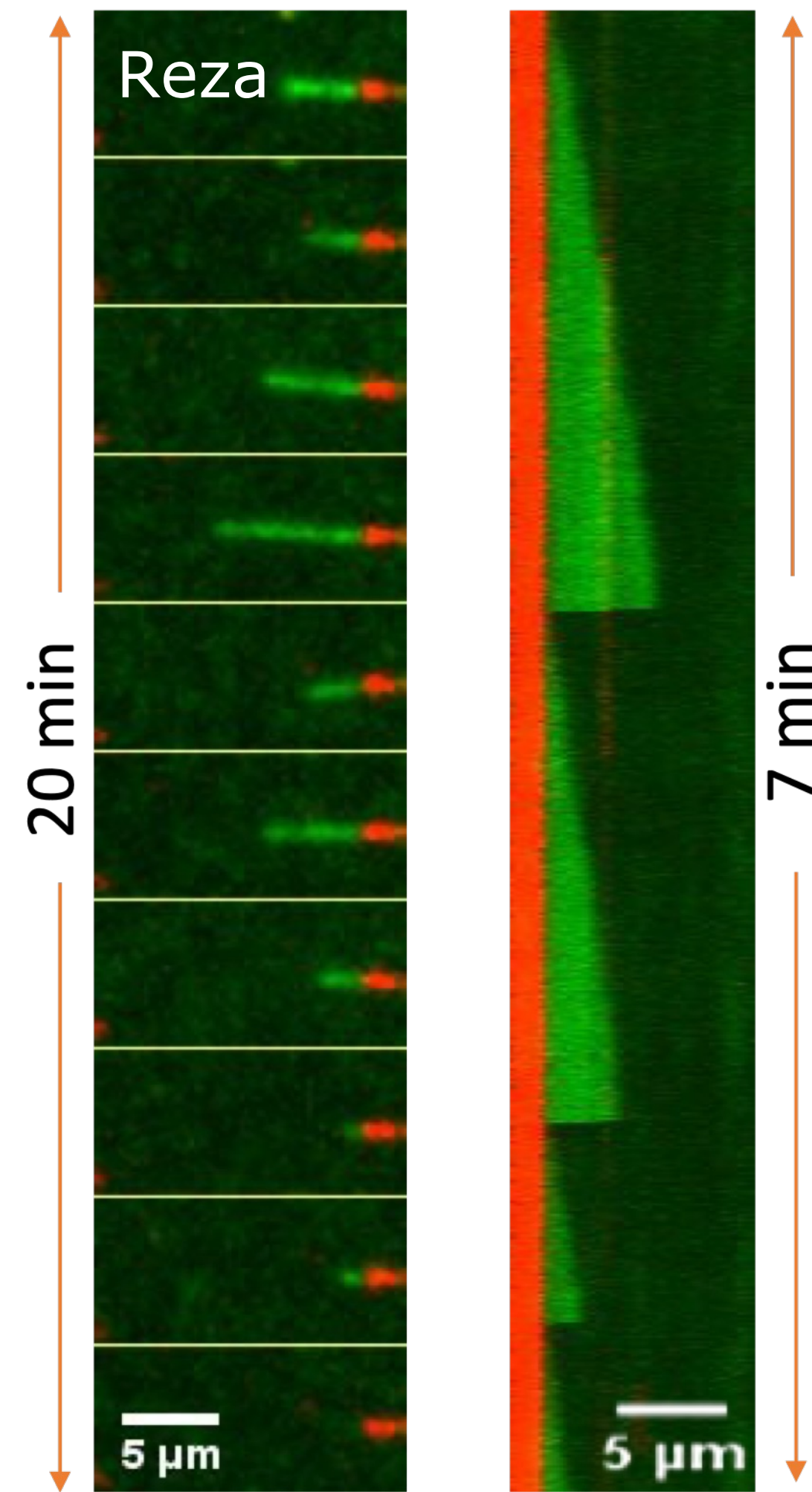
A minimal division machinery



From eukaryotic to bacterial filaments

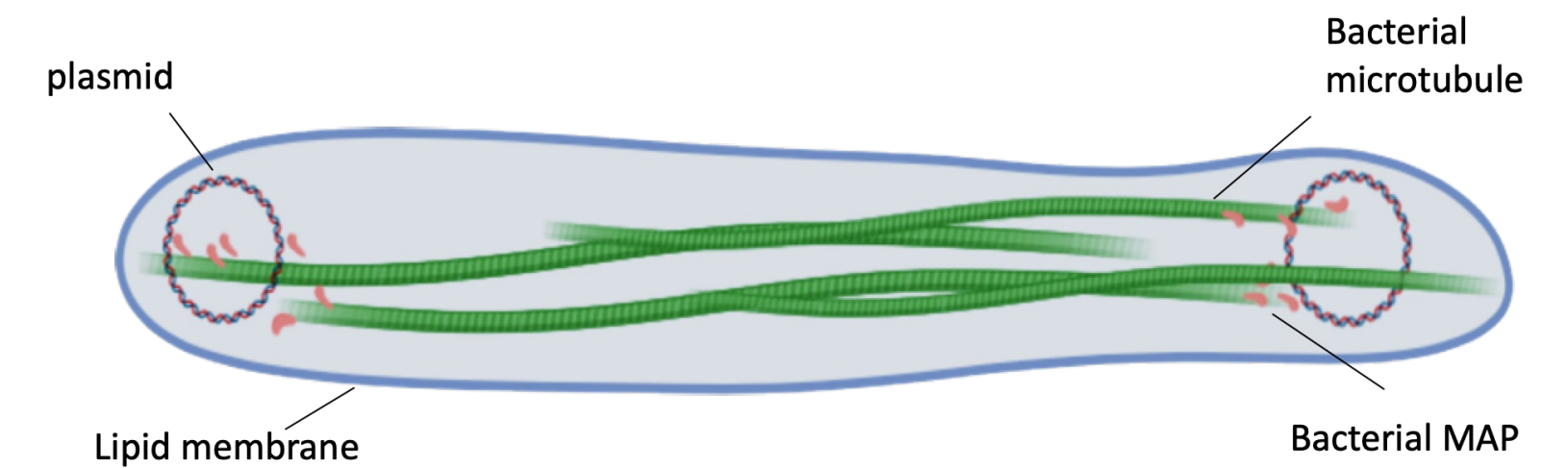
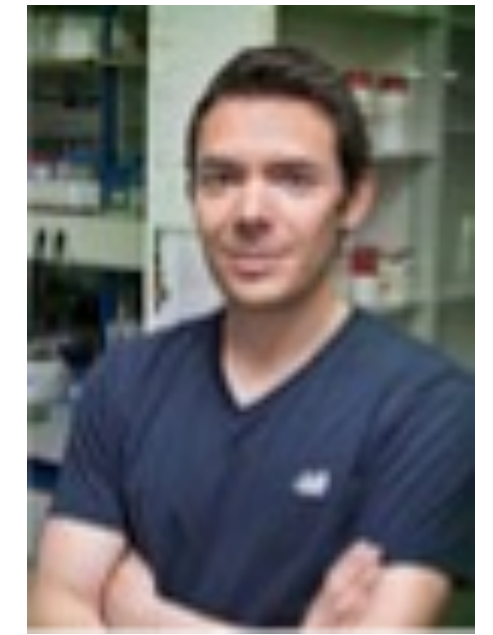
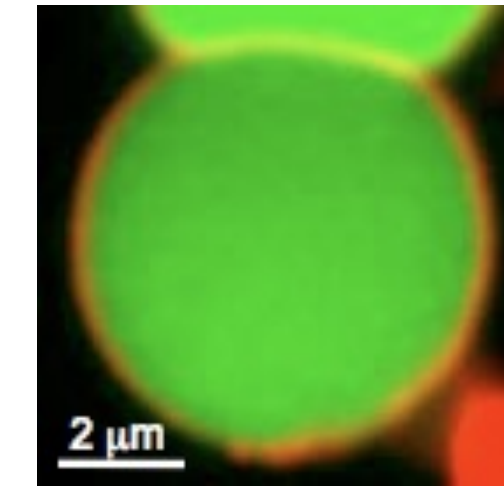


Deng et al, PNAS 2017

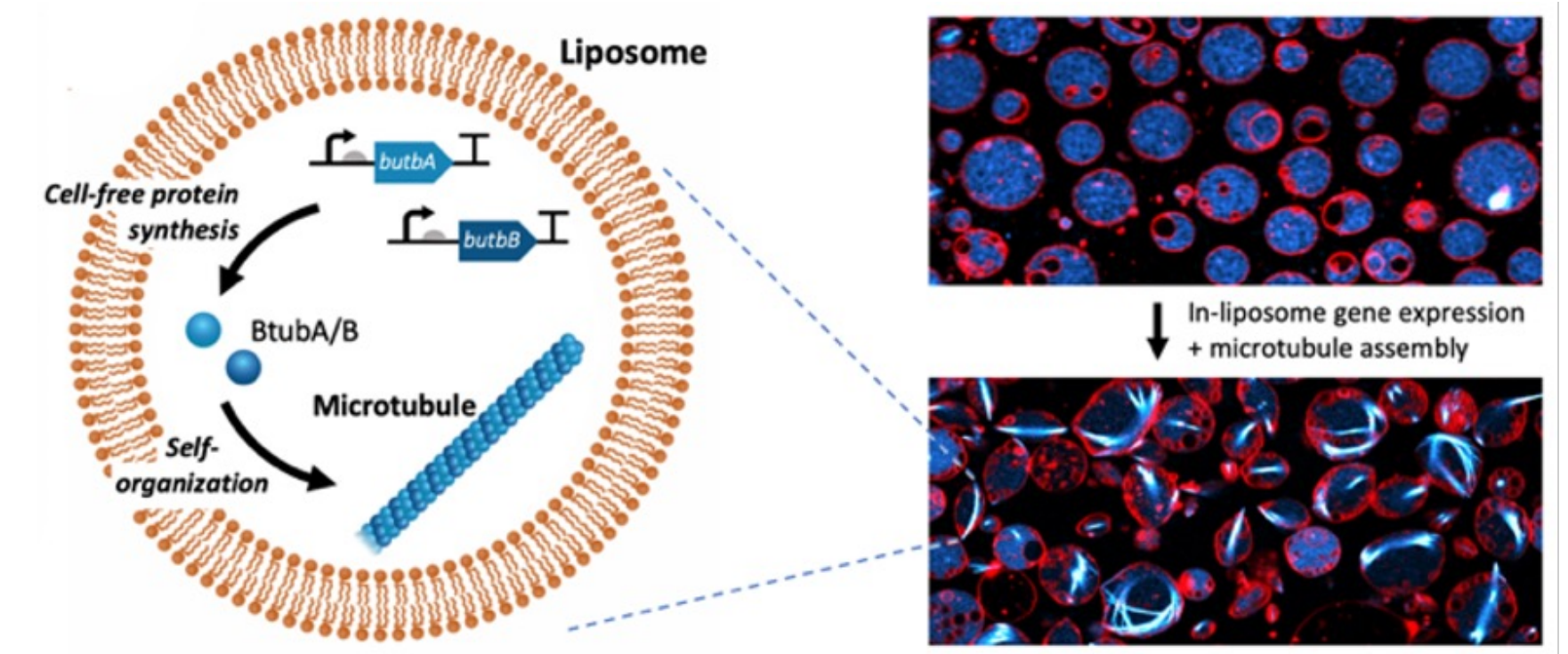


Bacterial microtubule:
dynamic instability

With
Christophe Danelon



For shape change and transport



Kattan et al., ACS Synthetic Biology 2021

Container growth

DNA processing

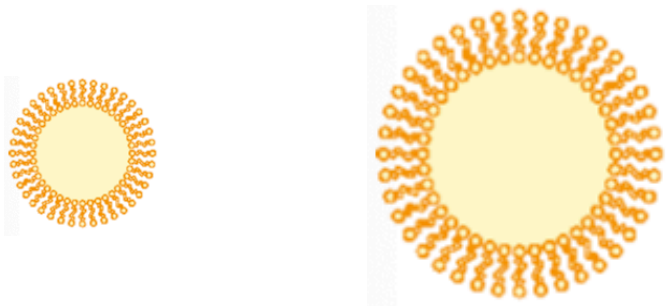
Segregation

Centering

Deformation

Splitting

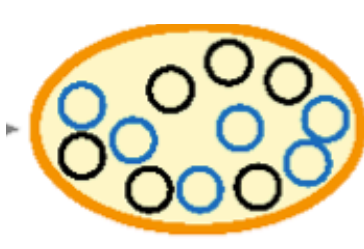
External feed



ATP, lipid
Synthesis

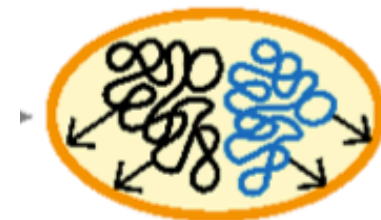


Multiple



Random

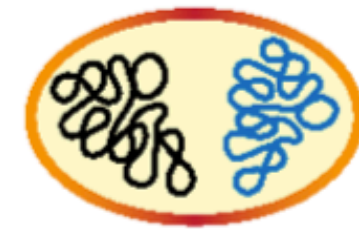
Active



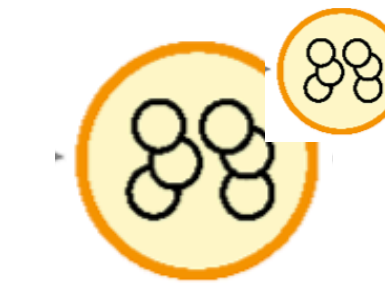
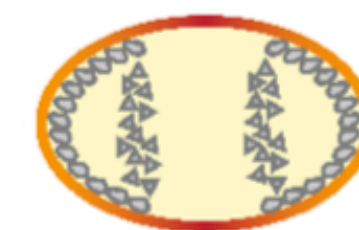
Entropy

External (light)

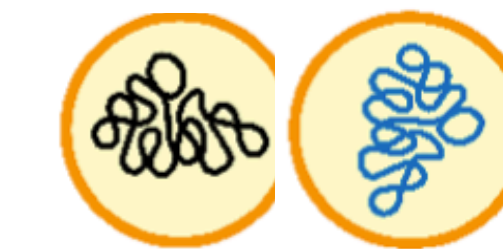
Nucleoid



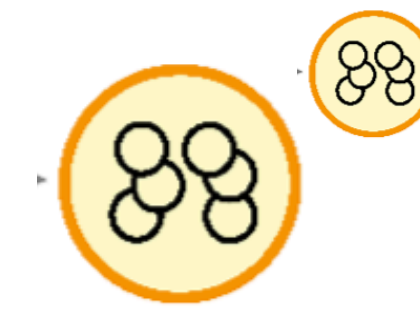
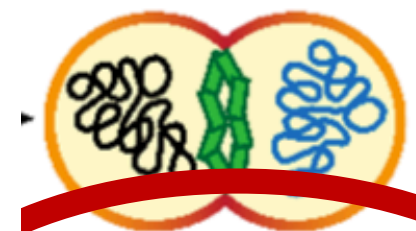
Proteins



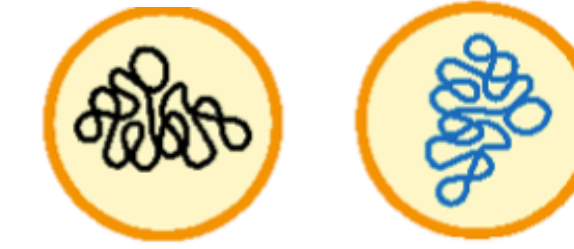
External feed



Proteins



External (mechanical)



Proteins



A. Asymmetric

B. Symmetric

C. Symmetric
Autonomous

Temporal control

Synthetic cells: 3 levels of autonomy / viability

Syn Cell A: Simplest and asymmetric (autonomy high, viability low)

Syn Cell B: Externally controlled and symmetric (autonomy low, viability high)

Syn Cell C: Internally controlled and symmetric (autonomy high, viability high)

What if it works?



Opportunities



But also questions

- Philosophical questions?
- Ethical issues?
- Safety?
- Technology: ownership?



Future Panel on Synthetic Life

<https://www.rathenau.nl/nl>

What does the public think?

Designer Mies Loogman

<https://www.rathenau.nl/nl>



Babyshower at the
Dutch design week 2021



Acknowledgements

Plus-tips:

Anna Akhmanova
Michel Steinmetz

Actin-microtubule crosstalk:

Gijsje Koenderink

Kinetochores:

Dim Huis in 't Veld

Dynein:

Sam Reck
Ron Vale

C elegans:

Sander v/o

Opto-control:

Lukas Kap

Modelling:

Nenad Pav
Frank Jülic
Bela Mulde
Harmen W

Pieter Rein ten Wolde

Tubulin PTMs:

Carsten Janke

Microfluidics:

Cees Dekker

cDICE:

Kristina Ganzinger



SWISS NATIONAL SCIENCE FOUNDATION



Thank you!

Marileen Dogterom

NWO Physics, April 4 2023, Basic Science for Sustainable Development



European Synthetic Cell Initiative

Nature is our next technology

