# General Agent Based Modeling in LAMMPS

## Andrew Jewett
## LAMMPS workshop
## August 15th, 2019

DNA

RIBOSOMES

RNA POLYMERASE

RNA

PROTEINS
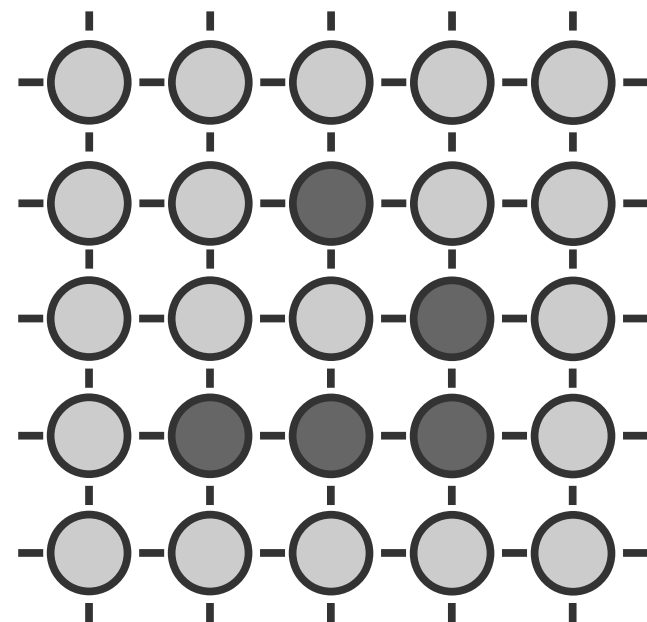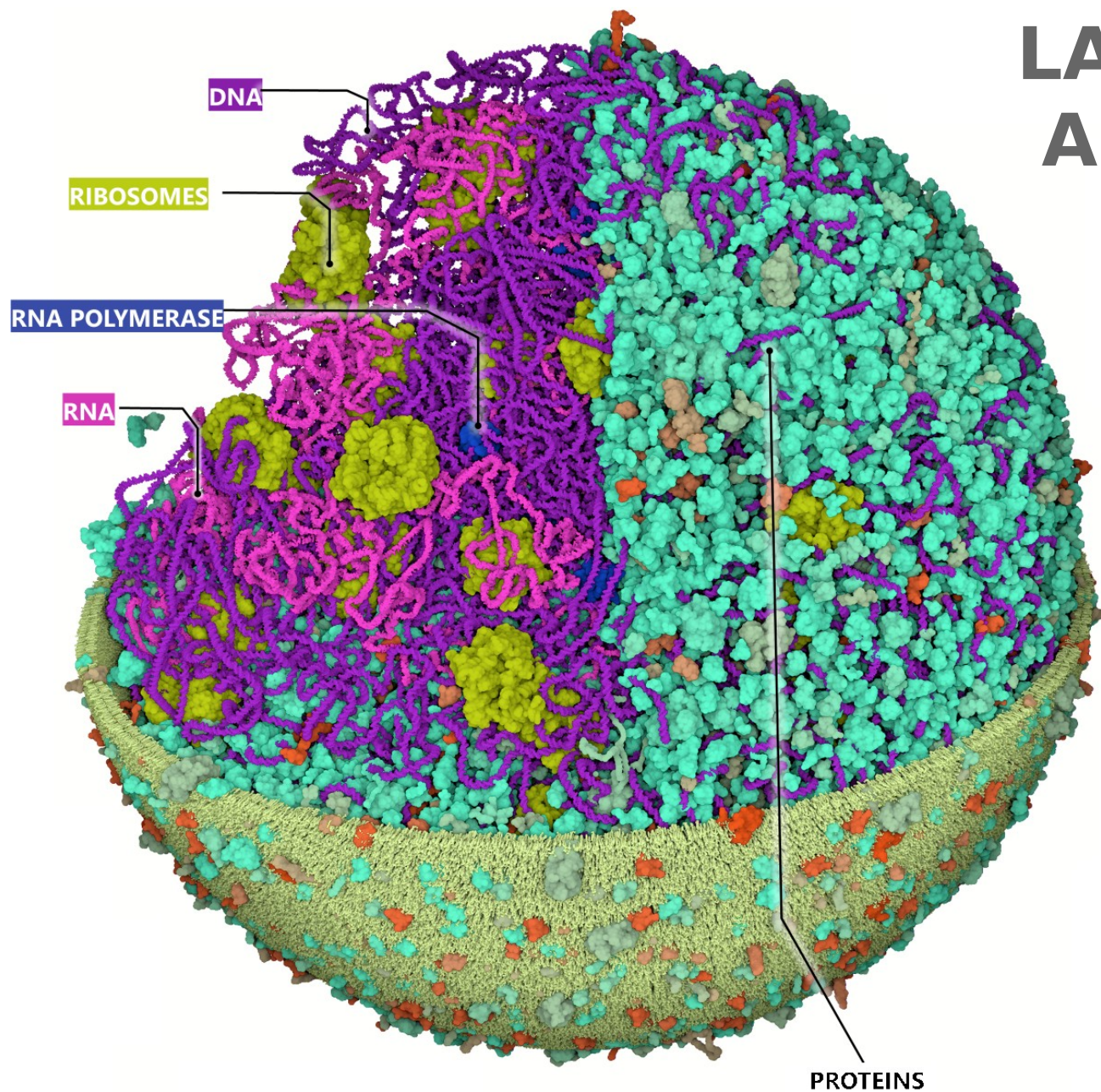
Scripps Research

# Definition: Molecular cellular automaton

A hybrid simulation method:
   a) run ordinary molecular dynamics for a short time,
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   c)     **goto** → a)     (repeat…)

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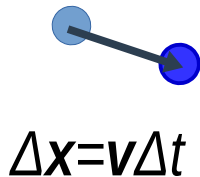
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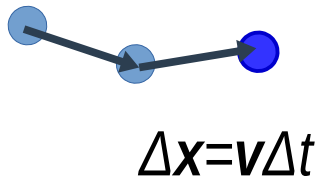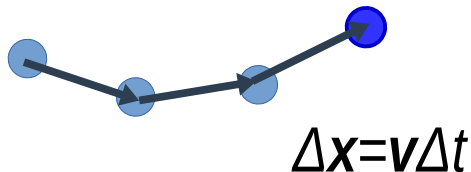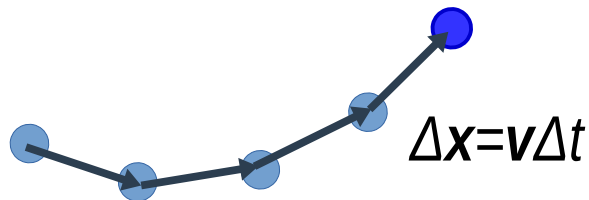   a) run ordinary molecular dynamics for a short time,
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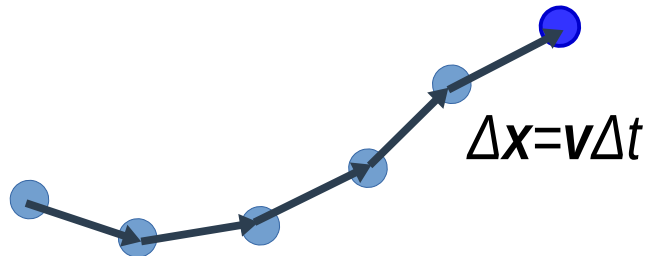
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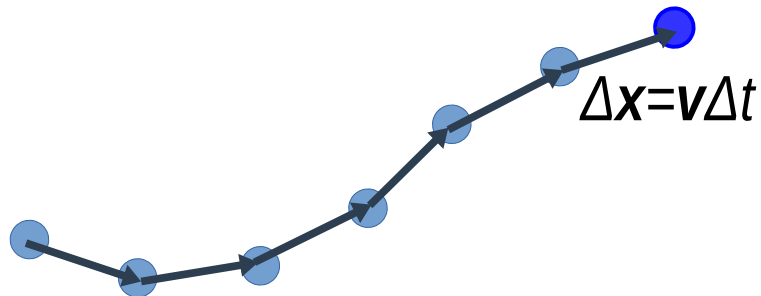
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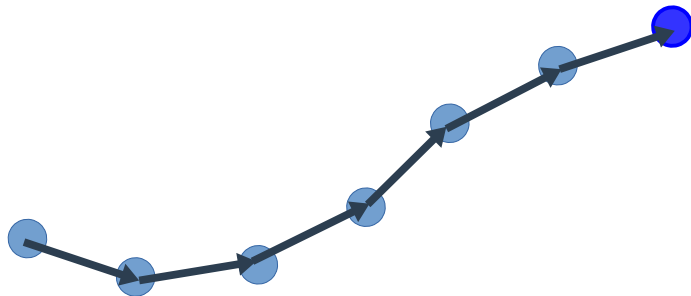
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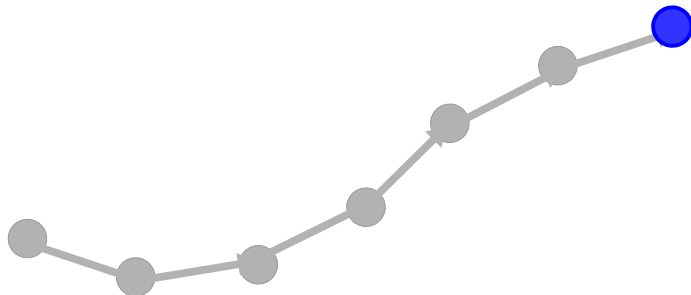# Definition: Molecular cellular automaton

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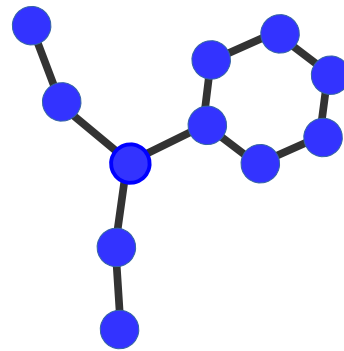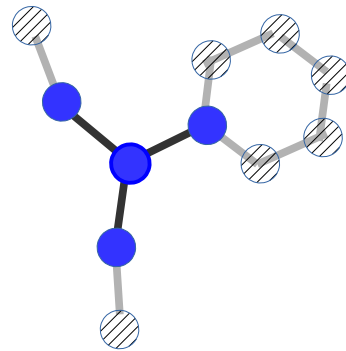# Definition: Molecular cellular automaton

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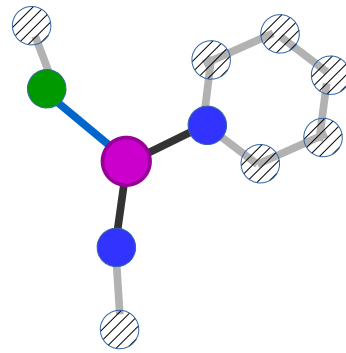
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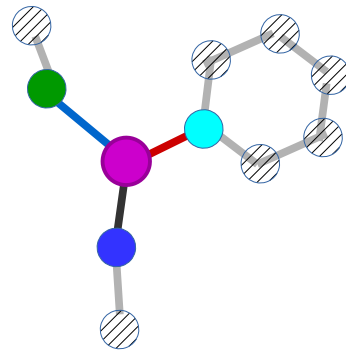# Definition: Molecular cellular automaton

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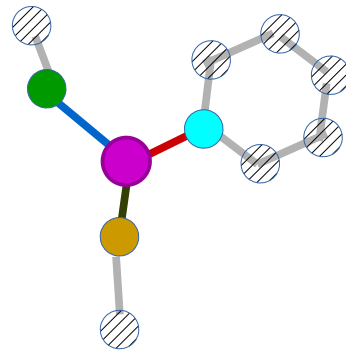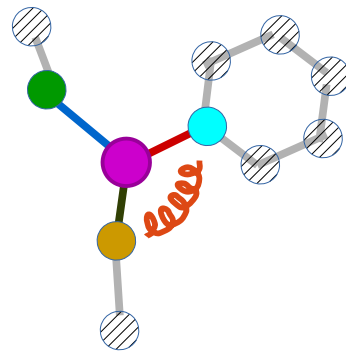# Definition: Molecular cellular automaton

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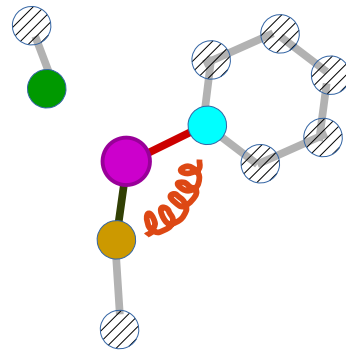# Definition: Molecular cellular automaton

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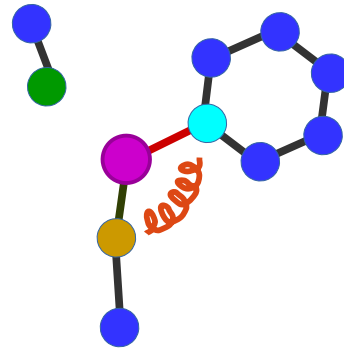# Definition: Molecular cellular automaton

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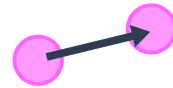
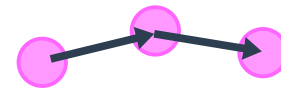# Definition: Molecular cellular automaton

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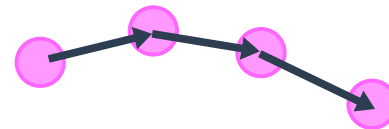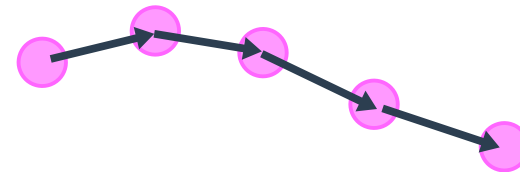
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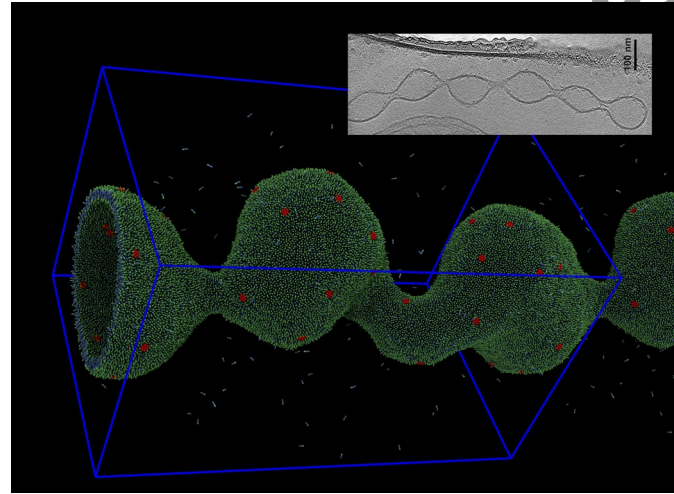# Definition: Molecular cellular automaton

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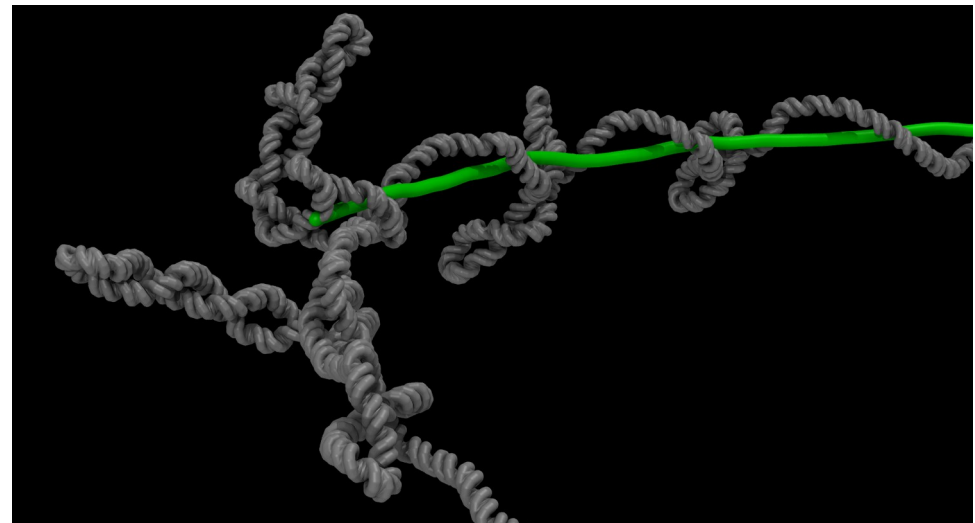   c)     **goto** → a)    (repeat…)
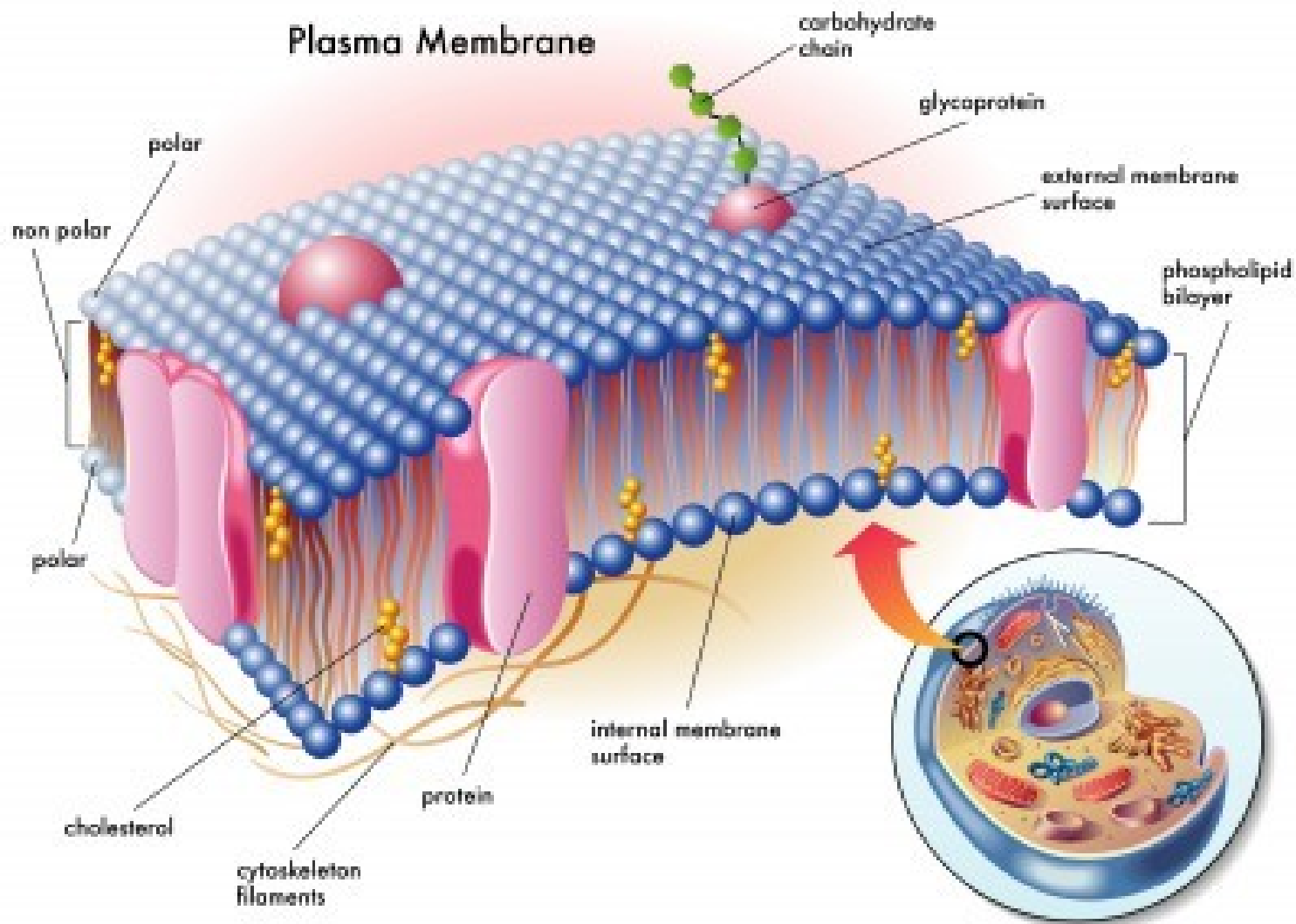
# Example Uses in Biology:

**membrane trafficking**

**cytoskeletal filament growth dynamics**

$5\mu M^{-1}s^{-1}$

$60s^{-1}$
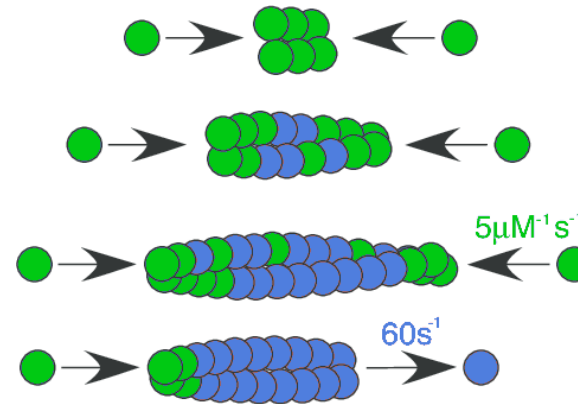
**transcriptional stalling**

# Background: cell membranes



https://biology.tutorvista.com/animal-and-plant-cells/plasma-membrane.html
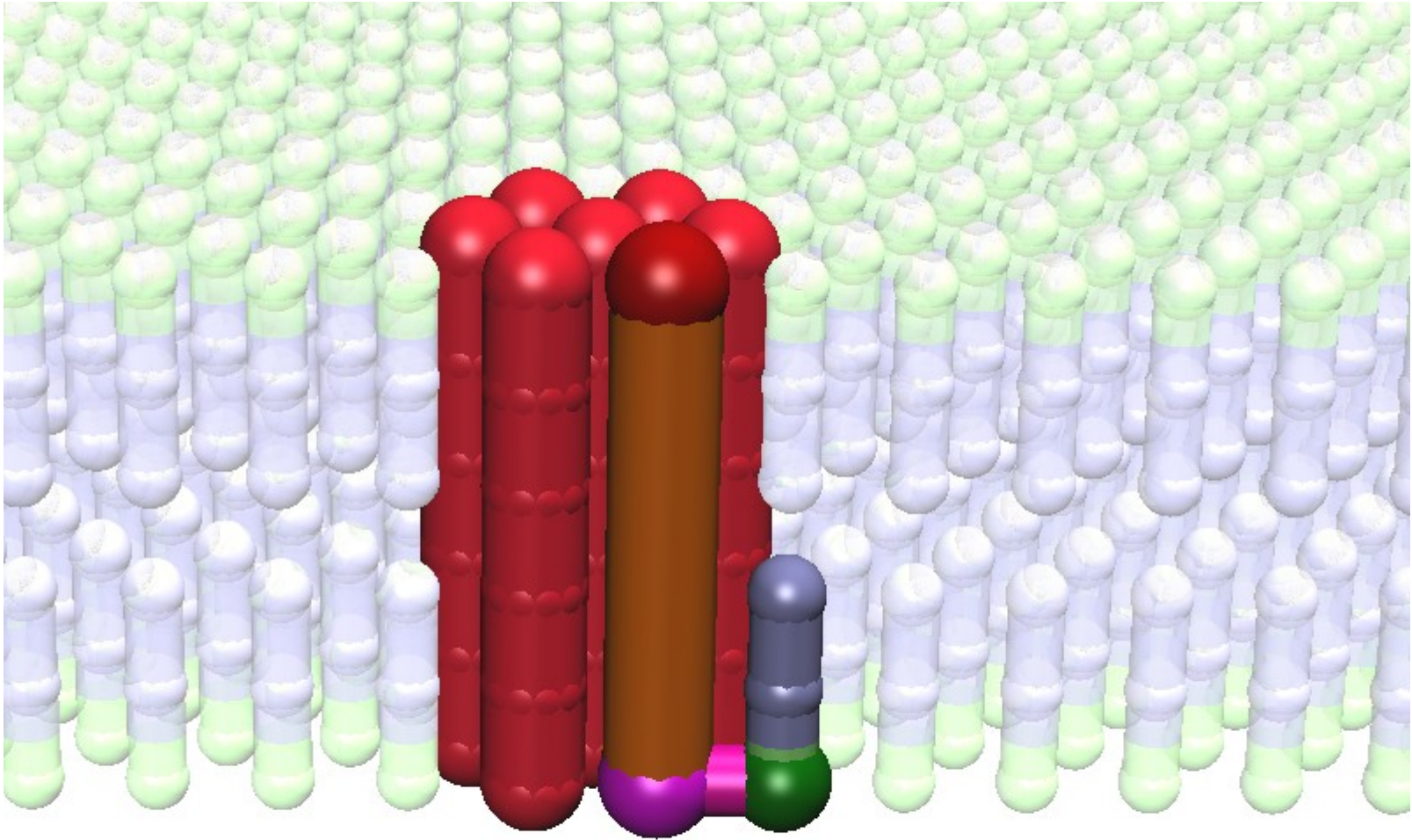
# Example: Flippase mediated membrane curvature
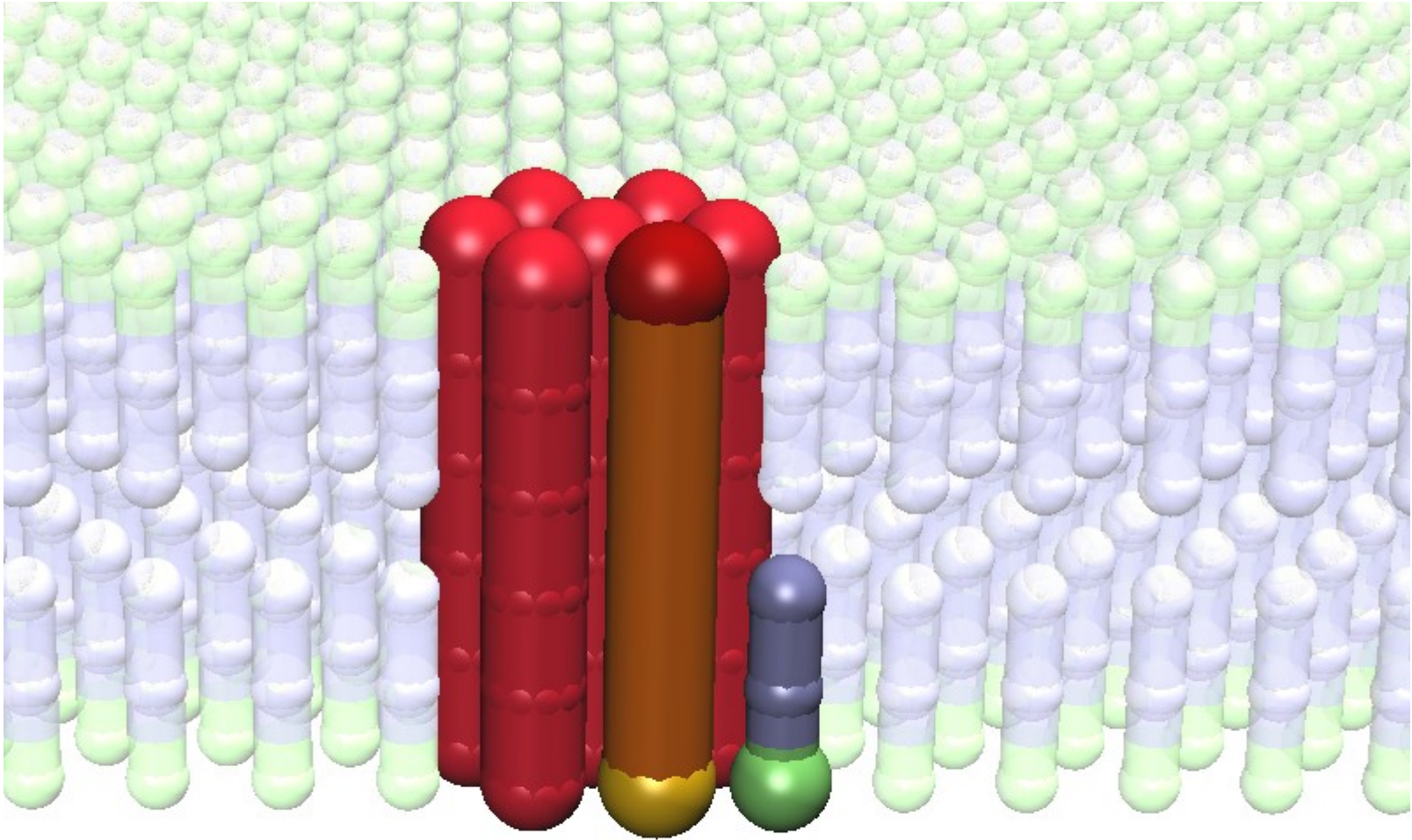
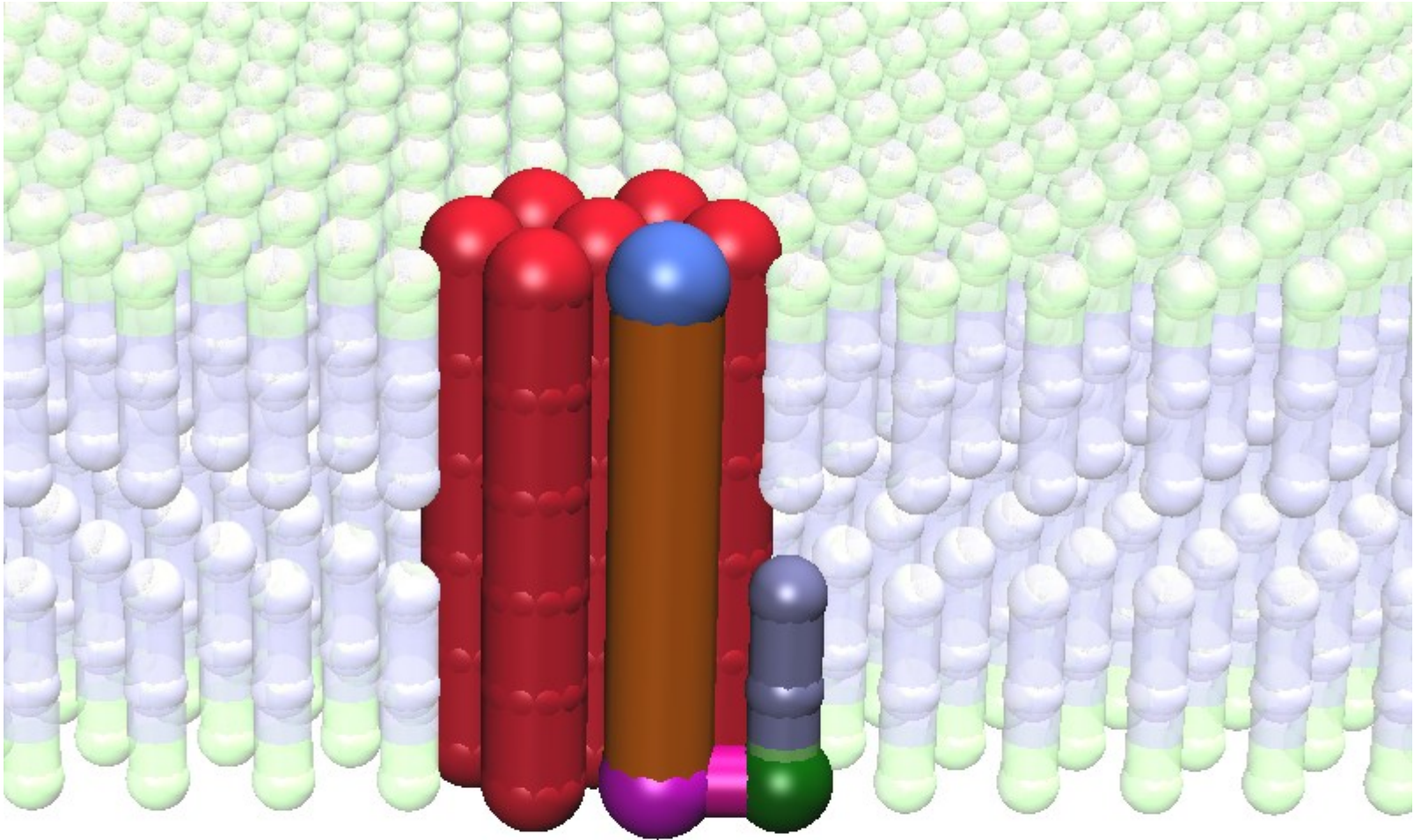# Example: Flippase mediated membrane curvature

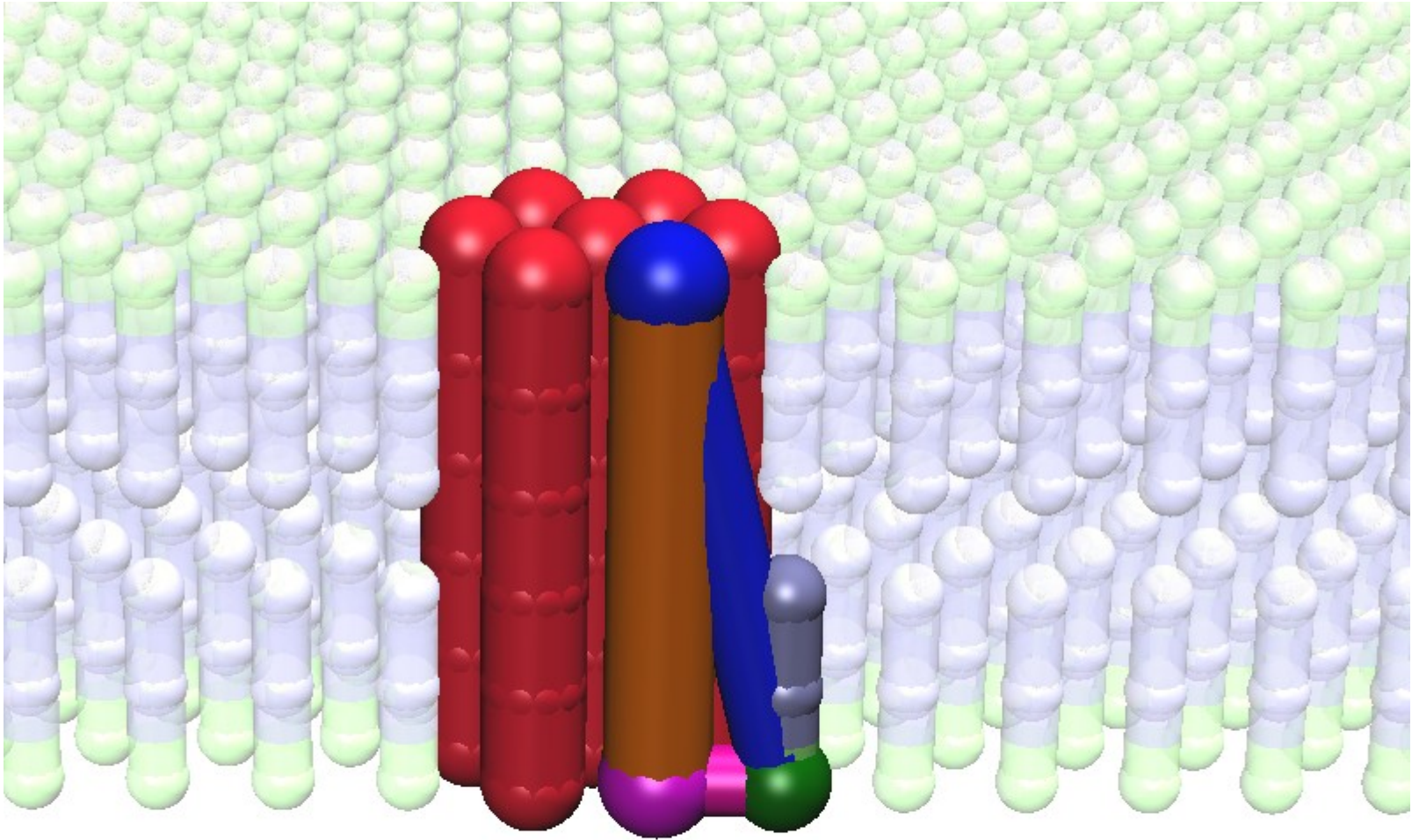**Flippase are motors which pull lipids (or proteins from one side of the membrane to the other)**
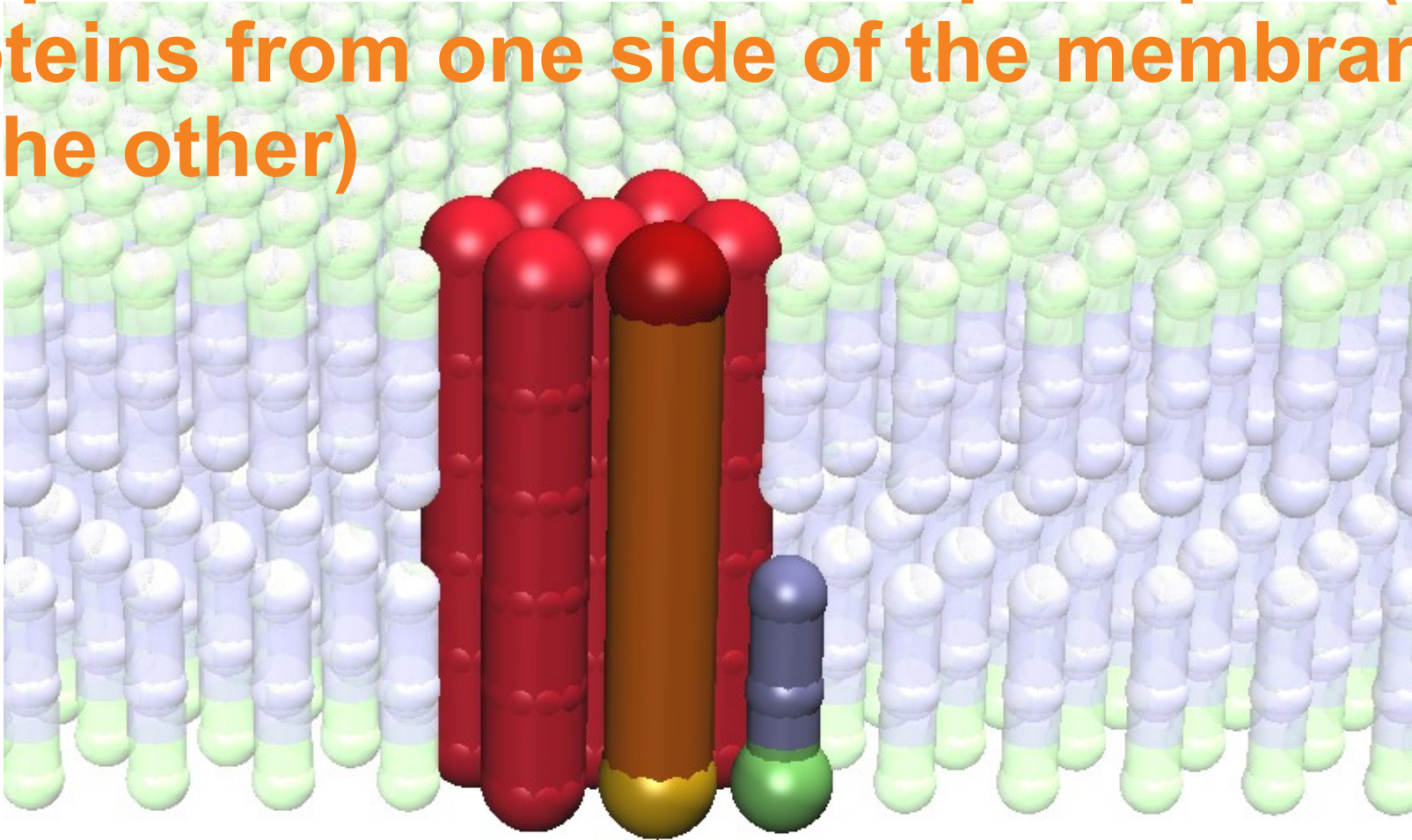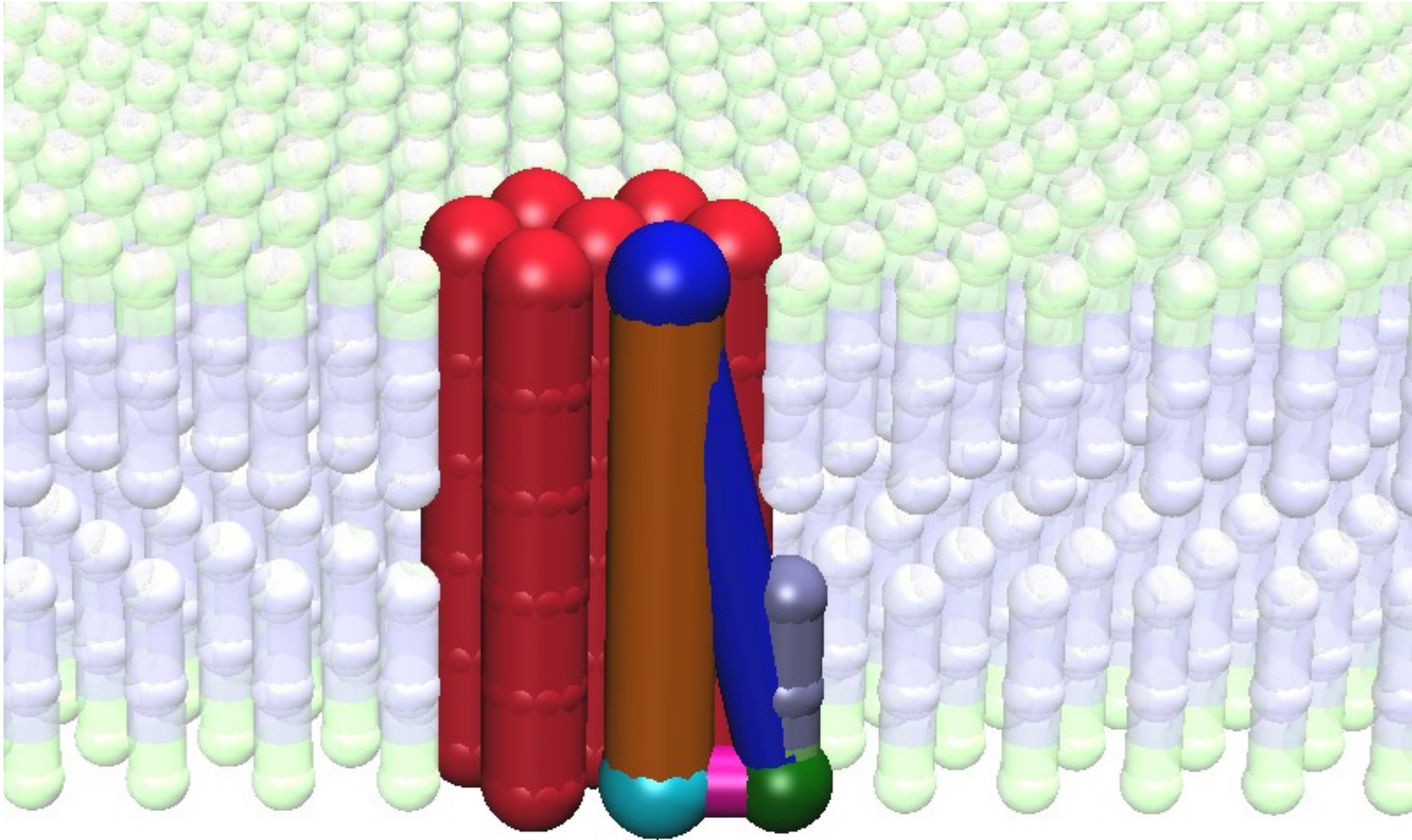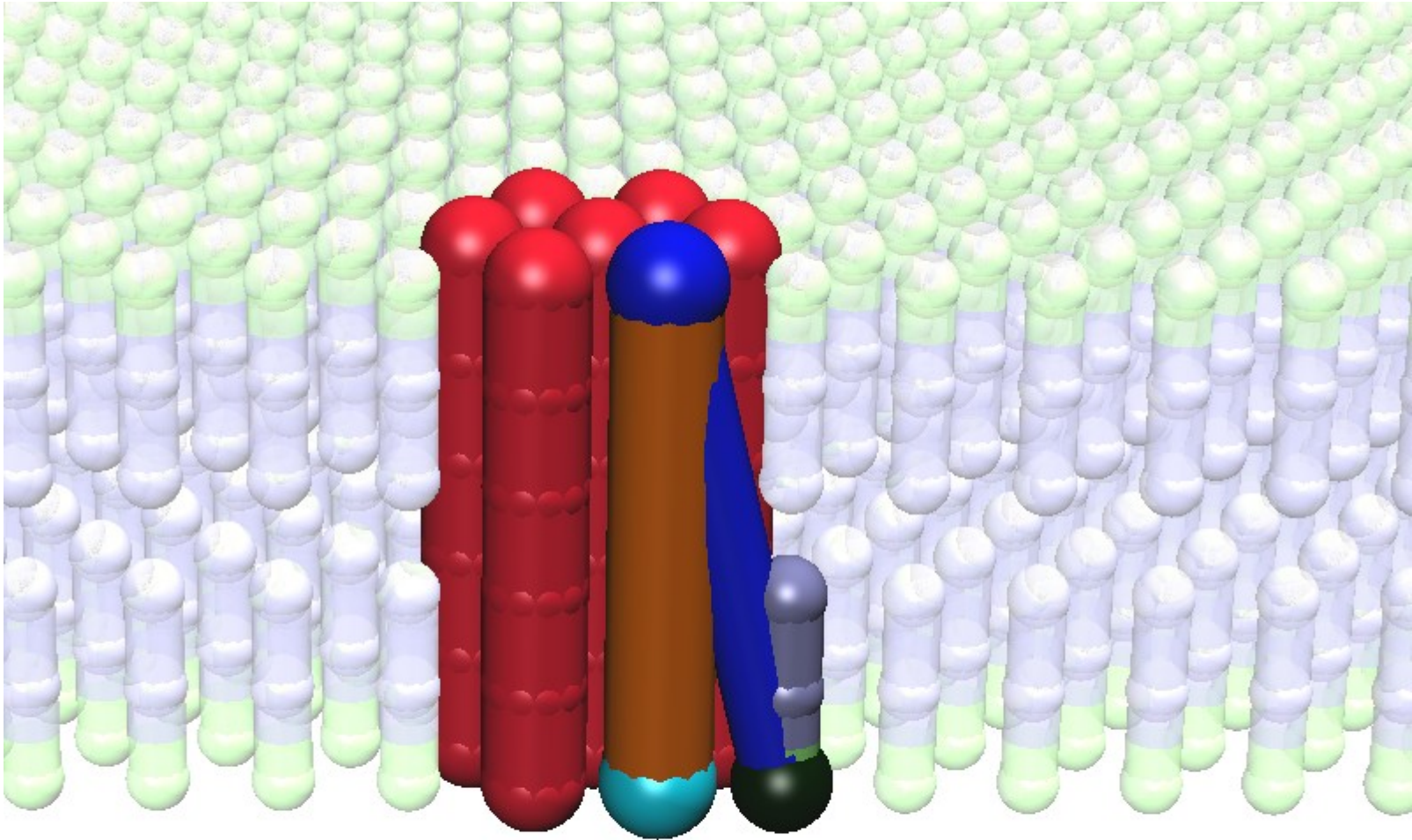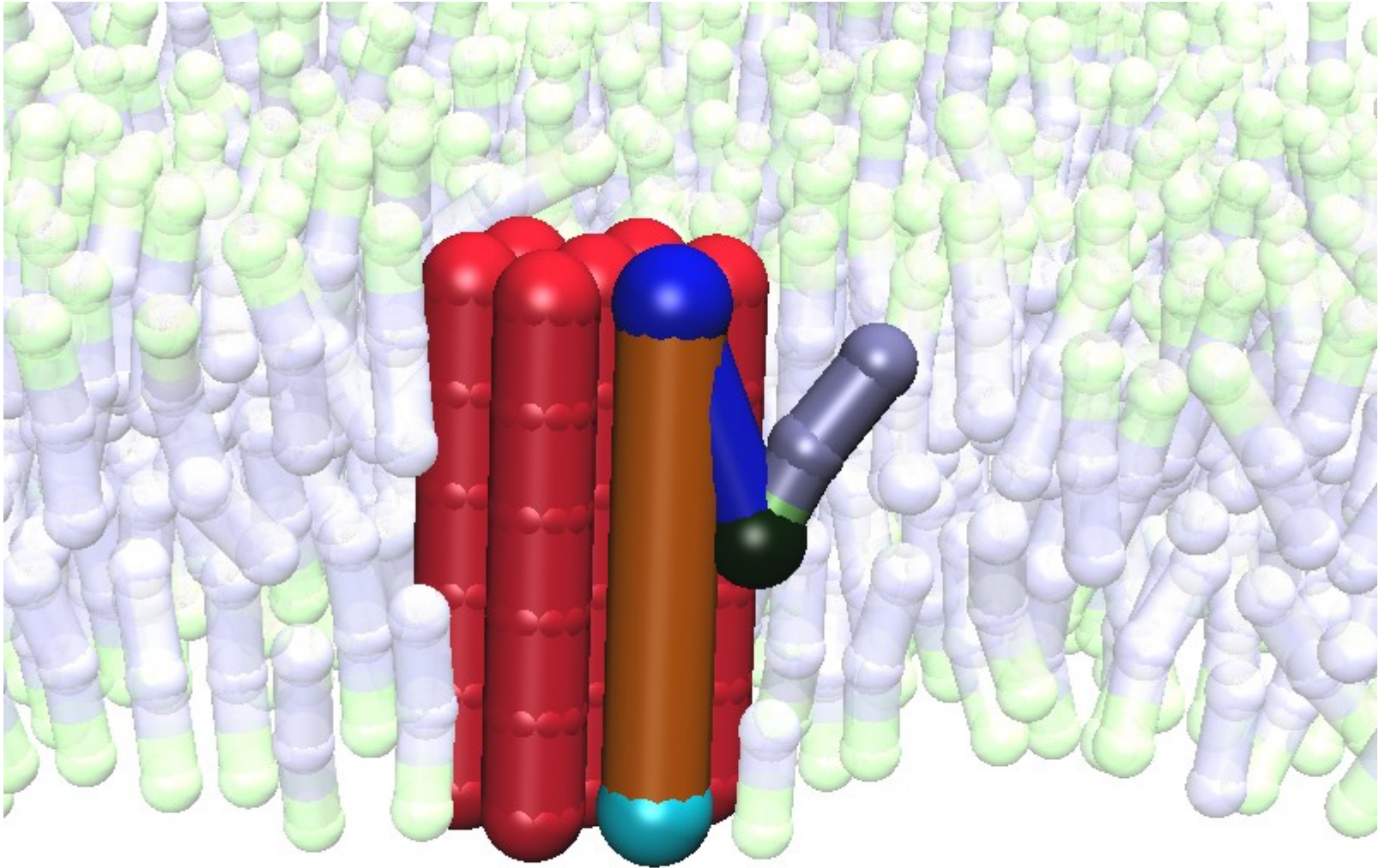
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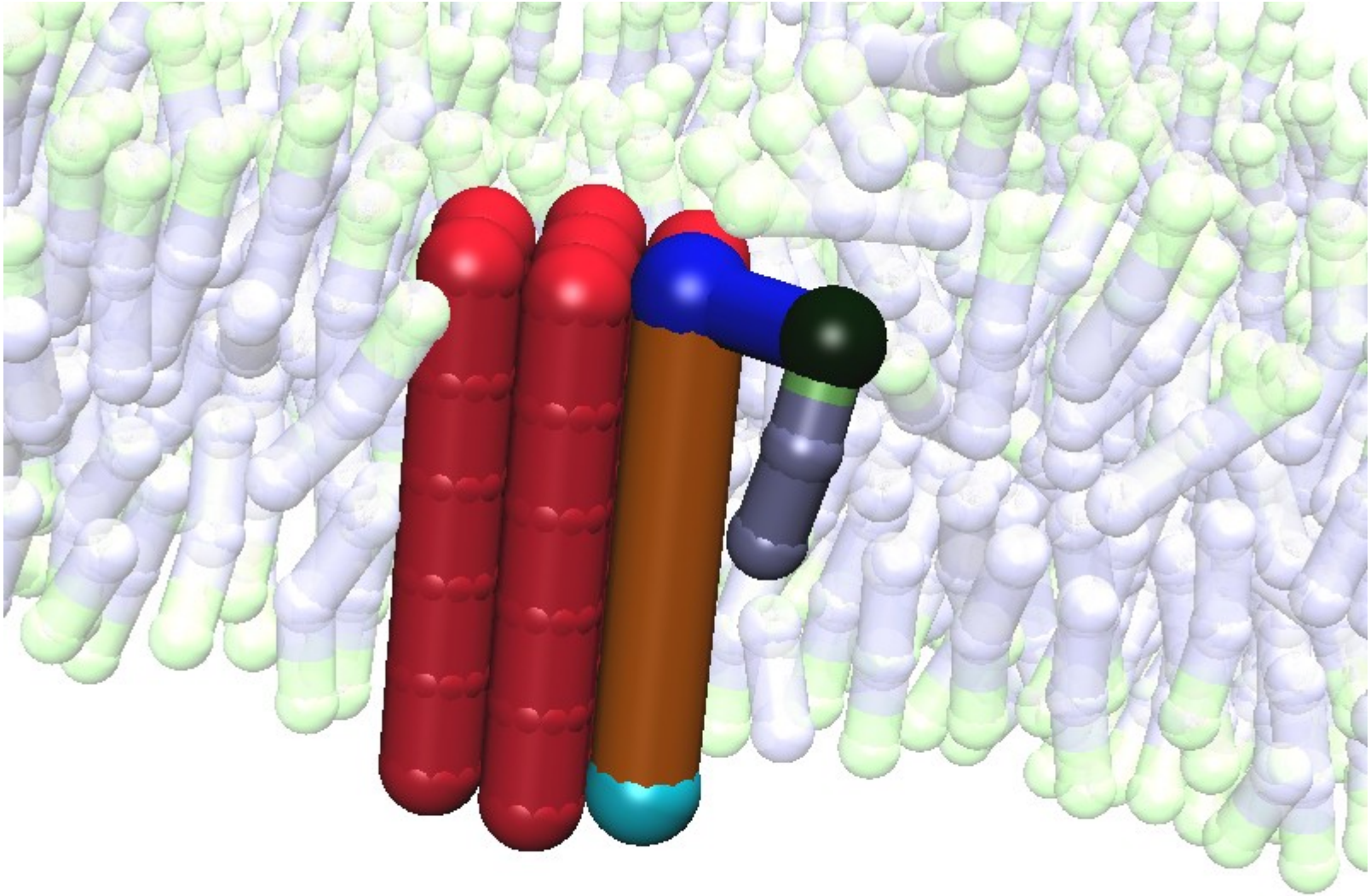# Example: Flippase mediated membrane curvature
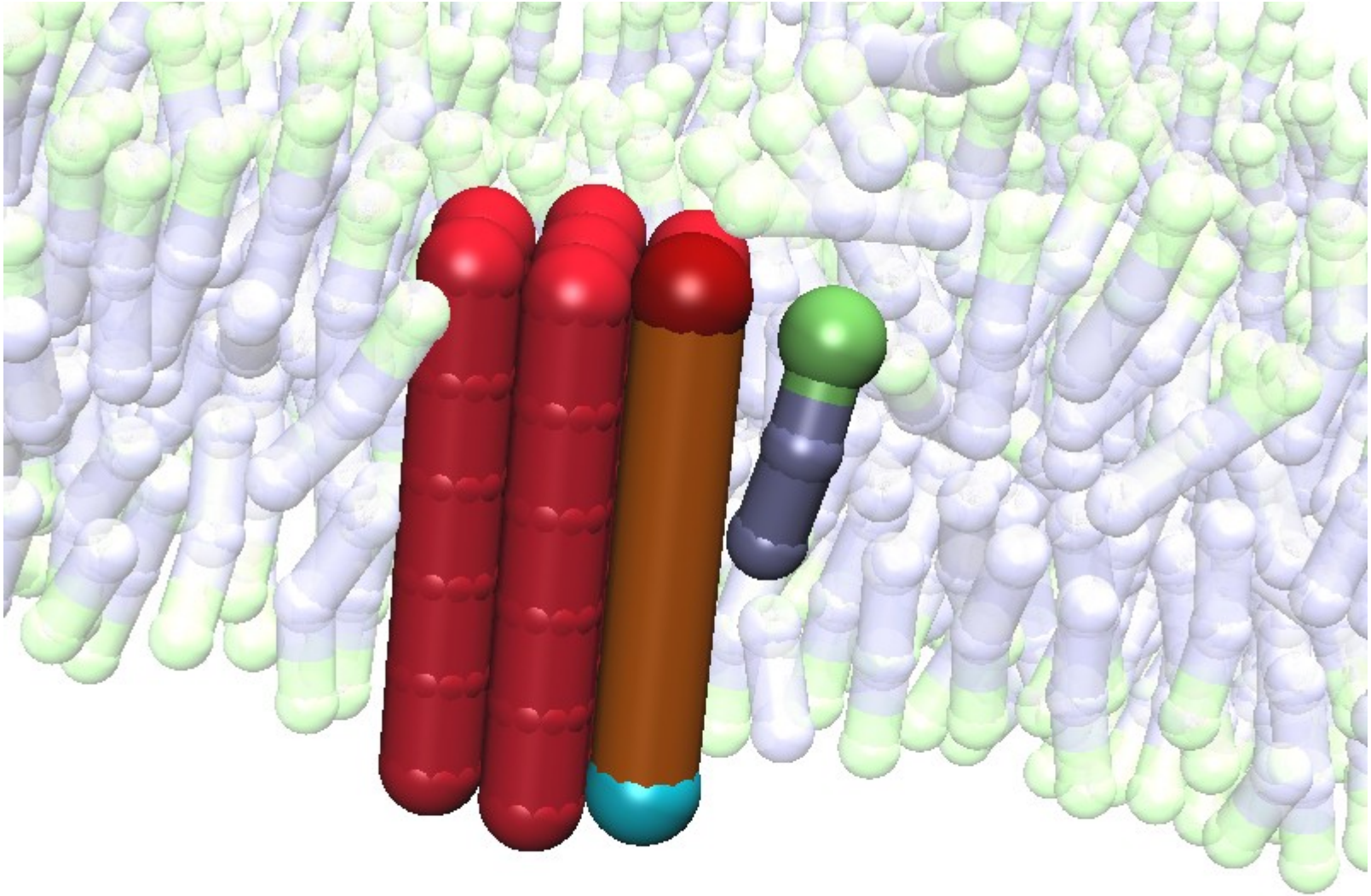
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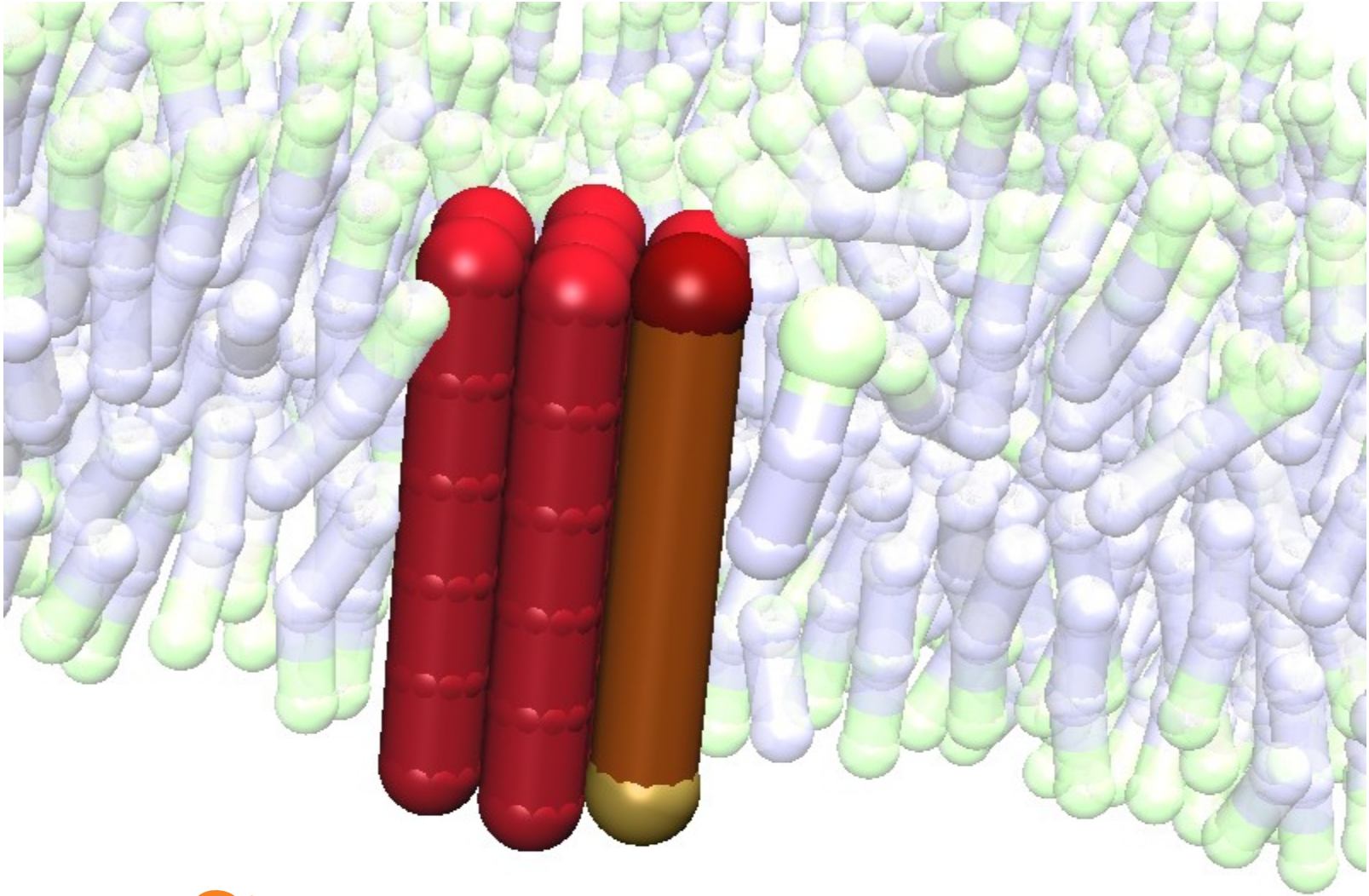# Example: Flippase mediated membrane curvature

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CYCLE REPEATS...

# Example: Flippase mediated membrane curvature

```
# Capture a lipid when it's "Head" bead strays to close to the "A" bead:
  if atoms @atom:A  @atom:H  and  distance <= 1.35  and  prob 0.1
then atoms @atom:At @atom:Ht  and  bond @bond:Capture

# Inform the bead at the other end of the flippase of the captured lipid:
if   atoms @atom:At @atom:B   and  bond @bond:AB
then atoms @atom:At @atom:Bt

# Create a bond that will pull the captured lipid's head to Bt:
if   atoms @atom:Bt @atom:Ht  and  distance <= 5.5
then atoms @atom:BT @atom:Ht  and  bond @bond:Pull

# Let the original atom ("A") know it's safe to release the lipid:
# First change the type back to "A".
if   atoms @atom:At @atom:BT
then atoms @atom:AT @atom:BT

# Then break the bond connecting "A" to the lipid's "Head" bead:
if   atoms @atom:AT @atom:Ht
then atoms @atom:AT @atom:H  and  bond BREAK

# When the lipids head group arrives at the other side
# break the bond connecting it to the Flippase bead ("B"):
if   atoms @atom:BT @atom:H  and  distance <= 1.3
then atoms @atom:B  @atom:H  and  bond BREAK

# Finally change the first bead back to the "A" state,
# enabling it to accept new lipids in the future:
if   atoms @atom:AT @atom:B
then atoms @atom:A  @atom:B
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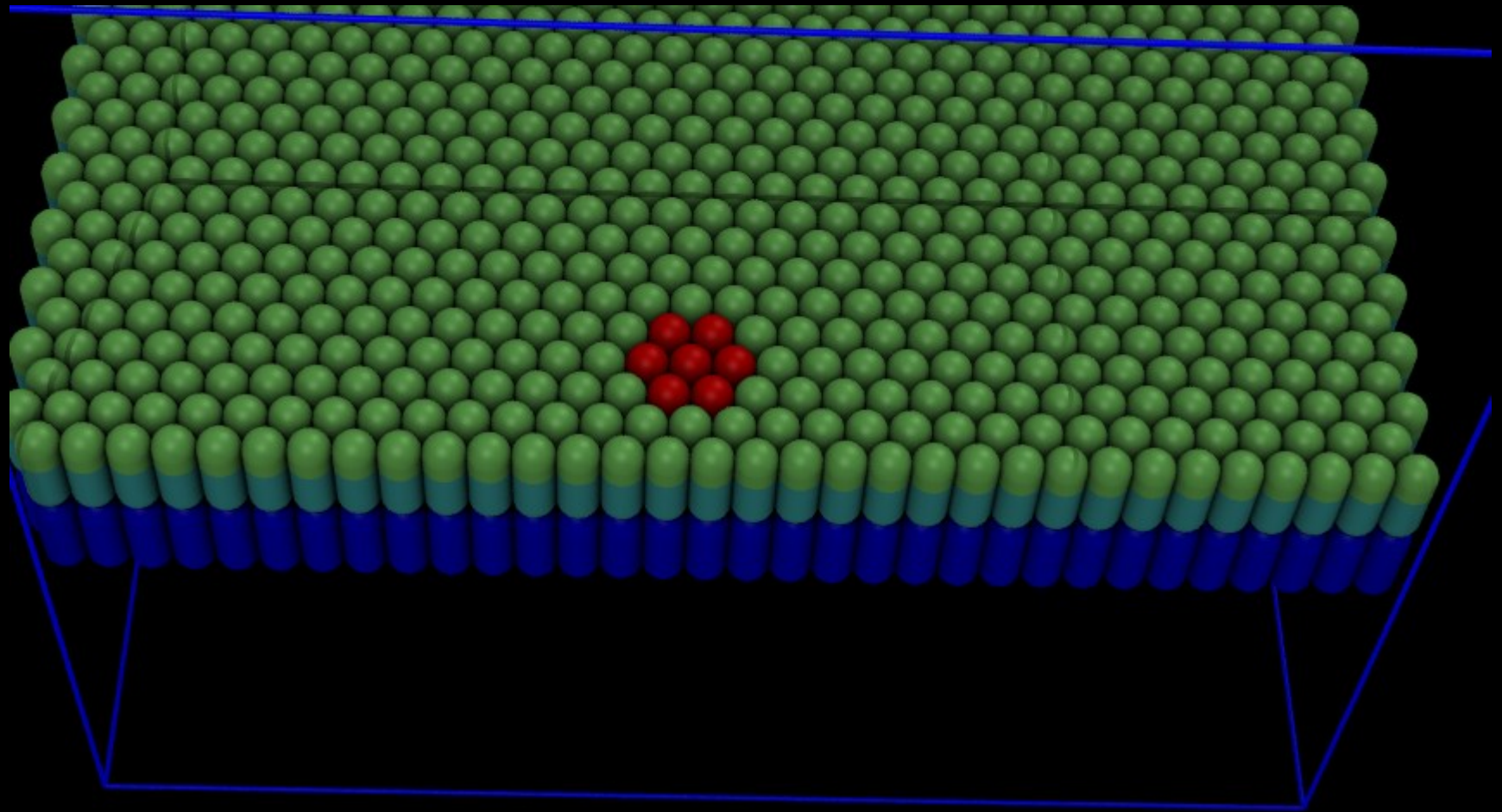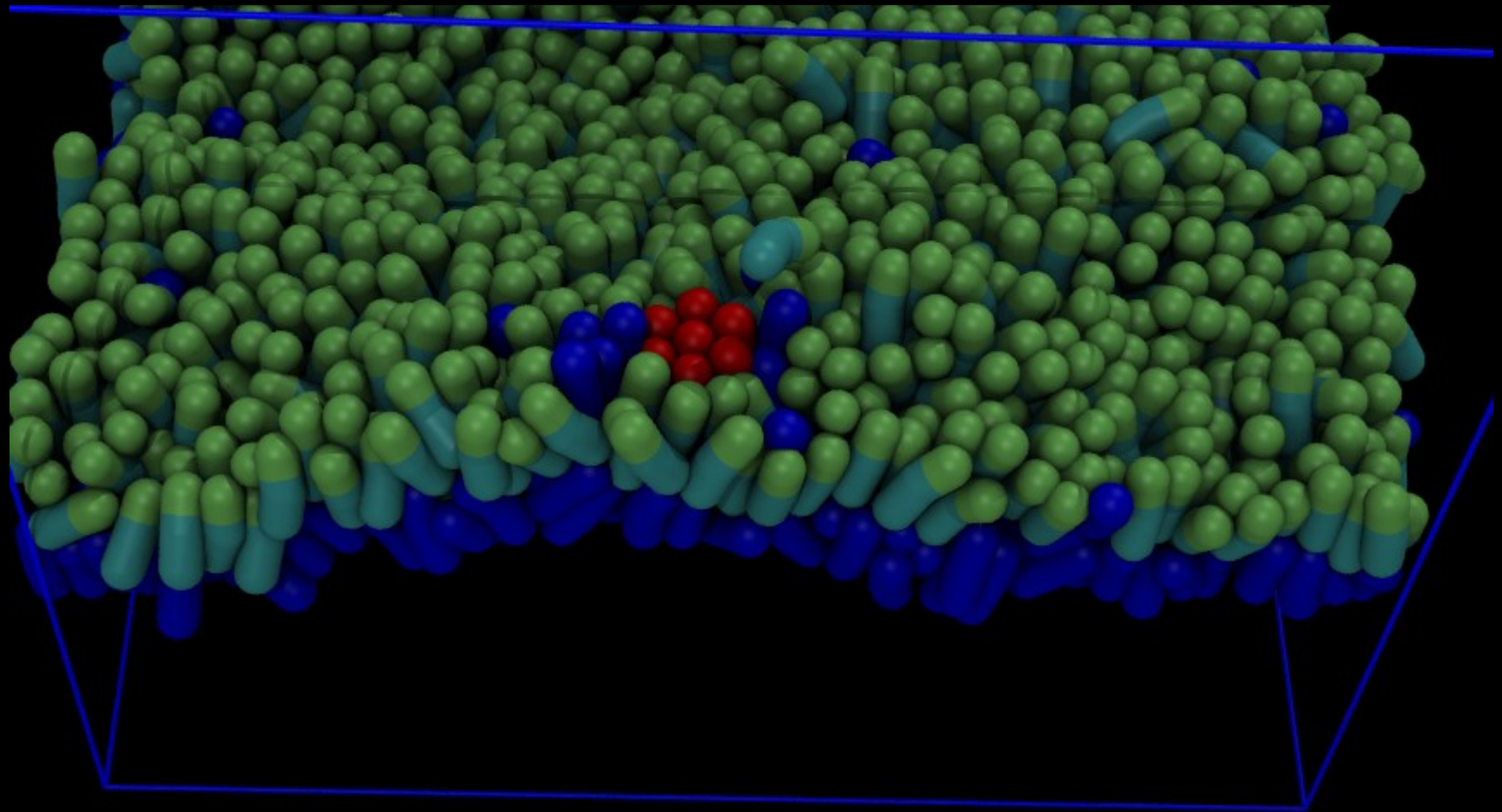
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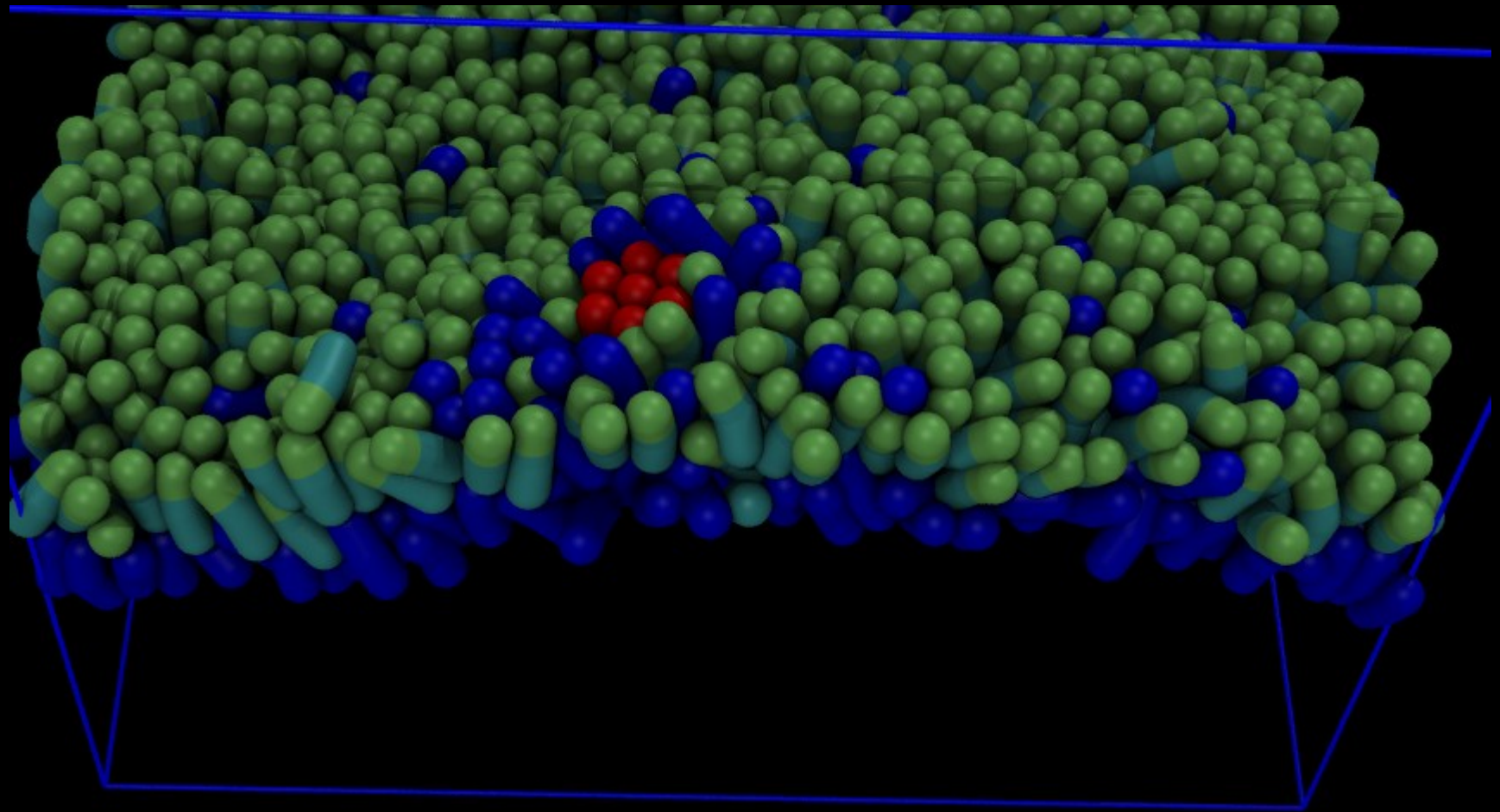Note: Syntax may change in the future...
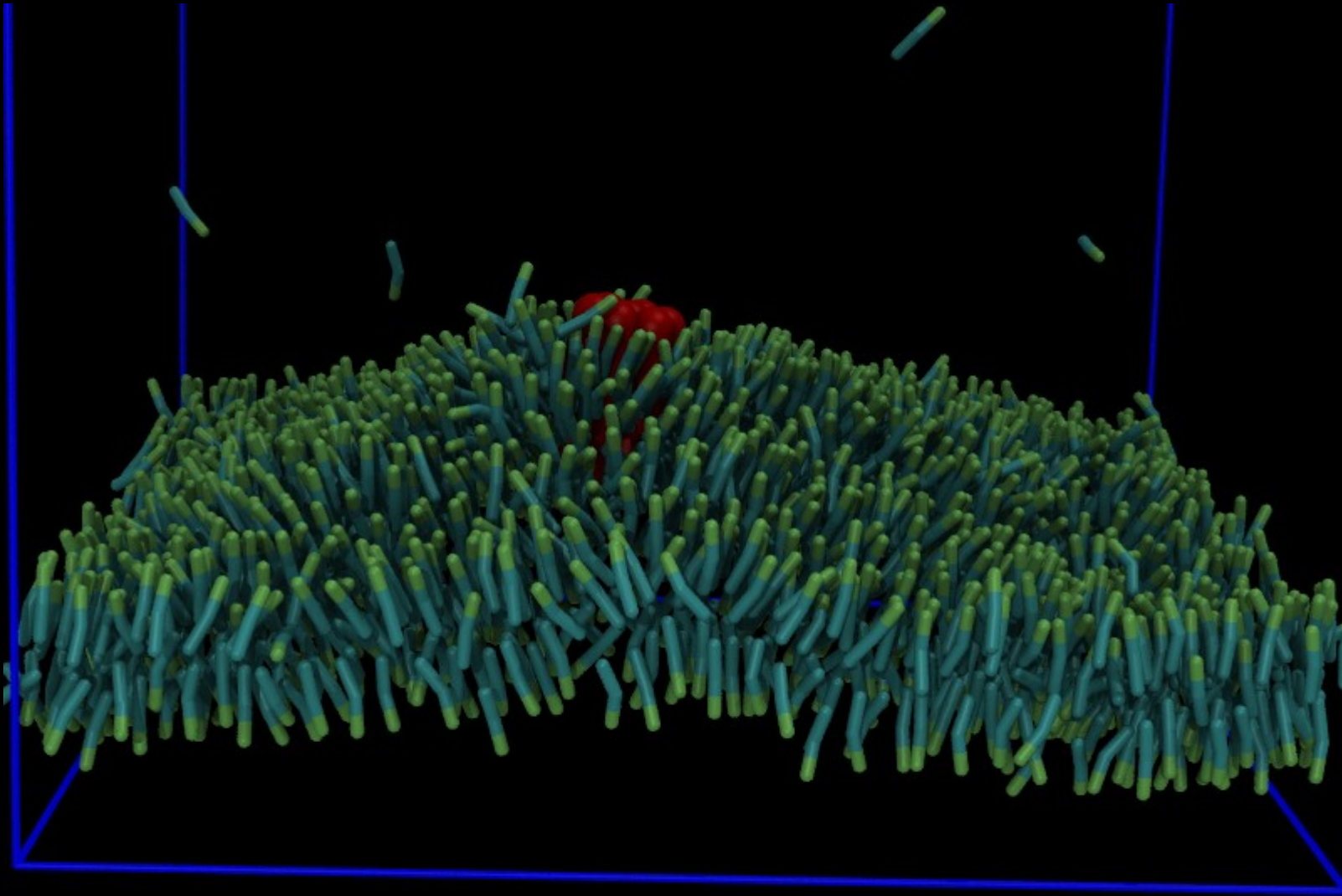
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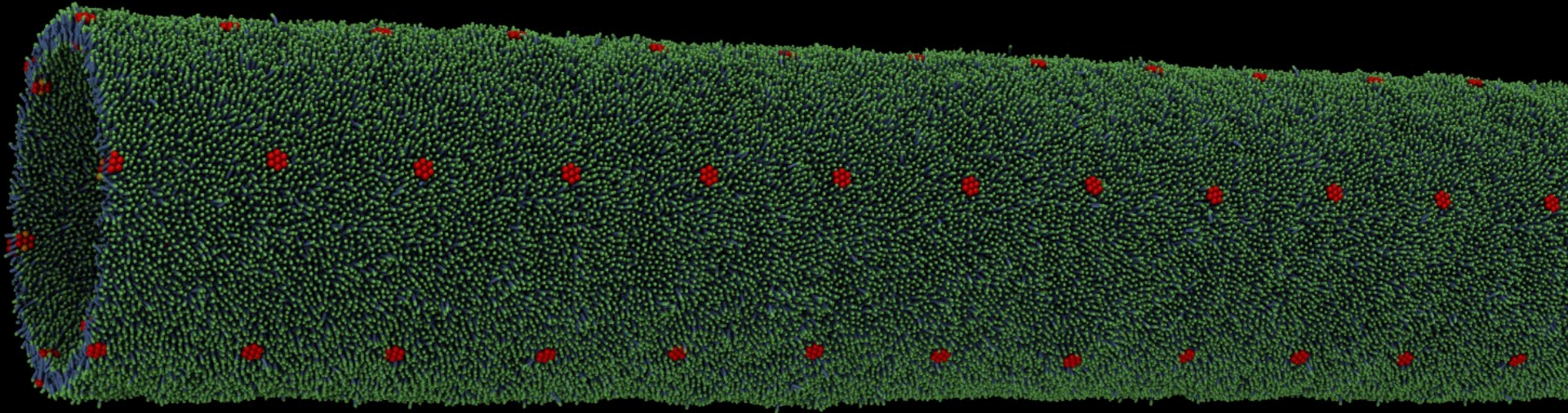Example: Flippase mediated membrane curvature

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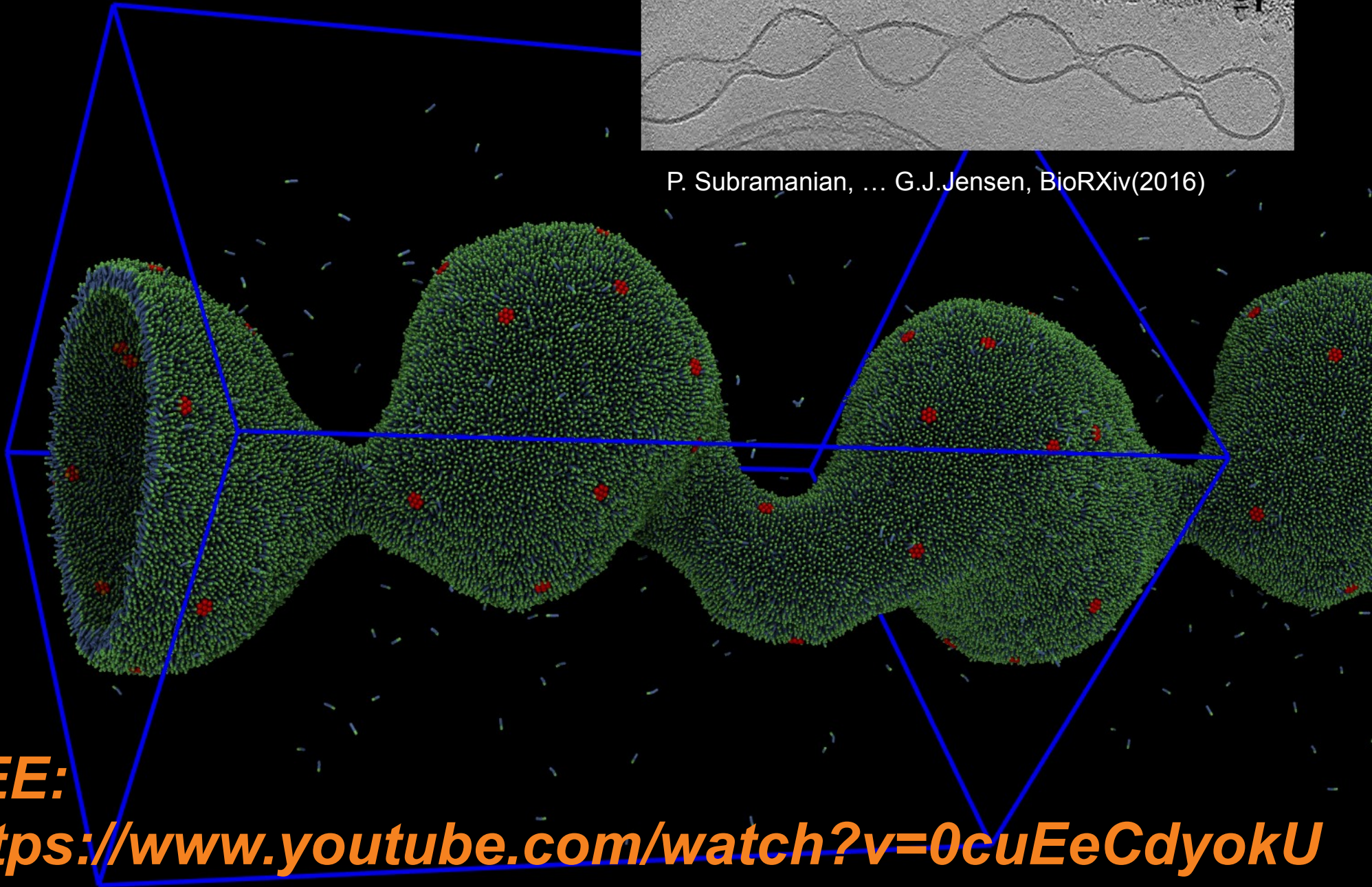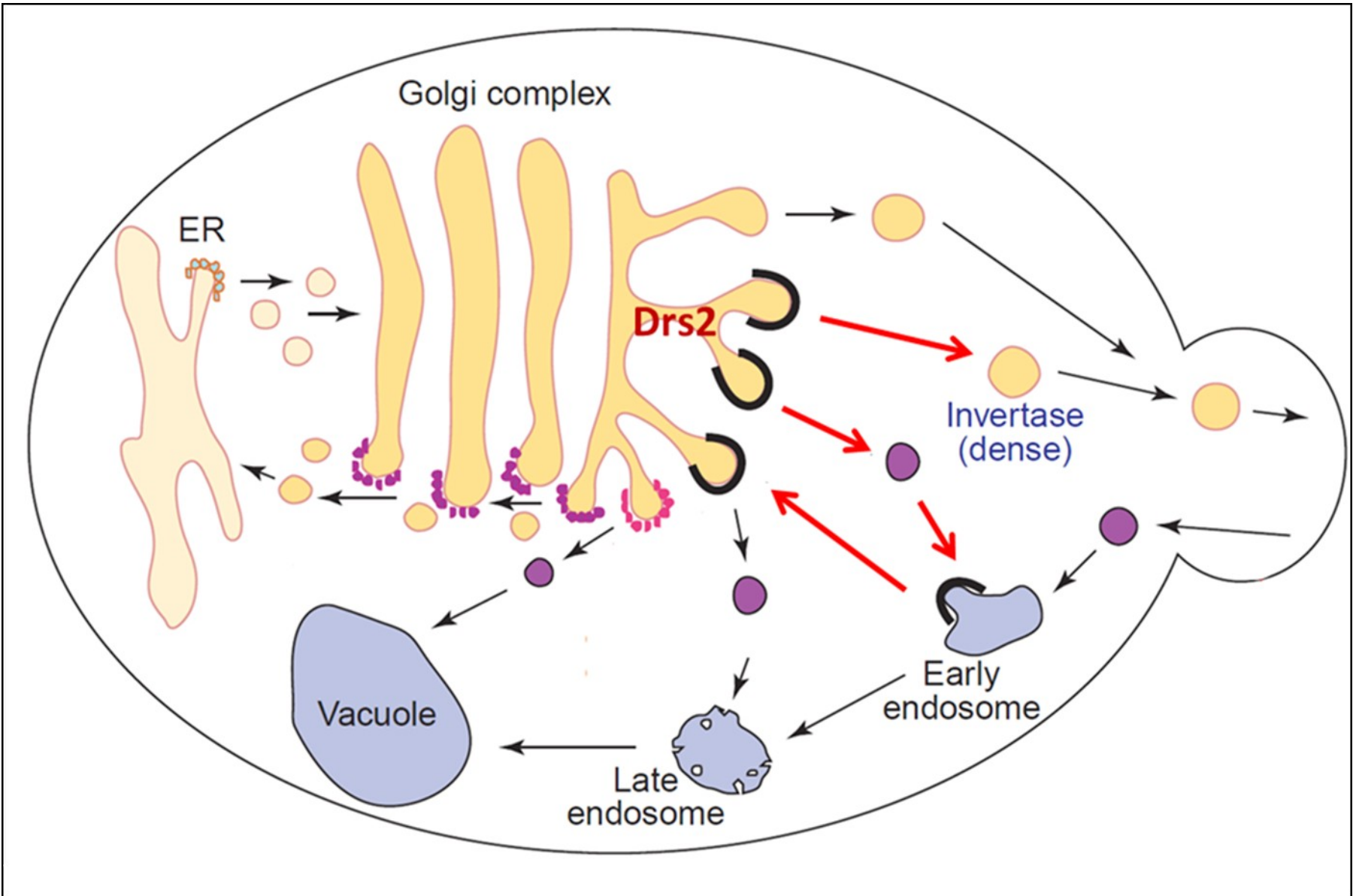
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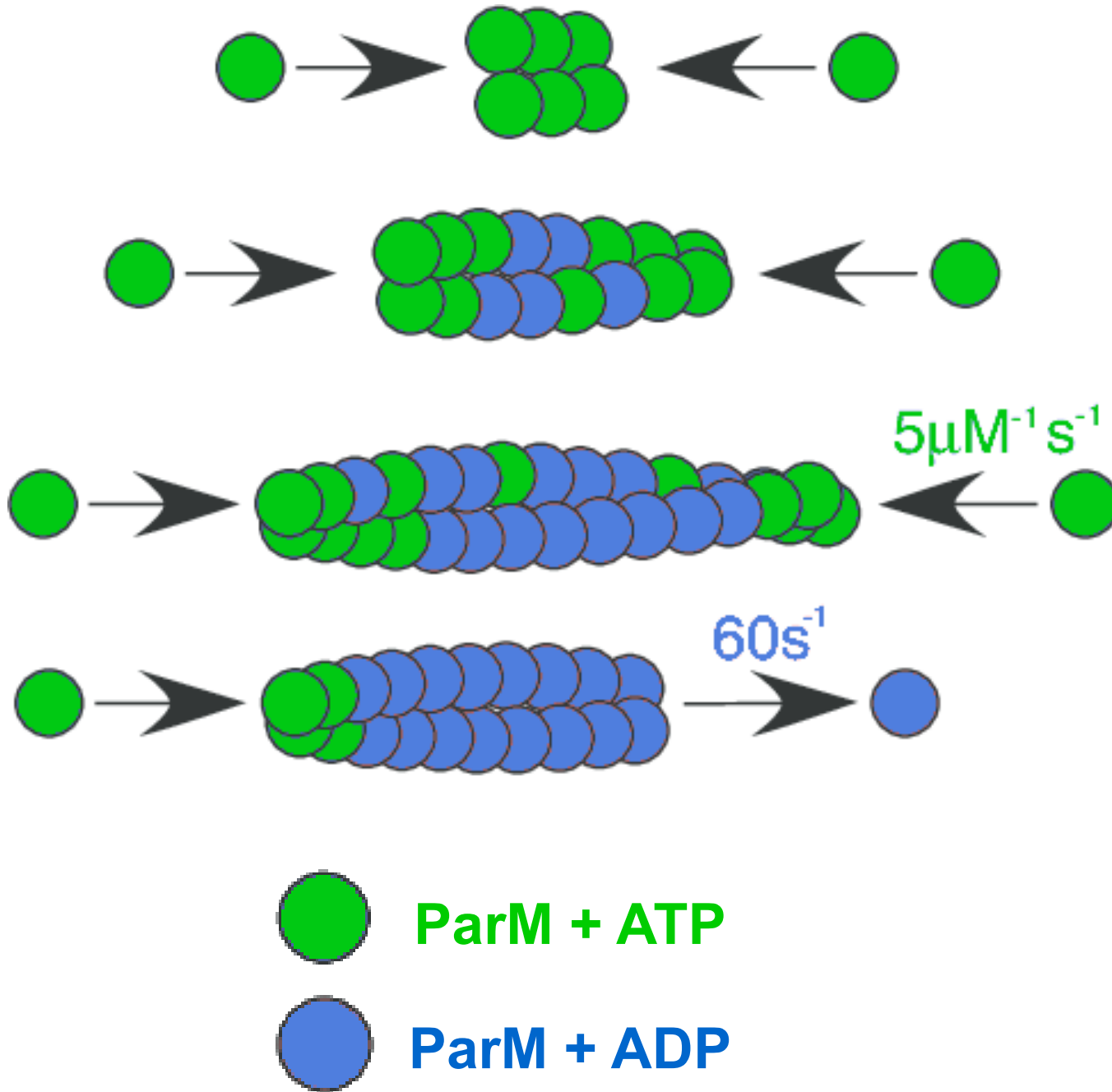


P. Subramanian, … G.J.Jensen, BioRXiv(2016)

*SEE:*
*https://www.youtube.com/watch?v=0cuEeCdyokU*

# Example: Flippase mediated membrane curvature



Graham Lab,
Vanderbilt, website

# Example: Dynamic Instabilty of ParM



$5\mu M^{-1}s^{-1}$

$60s^{-1}$

🟢 ParM + ATP

🔵 ParM + ADP

*Garner, ..., Mullins, Science (2004)*

# Example: Dynamic Instabilty of ParM

```
if atoms @atom:TF @atom:TF
   and distance <= 7.1 and prob 0.1
-> atoms @atom:TE @atom:TE and bond @bond:P


if atoms @atom:TE @atom:TE and prob 0.9
-> atoms @atom:TF @atom:TF and bond BREAK


if atoms @atom:TE @atom:TF
   and distance <= 7.1 and prob 0.25 &
-> atoms @atom:TB @atom:TE and bond @bond:P
 and angle @atom:S


if atom @atom:TB and prob 0.0015 -> atom @atom:DB


if atom @atom:TE and prob 0.0015 -> atom @atom:DE


if atoms @atom:DB @atom:DE
-> atoms @atom:DE @atom:DF and bond BREAK


if atoms @atom:DE @atom:DE
-> atoms @atom:DF @atom:DF and bond BREAK


if atom @atom:DF and prob 0.0007 -> atom @atom:TF
```
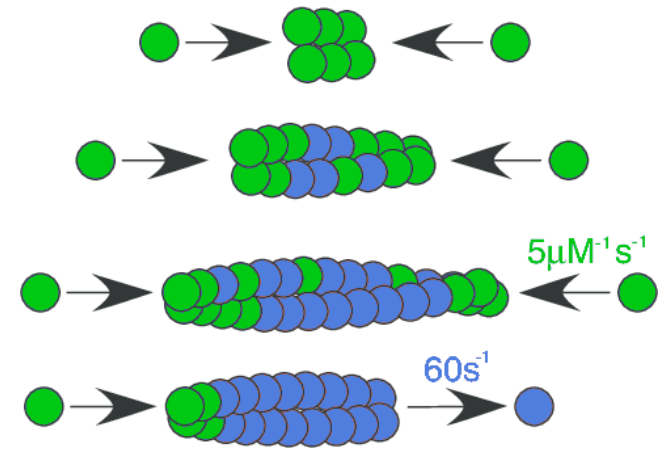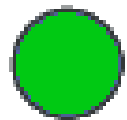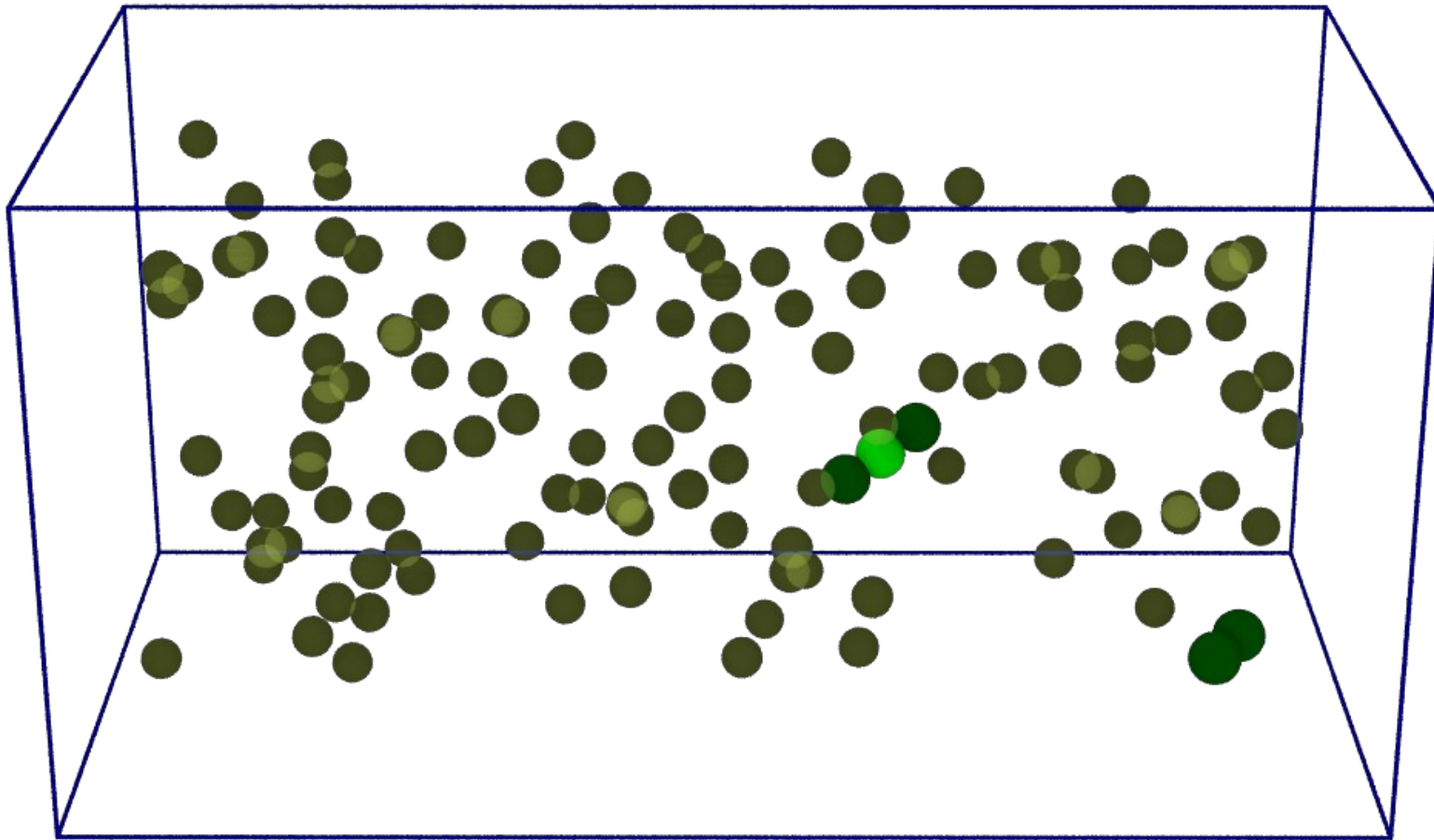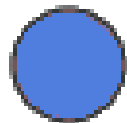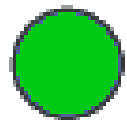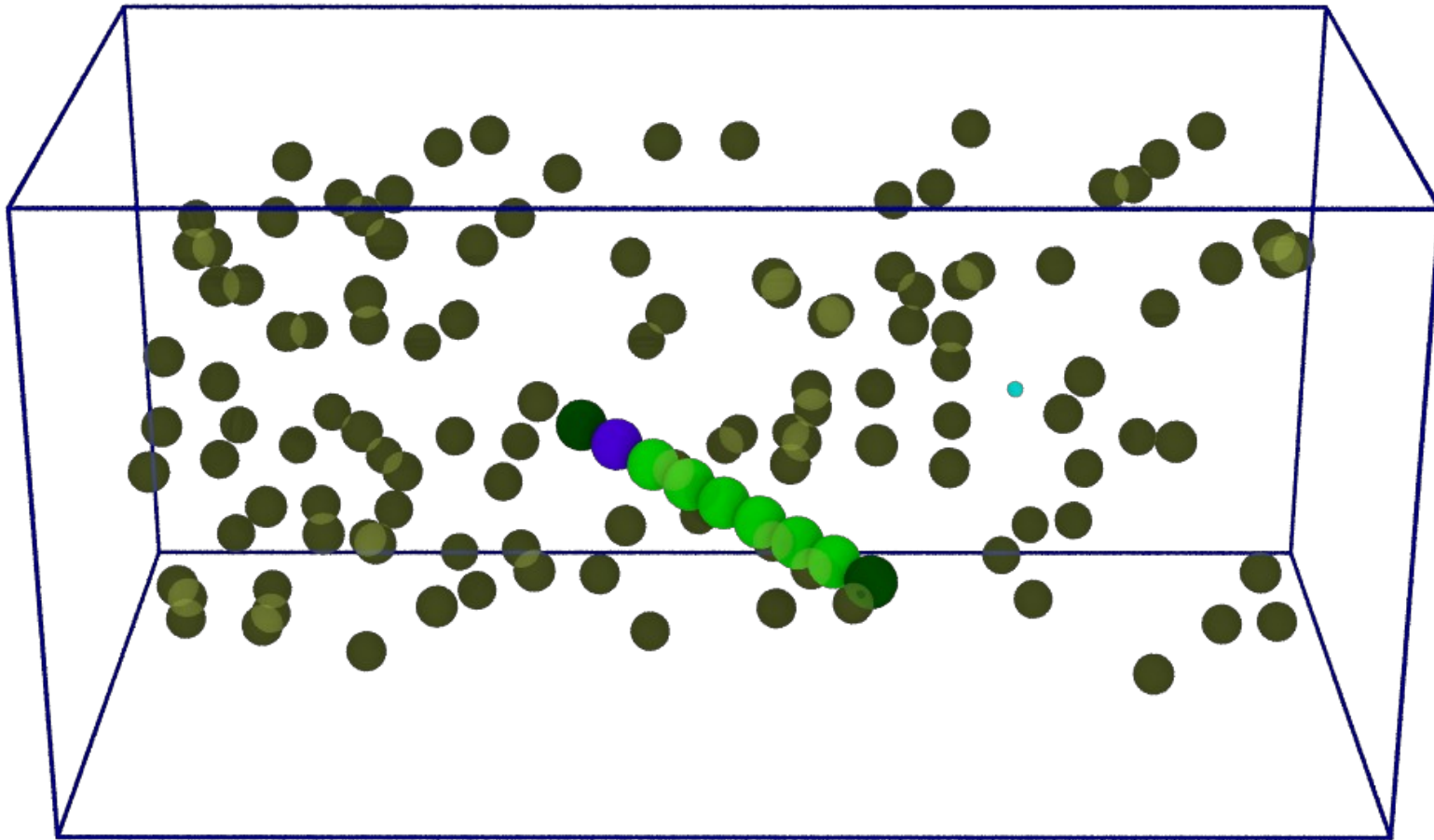


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● **ParM + ATP**

● **ParM + ADP**

*Garner, …, Mullins, Science (2004)*

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if atoms @atom:TF @atom:TF
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-> atoms @atom:TE @atom:TE and bond @bond:P


if atoms @atom:TE @atom:TE and prob 0.9
-> atoms @atom:TF @atom:TF and bond BREAK


if atoms @atom:TE @atom:TF
   and distance <= 7.1 and prob 0.25 &
-> atoms @atom:TB @atom:TE and bond @bond:P
 and angle @atom:S


if atom @atom:TB and prob 0.0015 -> atom @atom:DB


if atom @atom:TE and prob 0.0015 -> atom @atom:DE


if atoms @atom:DB @atom:DE
-> atoms @atom:DE @atom:DF and bond BREAK


if atoms @atom:DE @atom:DE
-> atoms @atom:DF @atom:DF and bond BREAK


if atom @atom:DF and prob 0.0007 -> atom @atom:TF
```

5μM⁻¹s⁻¹

60s⁻¹

ParM + ATP

ParM + ADP

*Garner, …, Mullins, Science (2004)*

*Note: Syntax may change in the future...*

# Example 2: Dynamic Instabilty of ParM



**ParM + ATP**

**ParM + ADP**

*Garner, …, Mullins, Science (2004)*

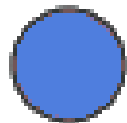# Example: Dynamic Instabilty of ParM



🟢 **ParM + ATP**

🔵 **ParM + ADP**

*Garner, …, Mullins, Science (2004)*
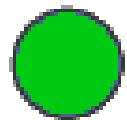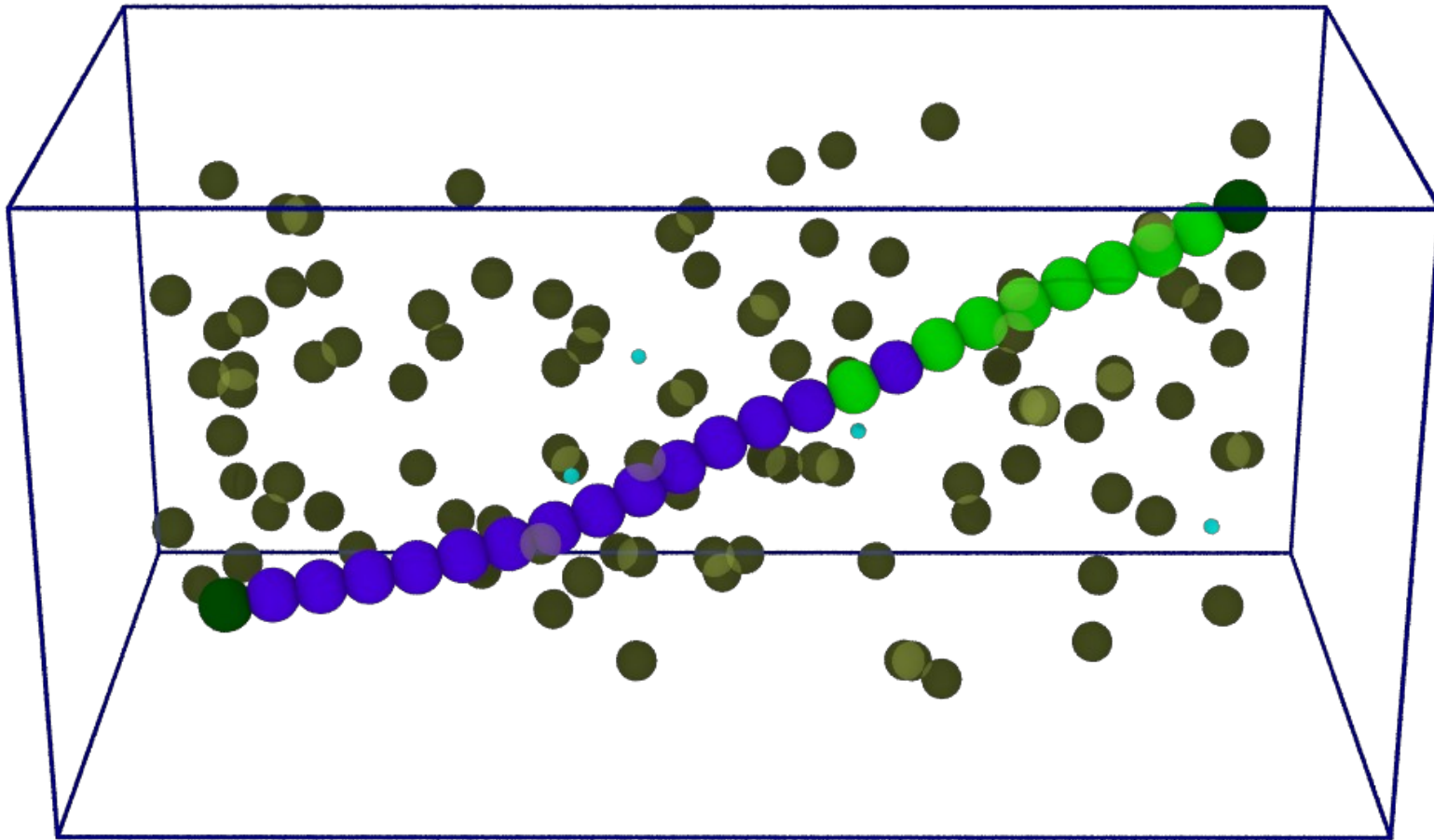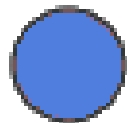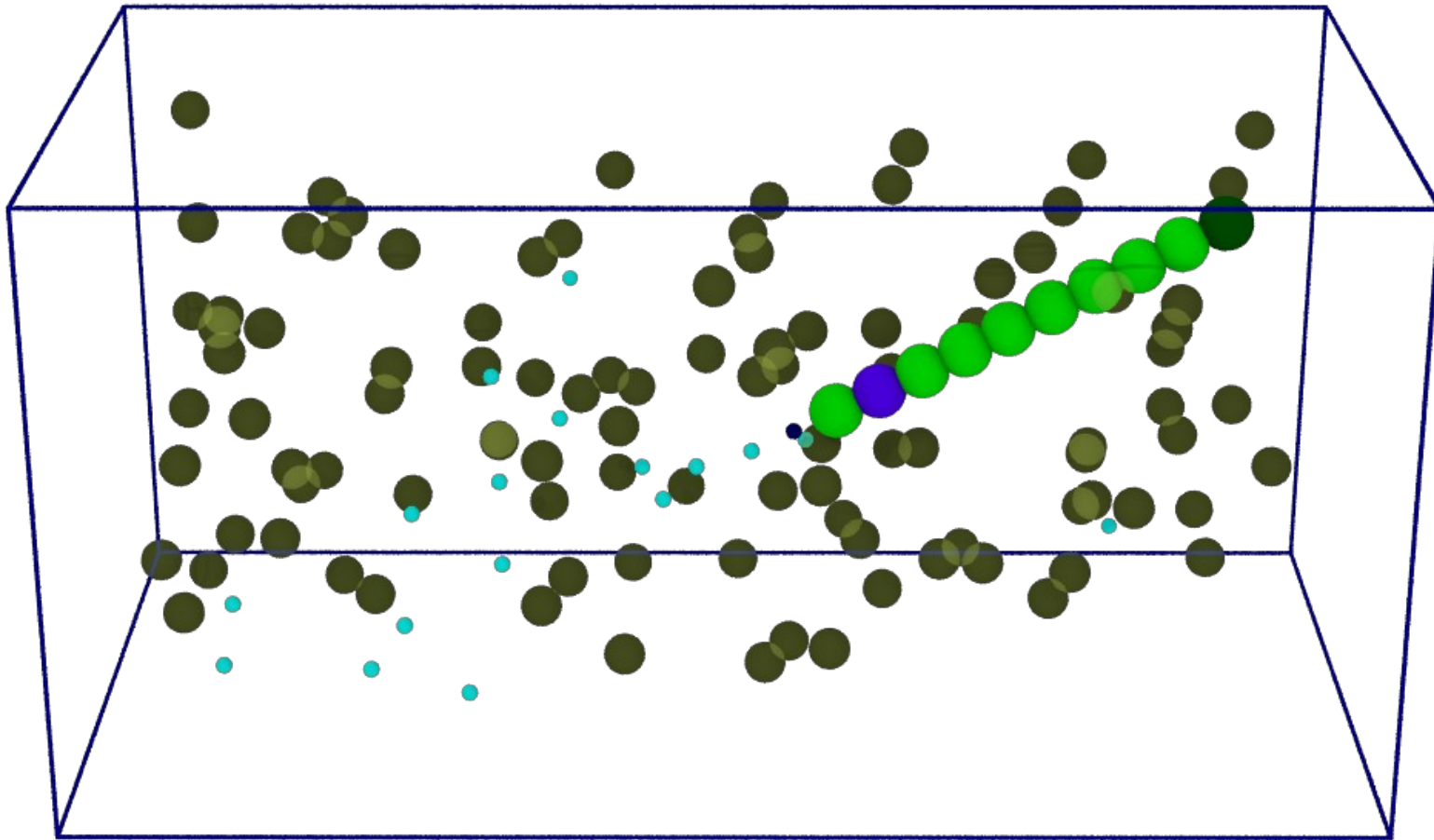
# Example: Dynamic Instabilty of ParM



ParM + ATP

ParM + ADP

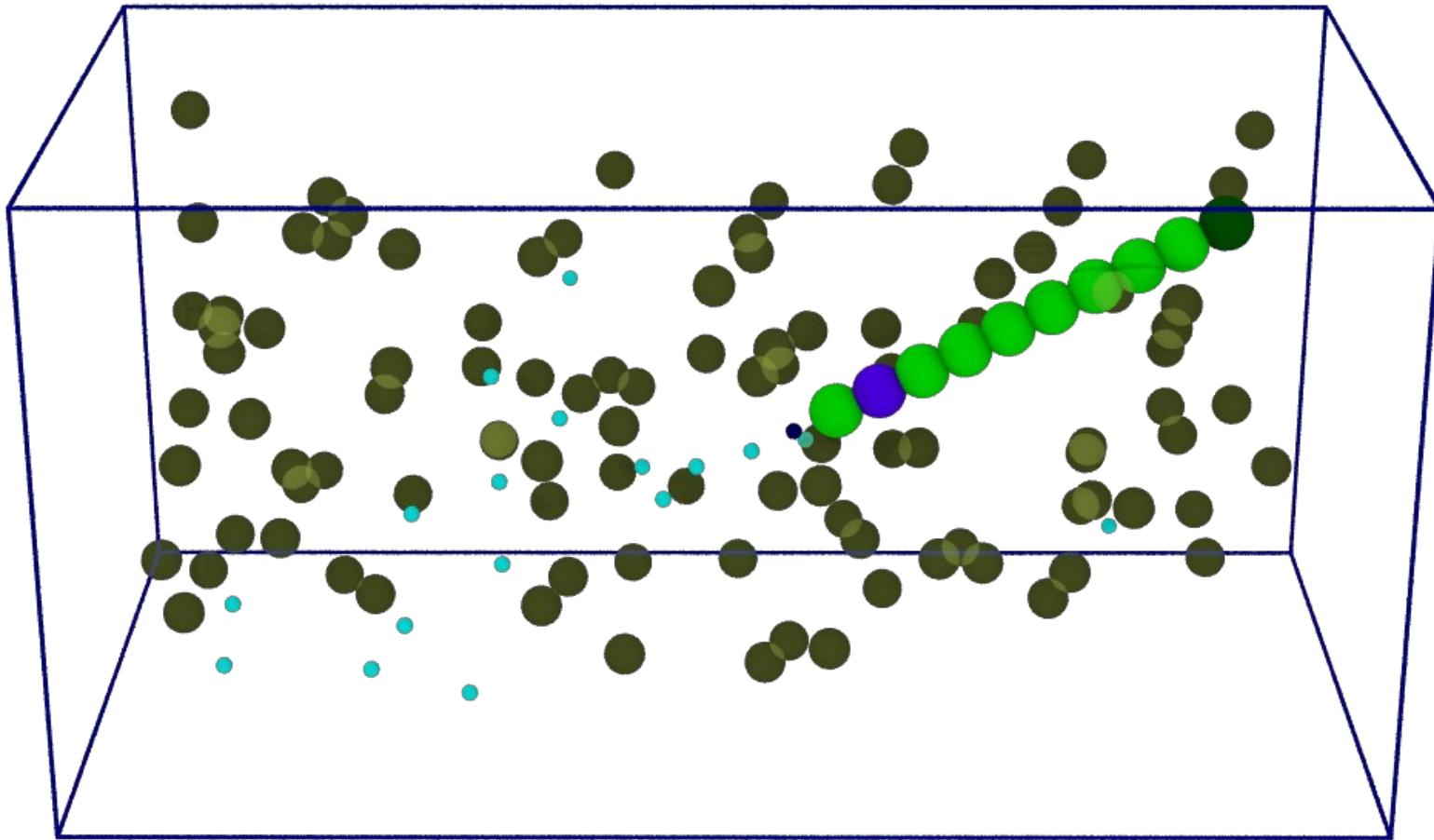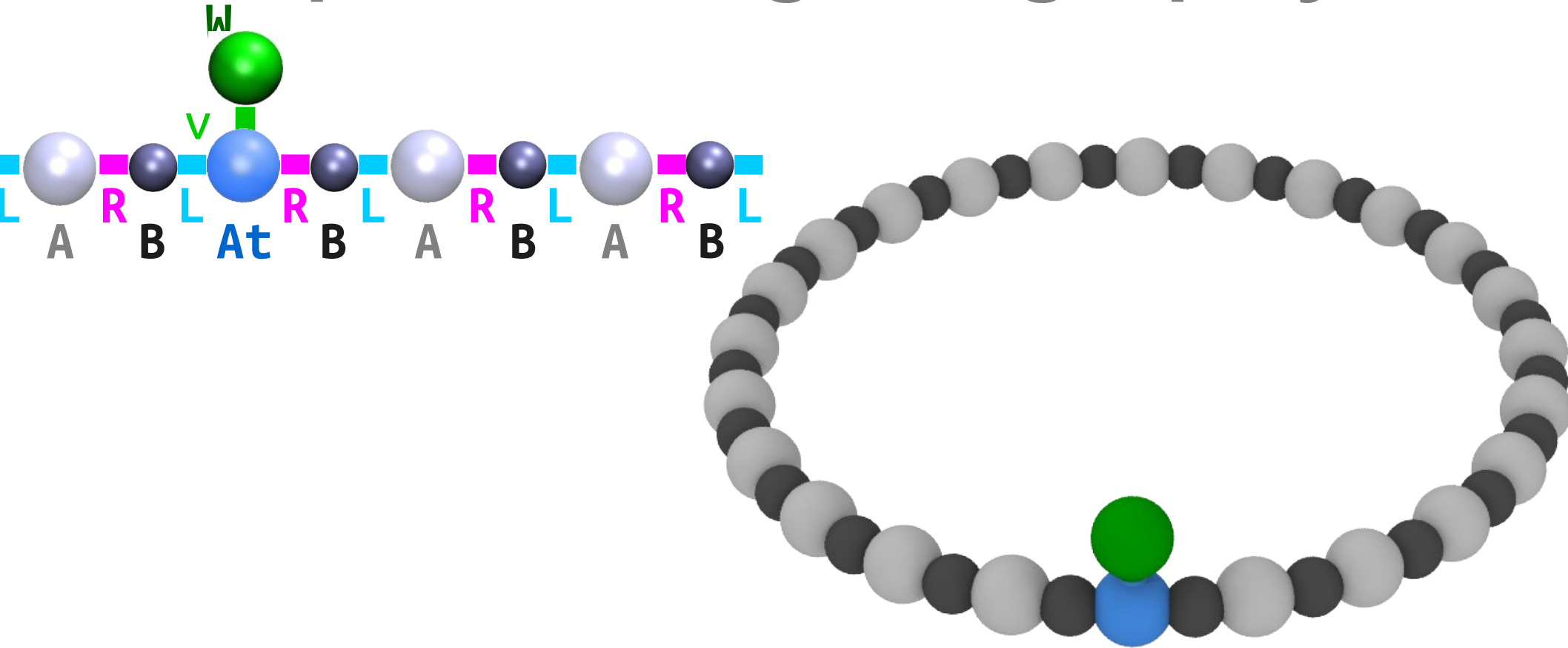*Garner, …, Mullins, Science (2004)*
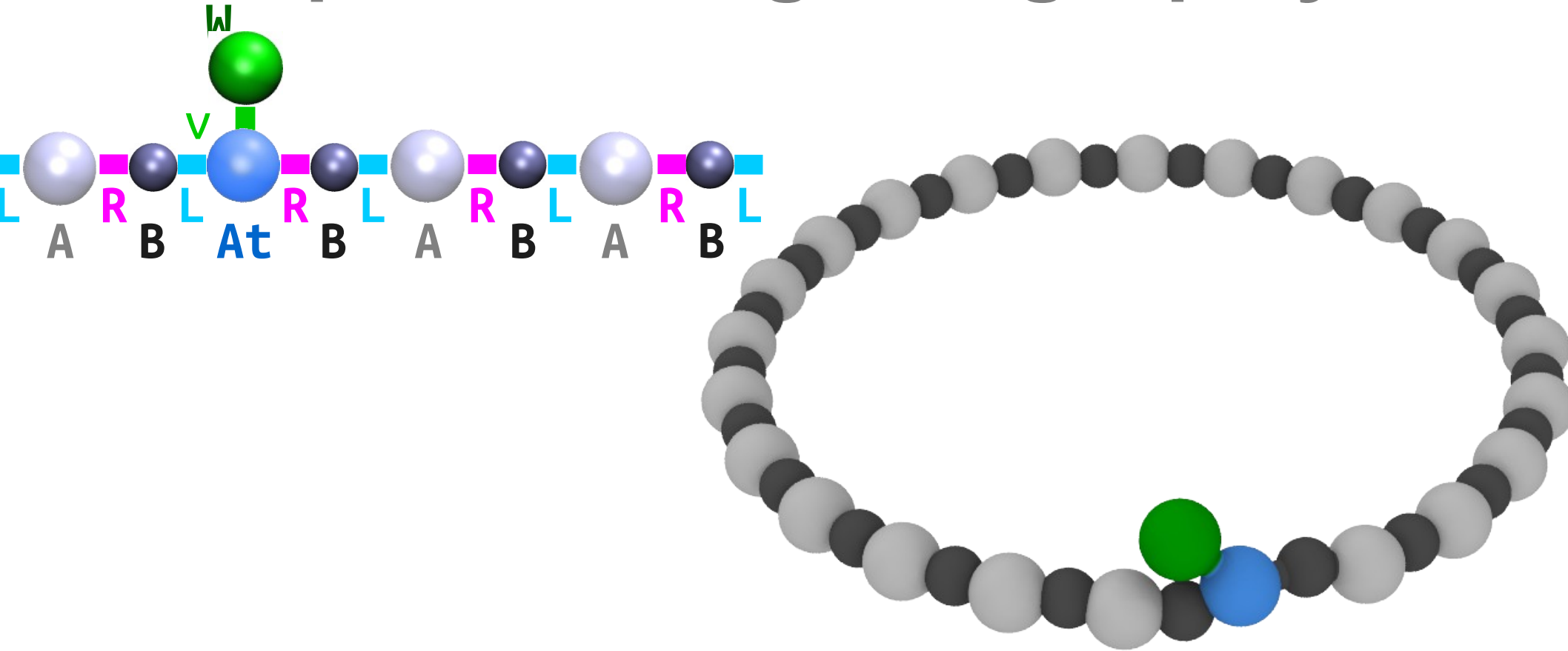
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# Example: Dynamic Instabilty of ParM
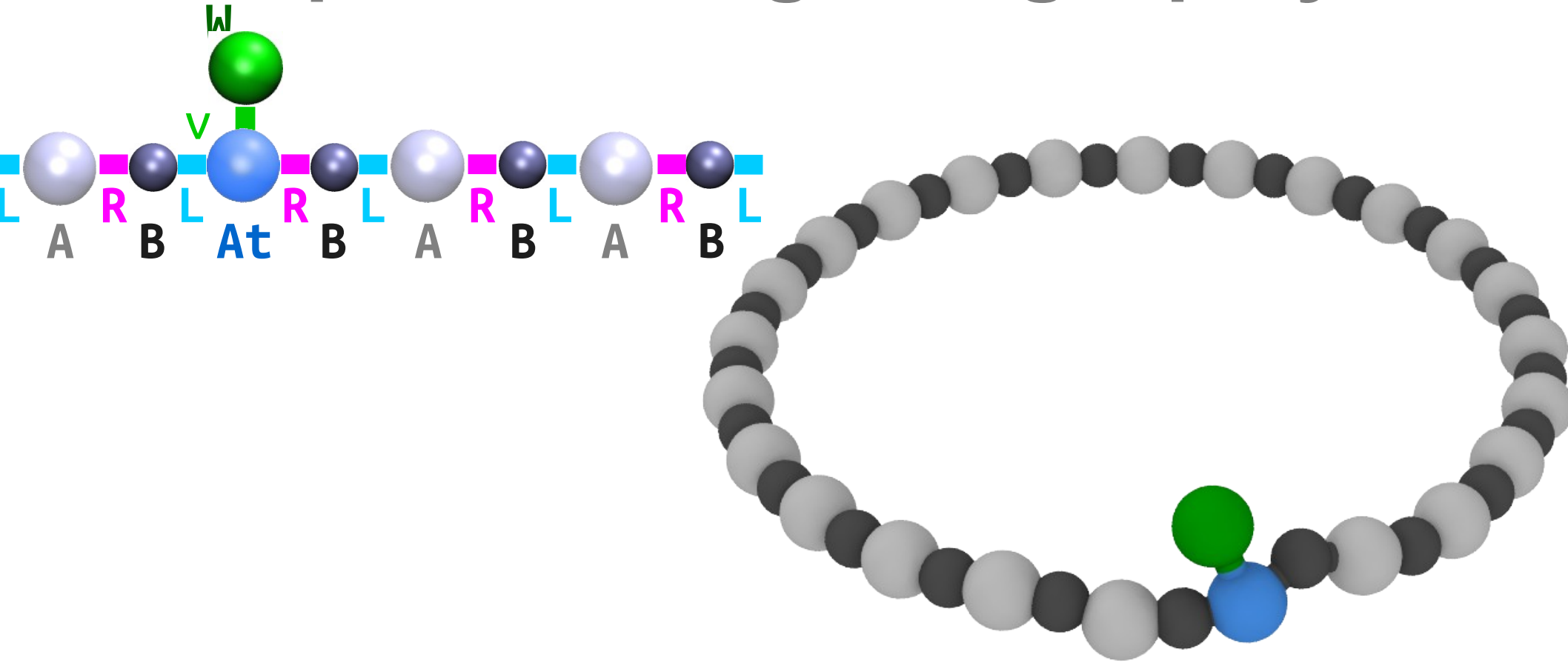
# Example: Walking along a polymer

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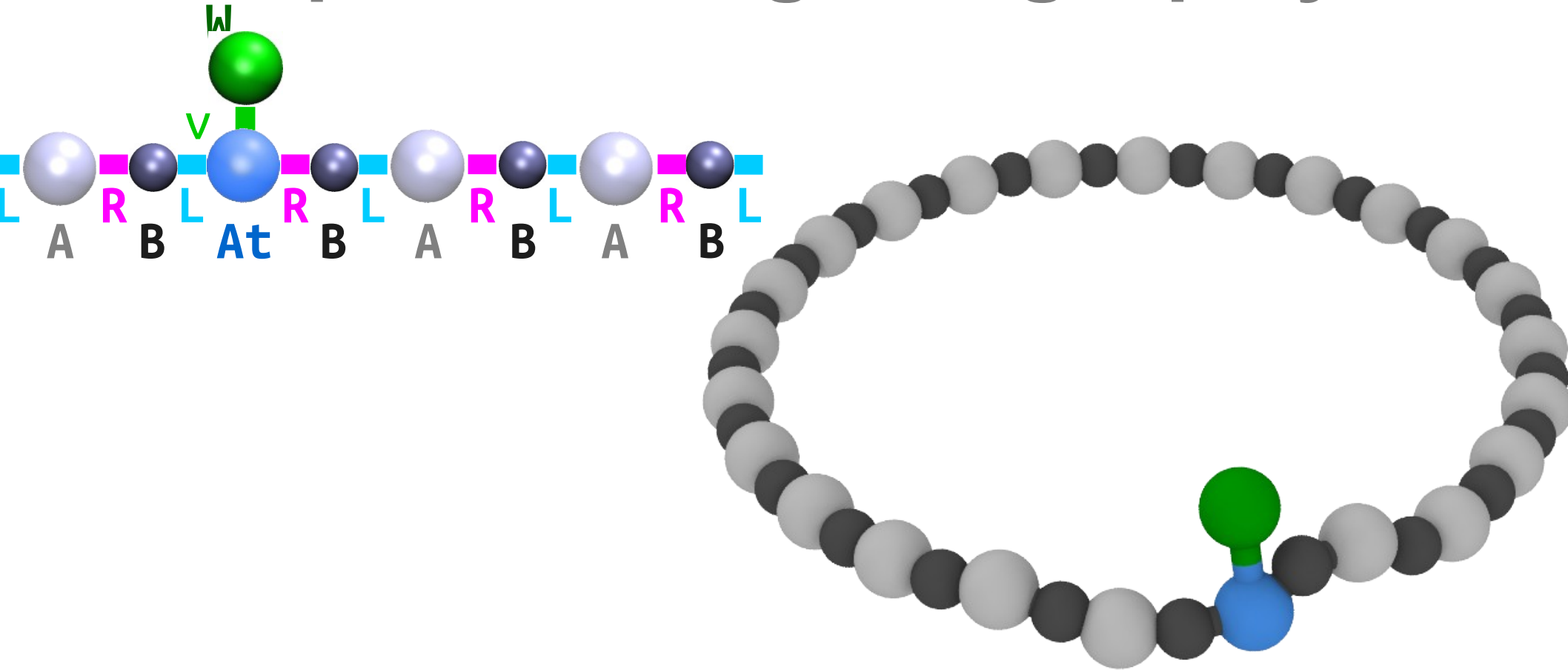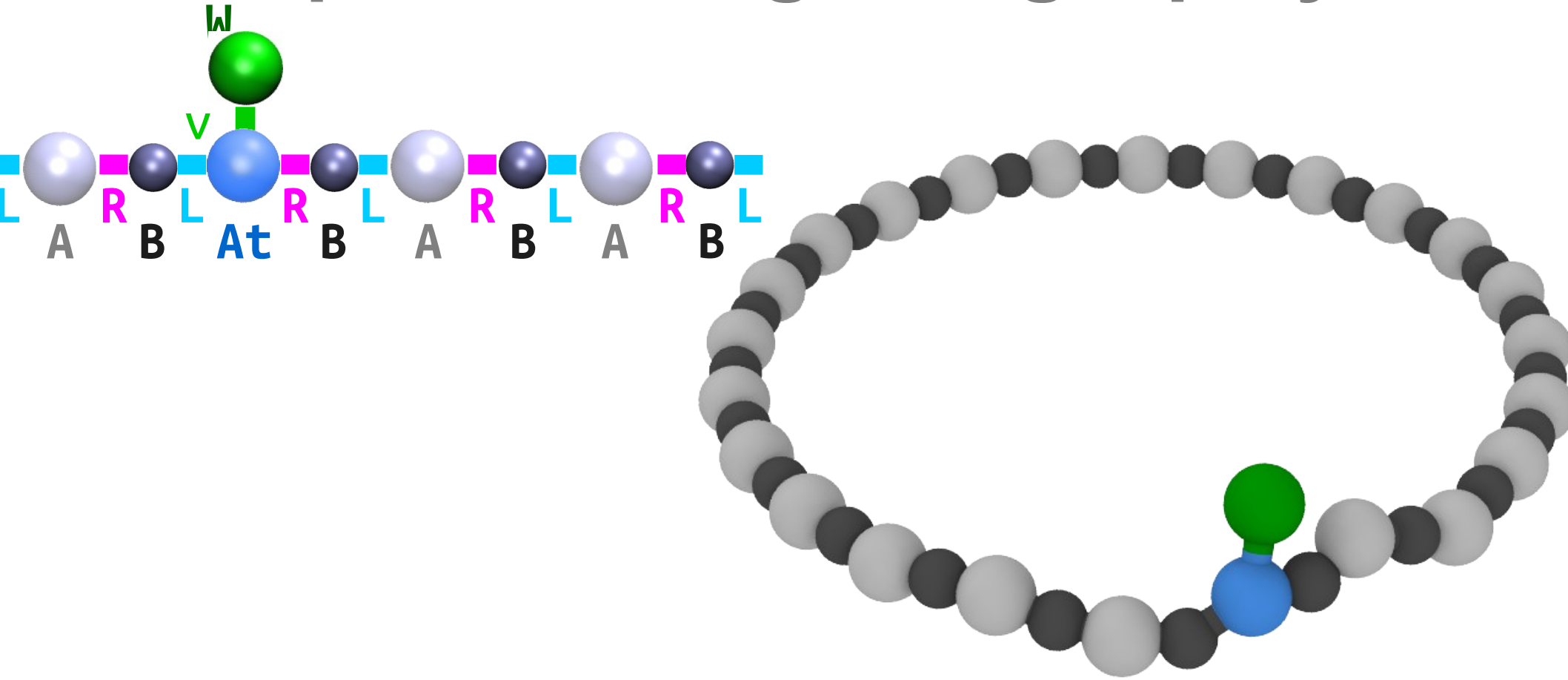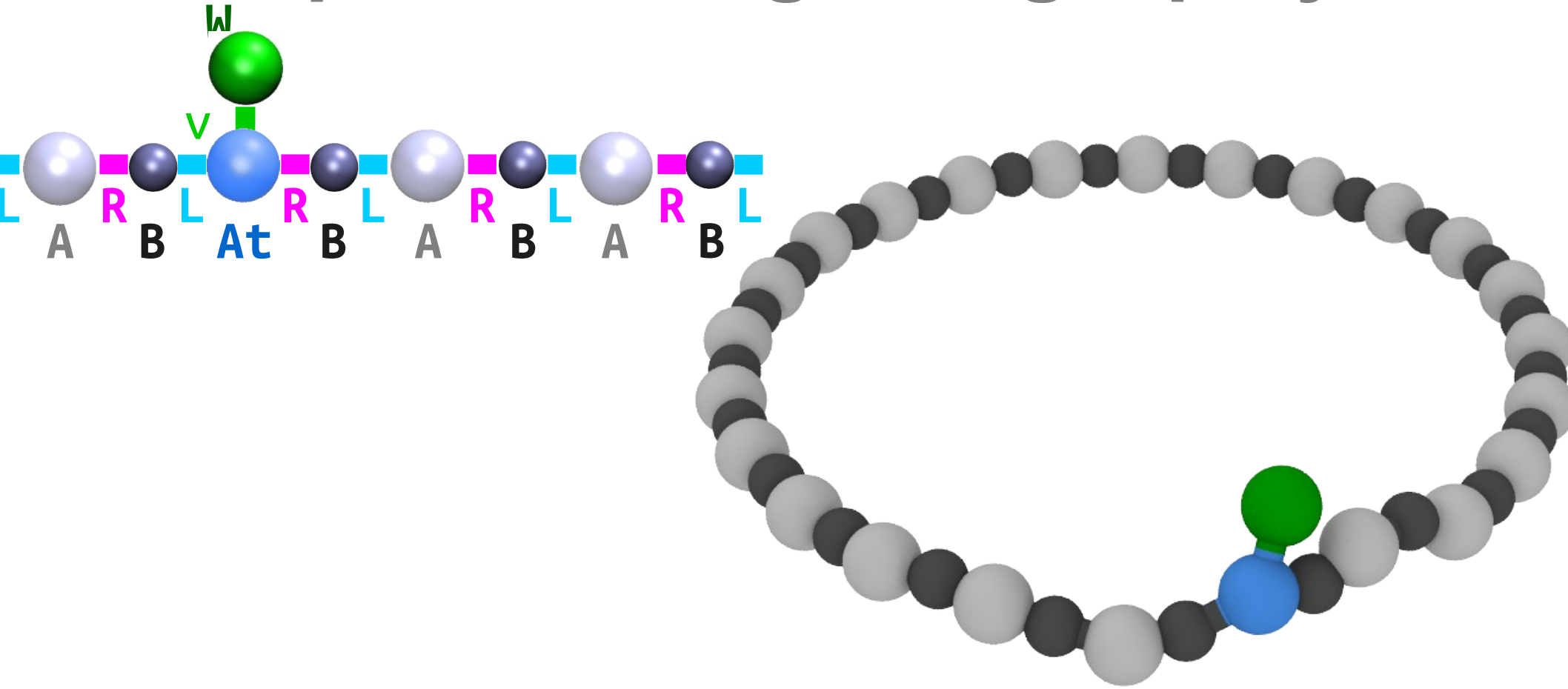# Example: Walking along a polymer

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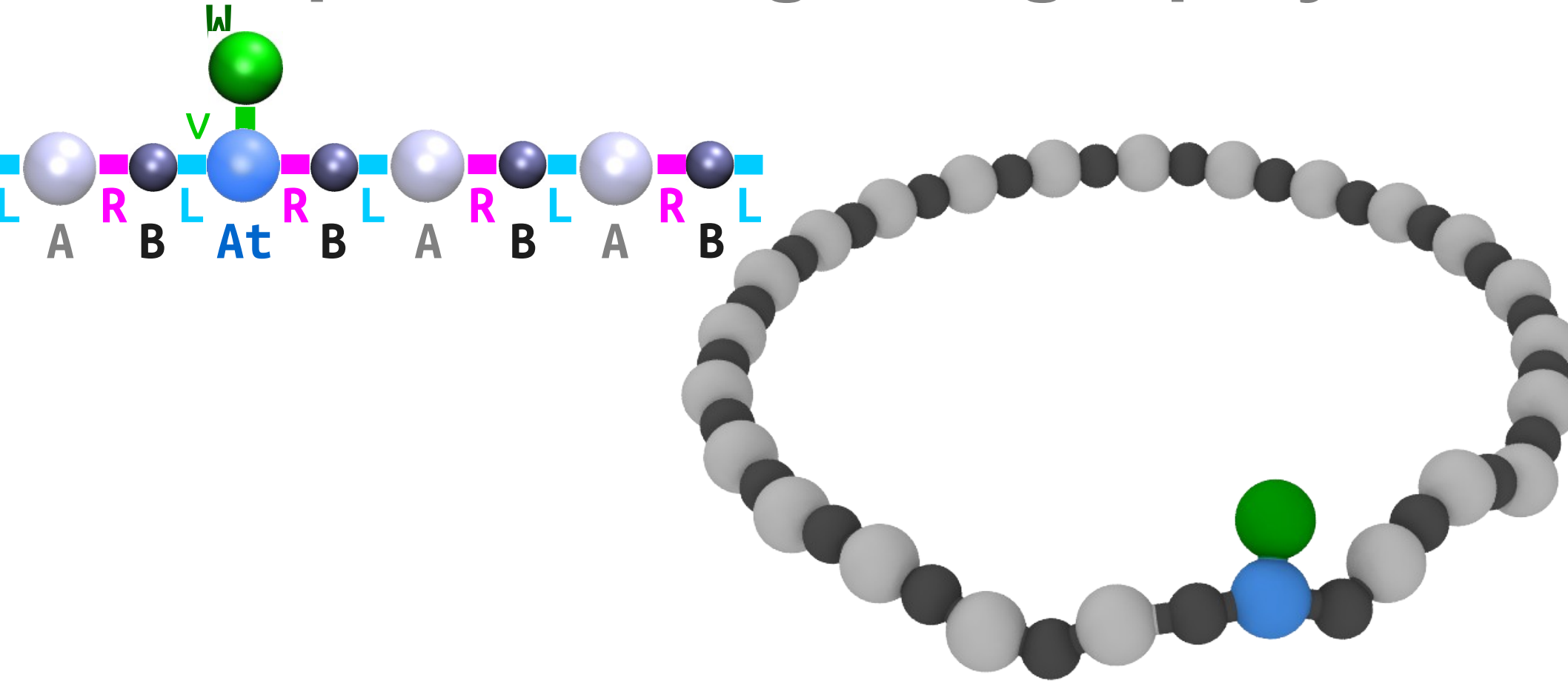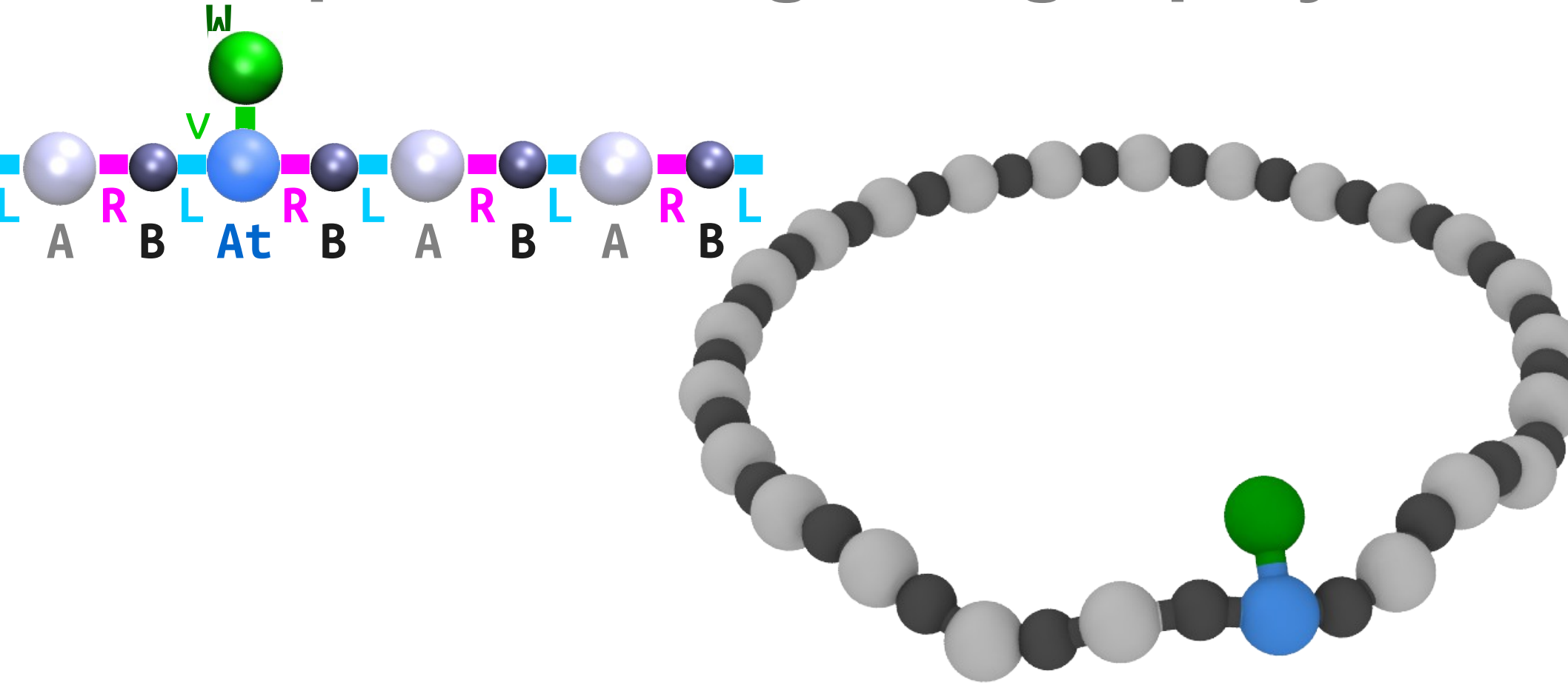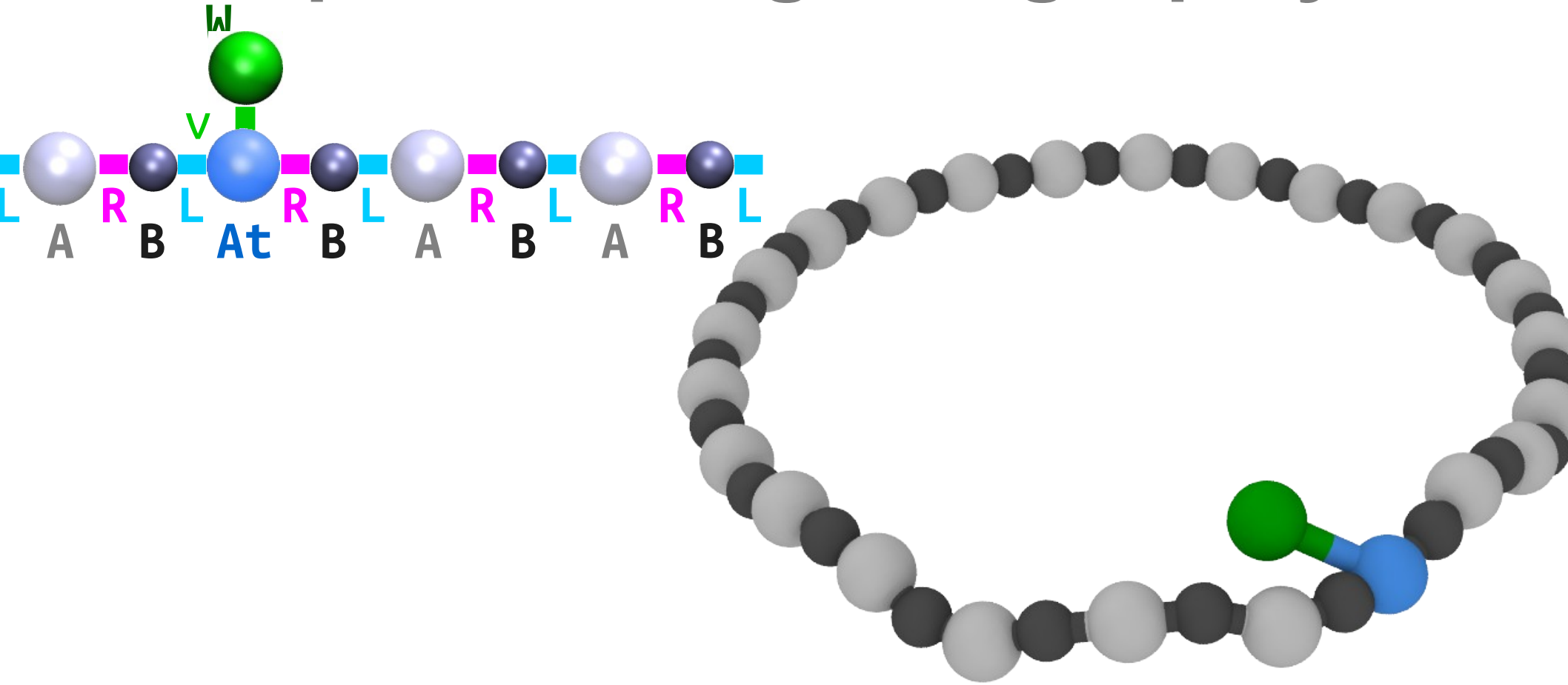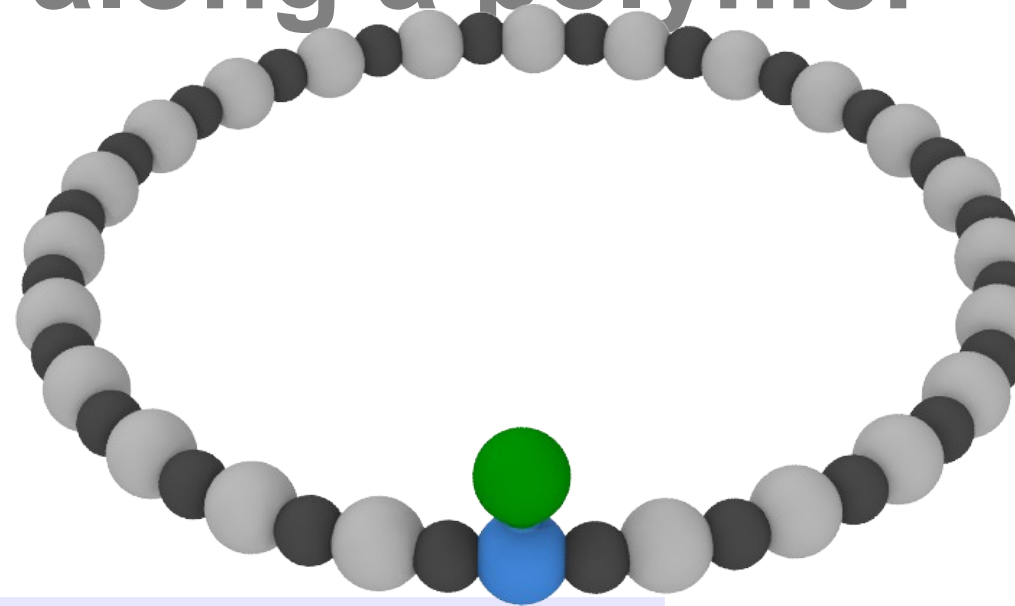# Example: Walking along a polymer

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SEE:
https://www.youtube.com/watch?v=QO4LbHGAgxU

# Example: Walking along a polymer



```
if    atoms @atom:At @atom:B    and   bond @bond:R
      and   prob 0.2
then  atoms @atom:A   @atom:Bt


if    atoms @atom:Bt @atom:A    and   bond @bond:L
then  atoms @atom:B   @atom:AT


if    atoms @atom:W   @atom:AT   and   distance <= 1.5
then  atoms @atom:Wt @atom:At    and   bond @bond:V
      and angle @angle:Ra   @atom:B @atom:Aw @atom:W


if    atoms @atom:Wt @atom:A    and   bond @bond:V
then  atoms @atom:W   @atom:A    and   bond BREAK
```
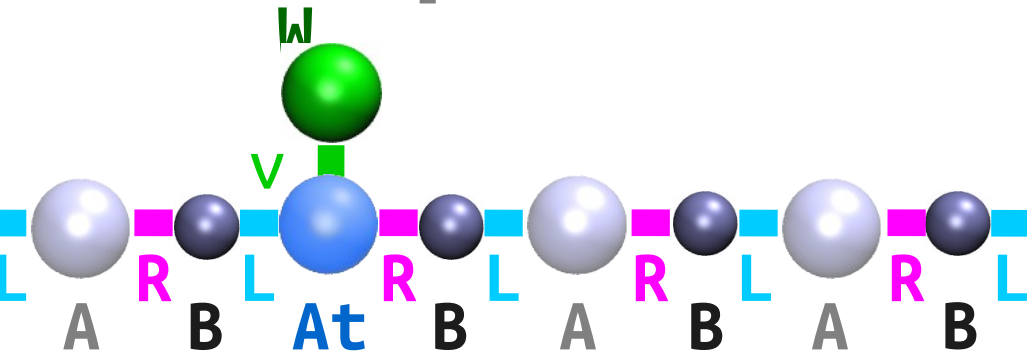
# Example: Walking along a polymer
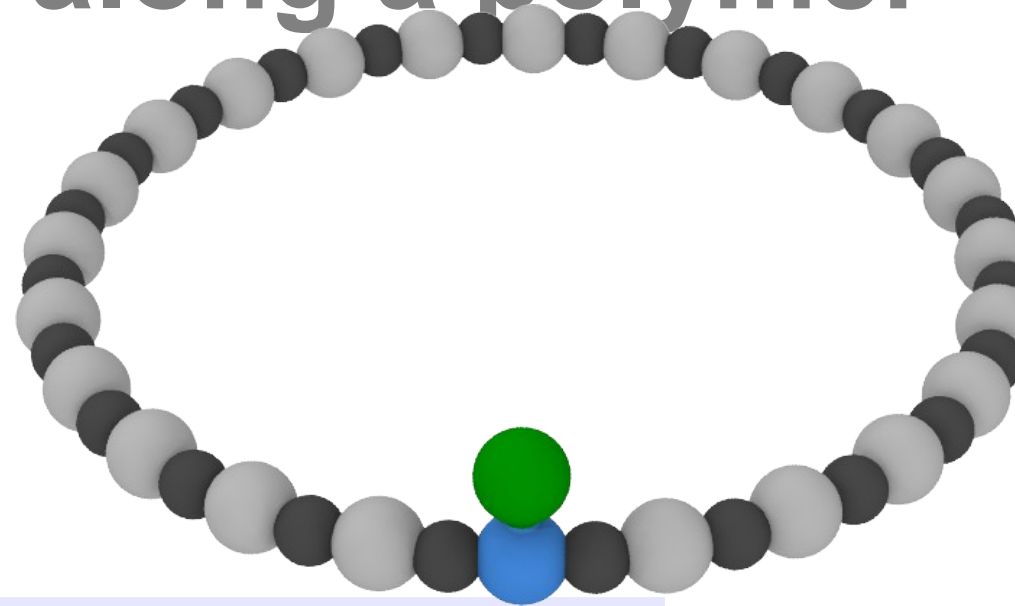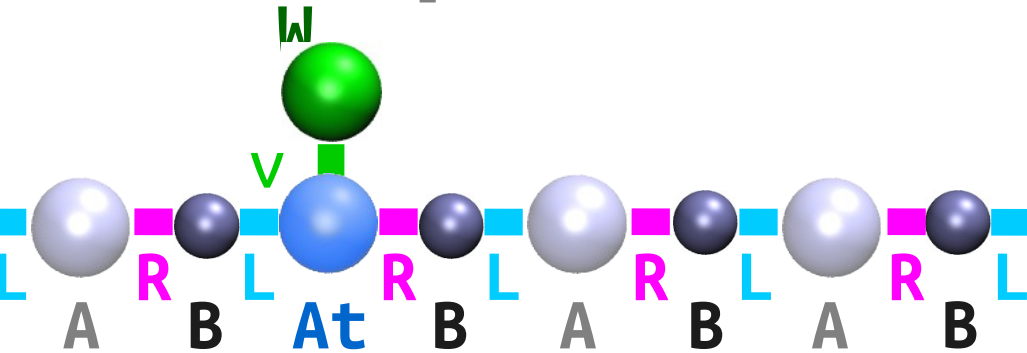


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if    atoms @atom:At @atom:B   and  bond @bond:R
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if    atoms @atom:W  @atom:AT   and   distance <= 1.5
then  atoms @atom:Wt @atom:At   and   bond @bond:V
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if    atoms @atom:Wt @atom:A   and   bond @bond:V
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```
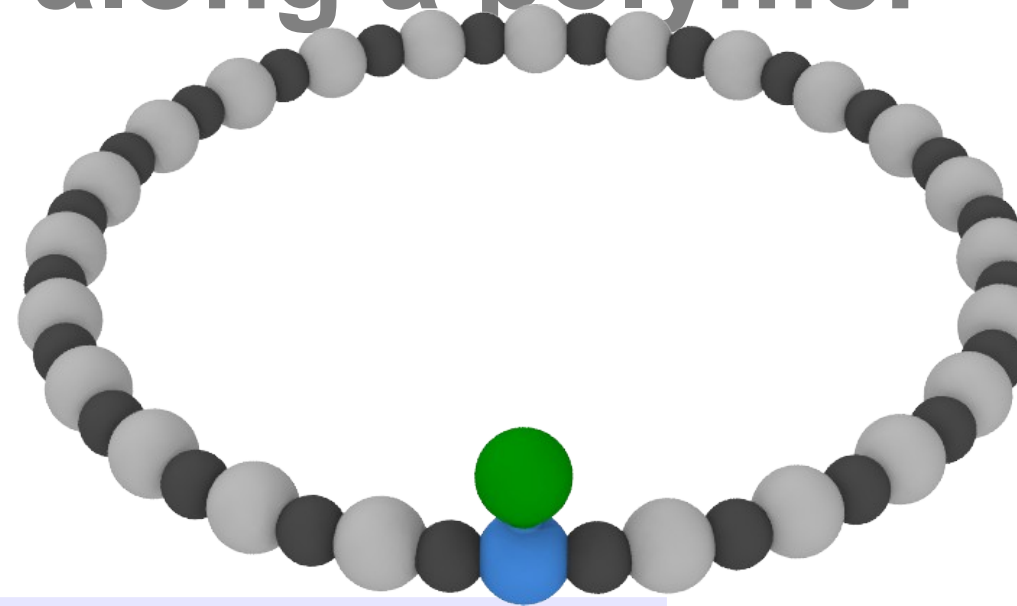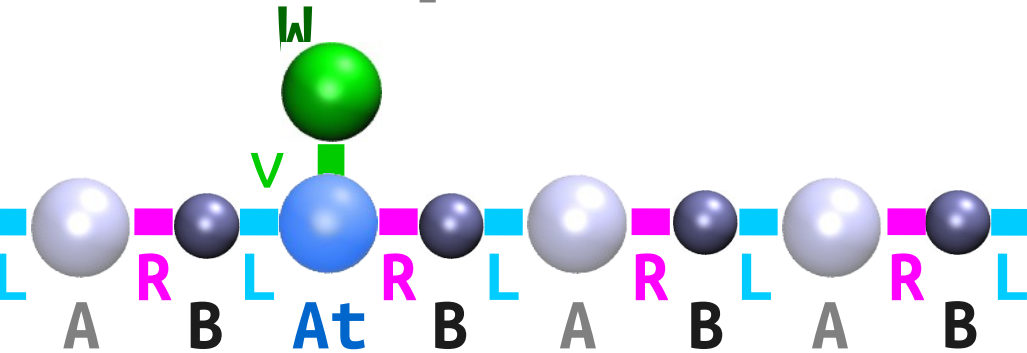
*Note: Syntax may change in the future...*

# Example: Walking along a polymer



```
if    atoms @atom:At @atom:B    and   bond @bond:R
      and   prob 0.2
then  atoms @atom:A   @atom:Bt

if    atoms @atom:Bt @atom:A    a
then  atoms @atom:B   @atom:AT

if    atoms @atom:W   @atom:AT   a
then  atoms @atom:Wt @atom:At   a
      and angle @angle:Ra   @atom

if    atoms @atom:Wt @atom:A    a
then  atoms @atom:W   @atom:A    a
```
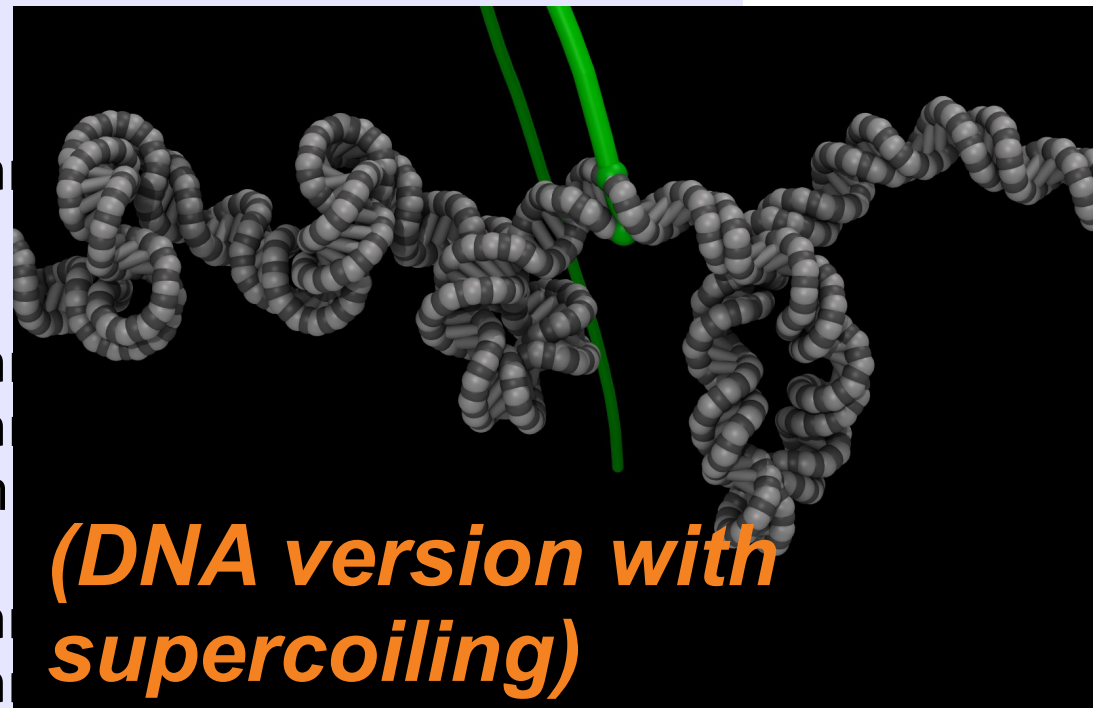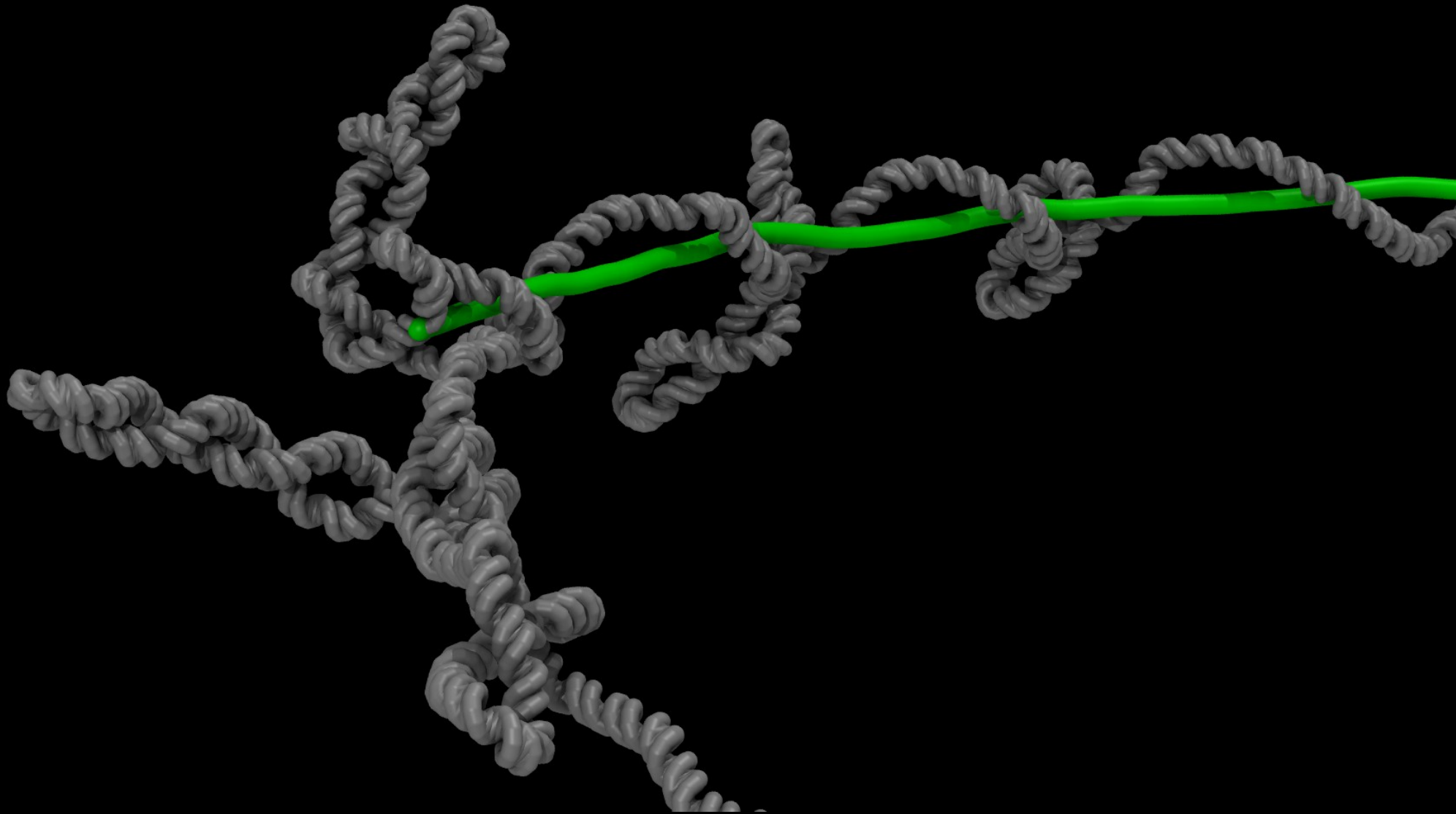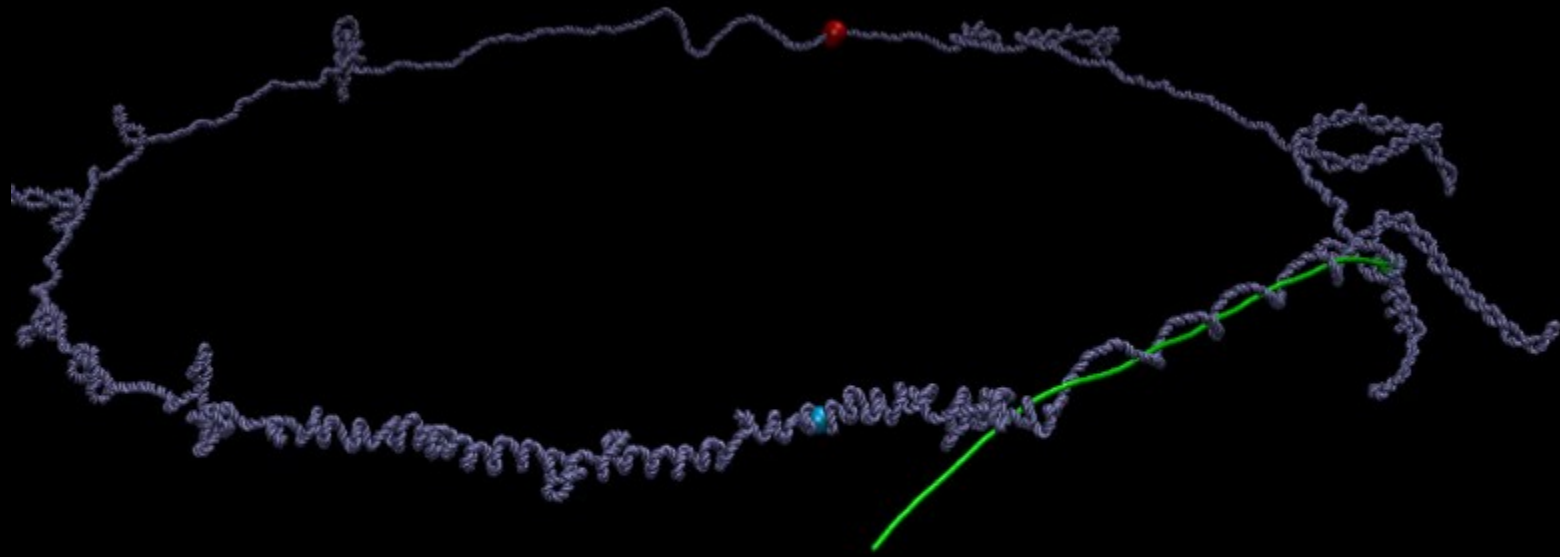
*(DNA version with supercoiling)*

# Example: DNA supercoiling during transcription

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**Example: DNA supercoiling during transcription**
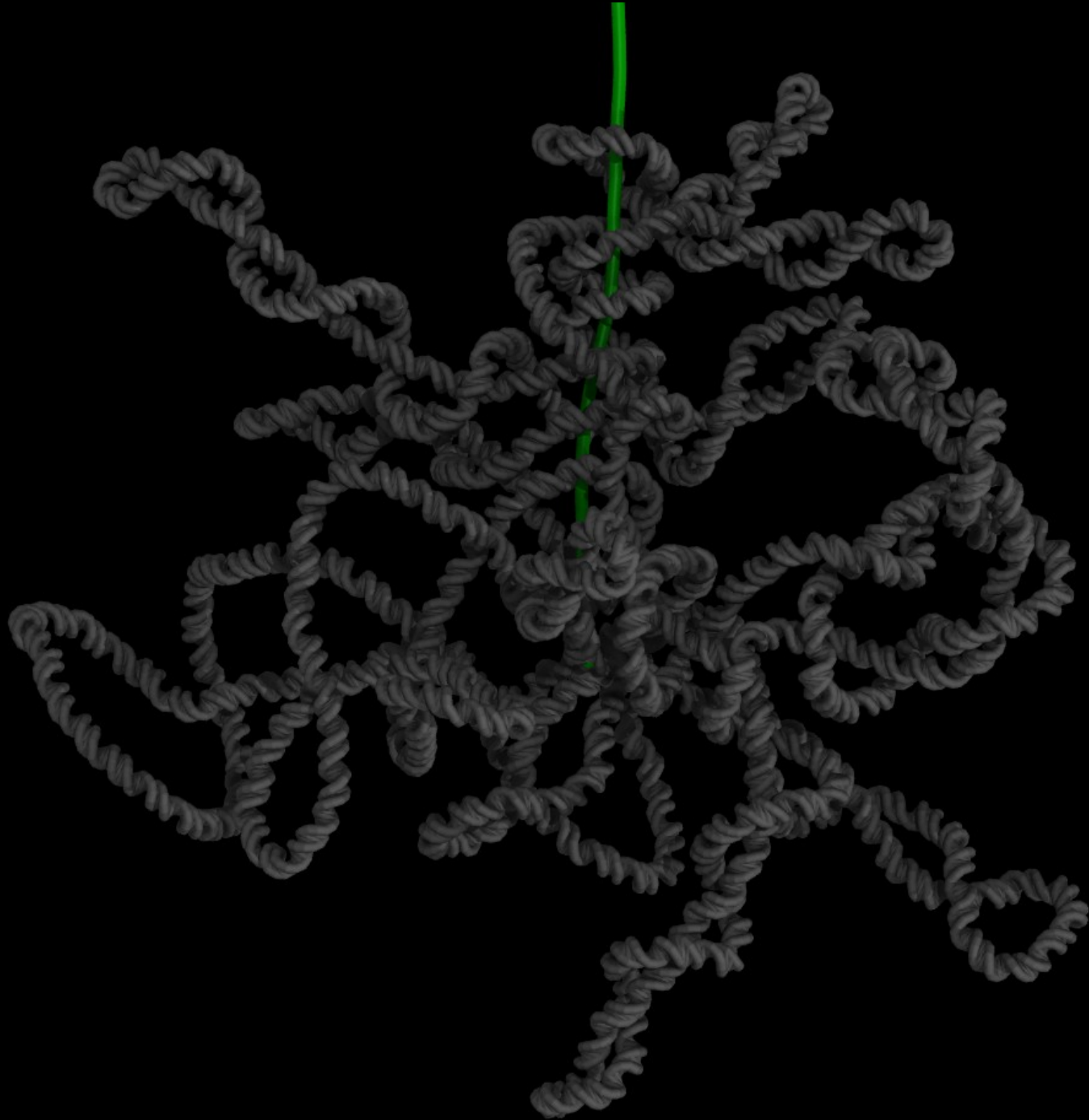
# Example: Loop Extrusion and Genome Folding
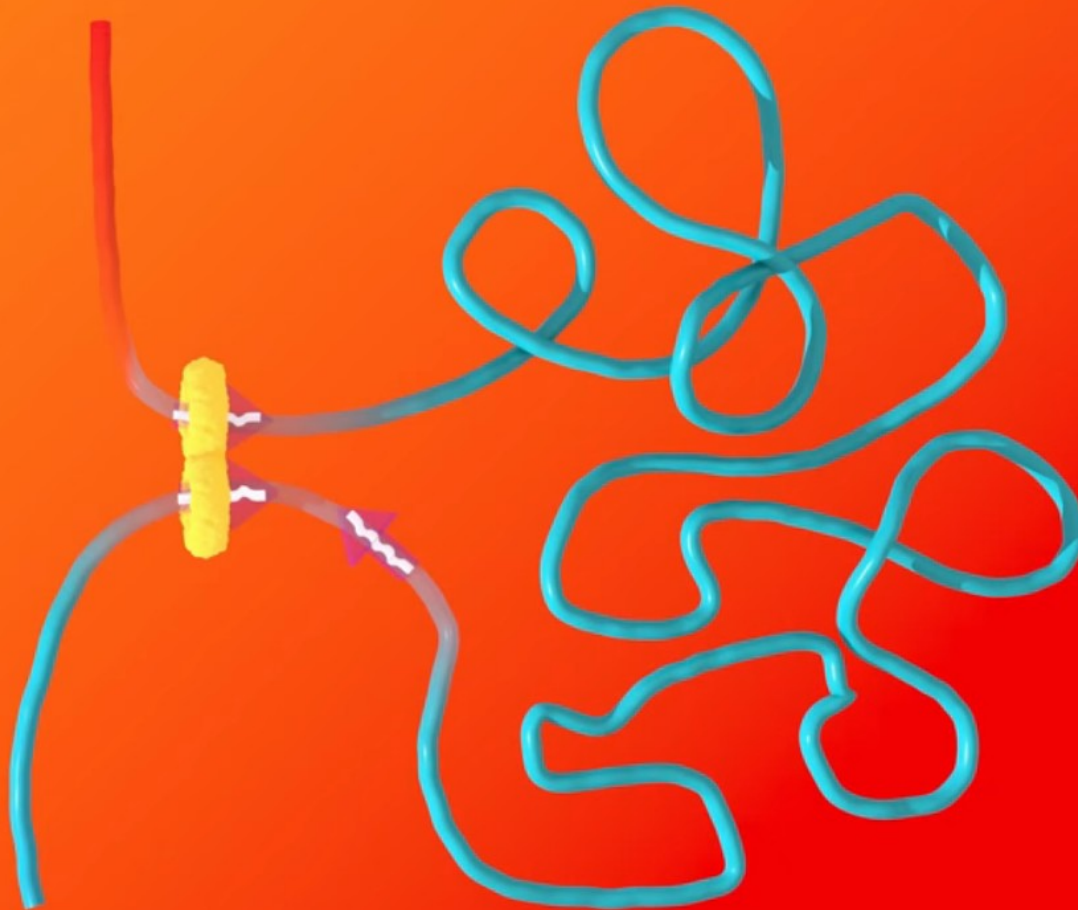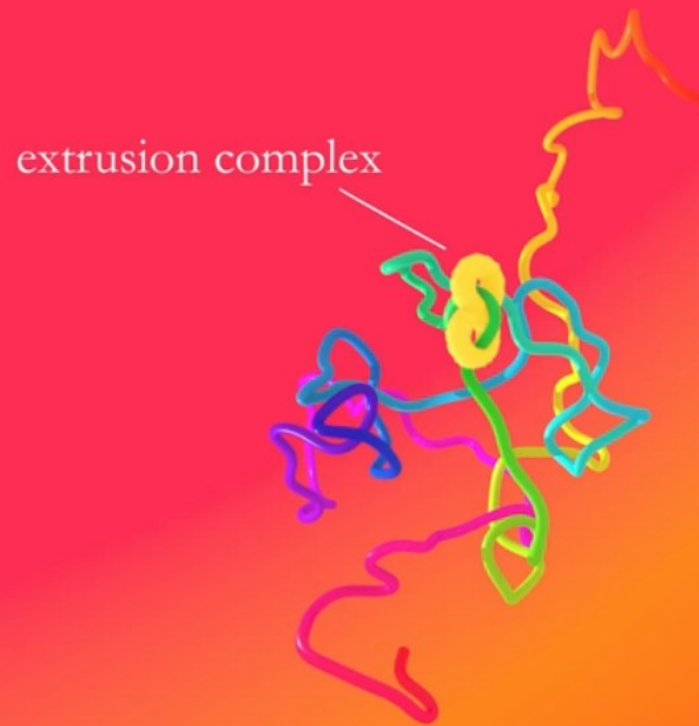
**Example: Loop Extrusion and Genome Folding**

# Example: Loop Extrusion and Genome Folding



How does DNA fold? The loop extrusion model
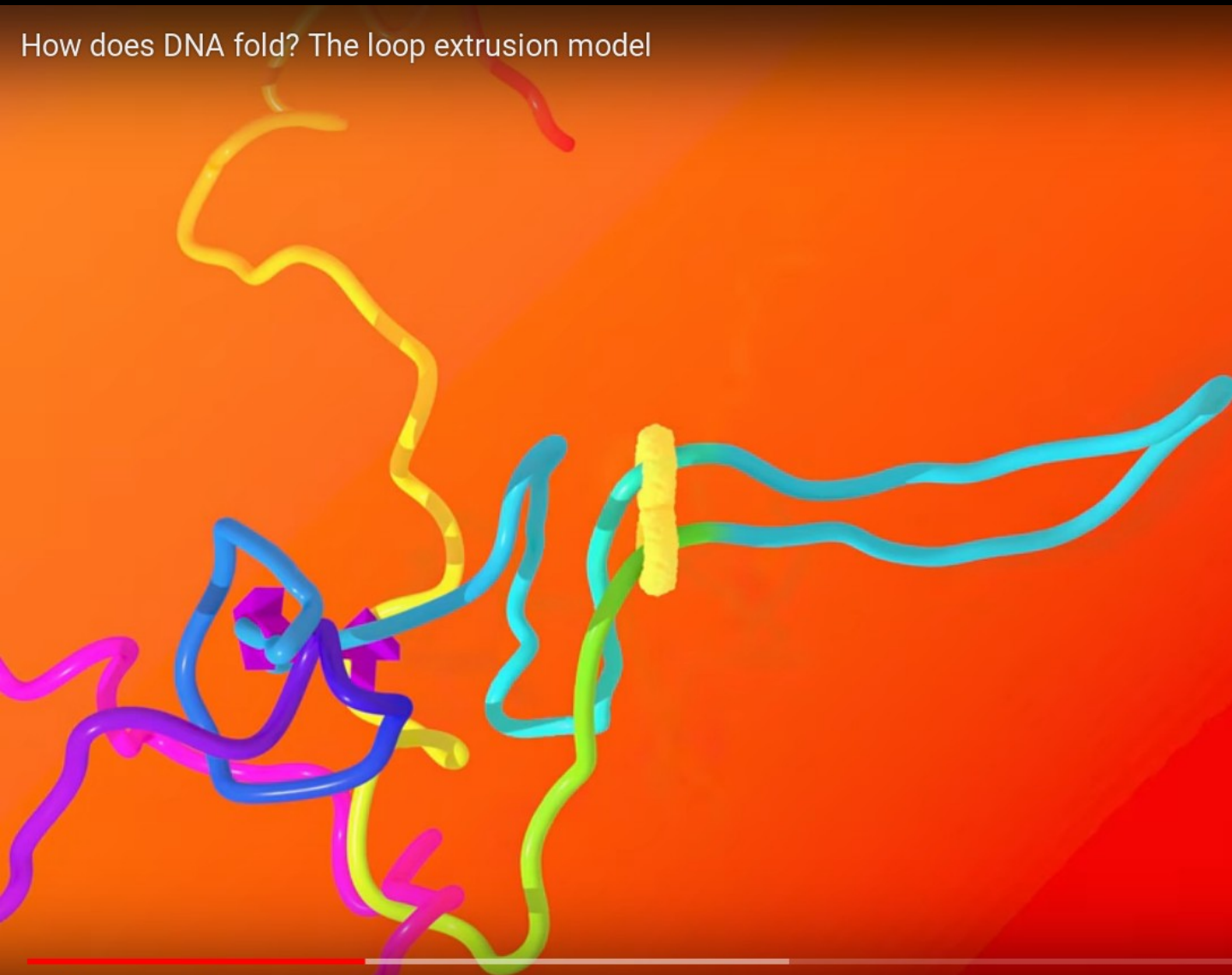
0:37 / 3:16

# Example: Loop Extrusion and Genome Folding



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0:39 / 3:16

How does DNA fold? The loop extrusion model
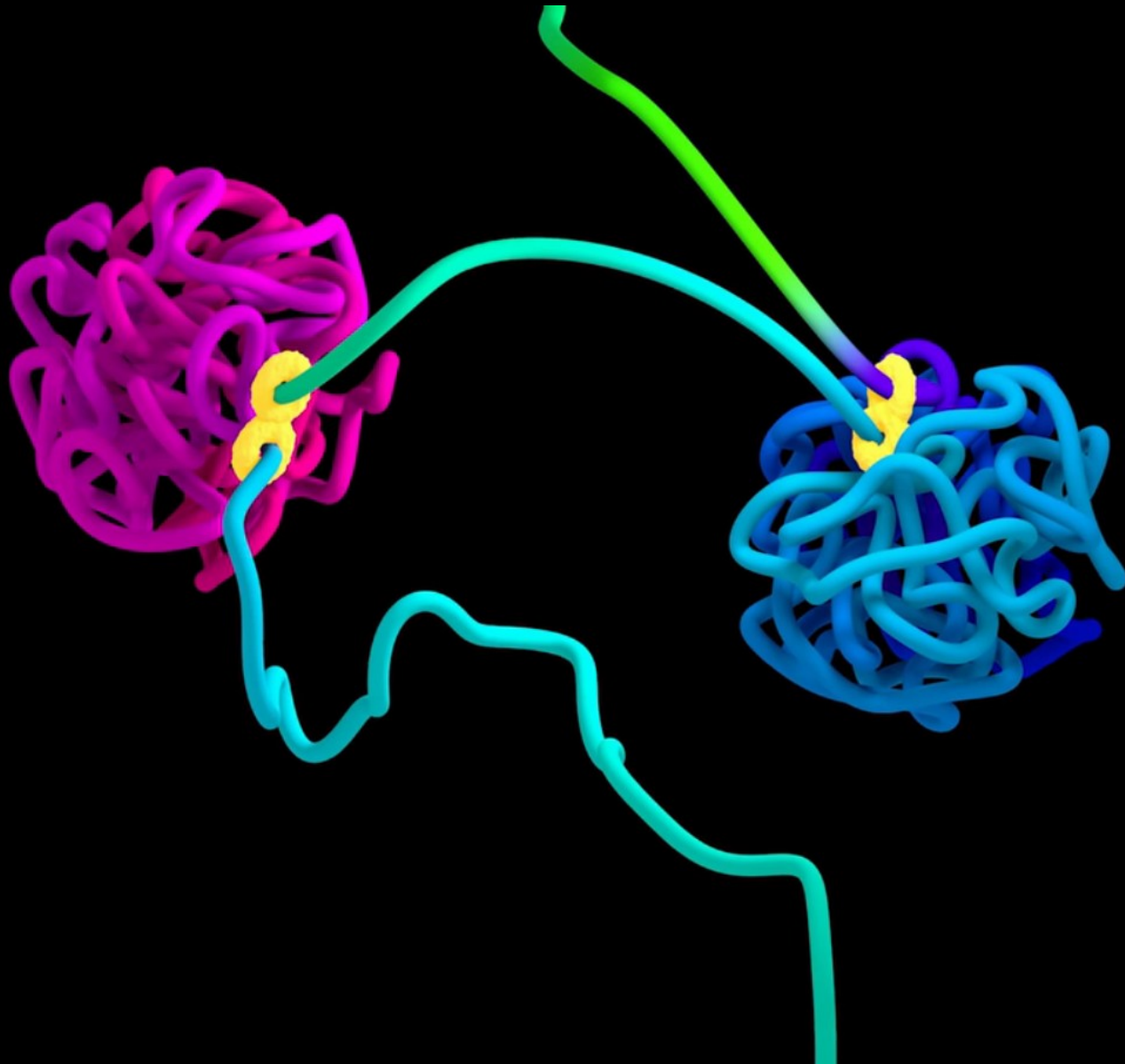
# Example: Loop Extrusion and Genome Folding

Chromatin extrusion explains
key features of loop and domain formation
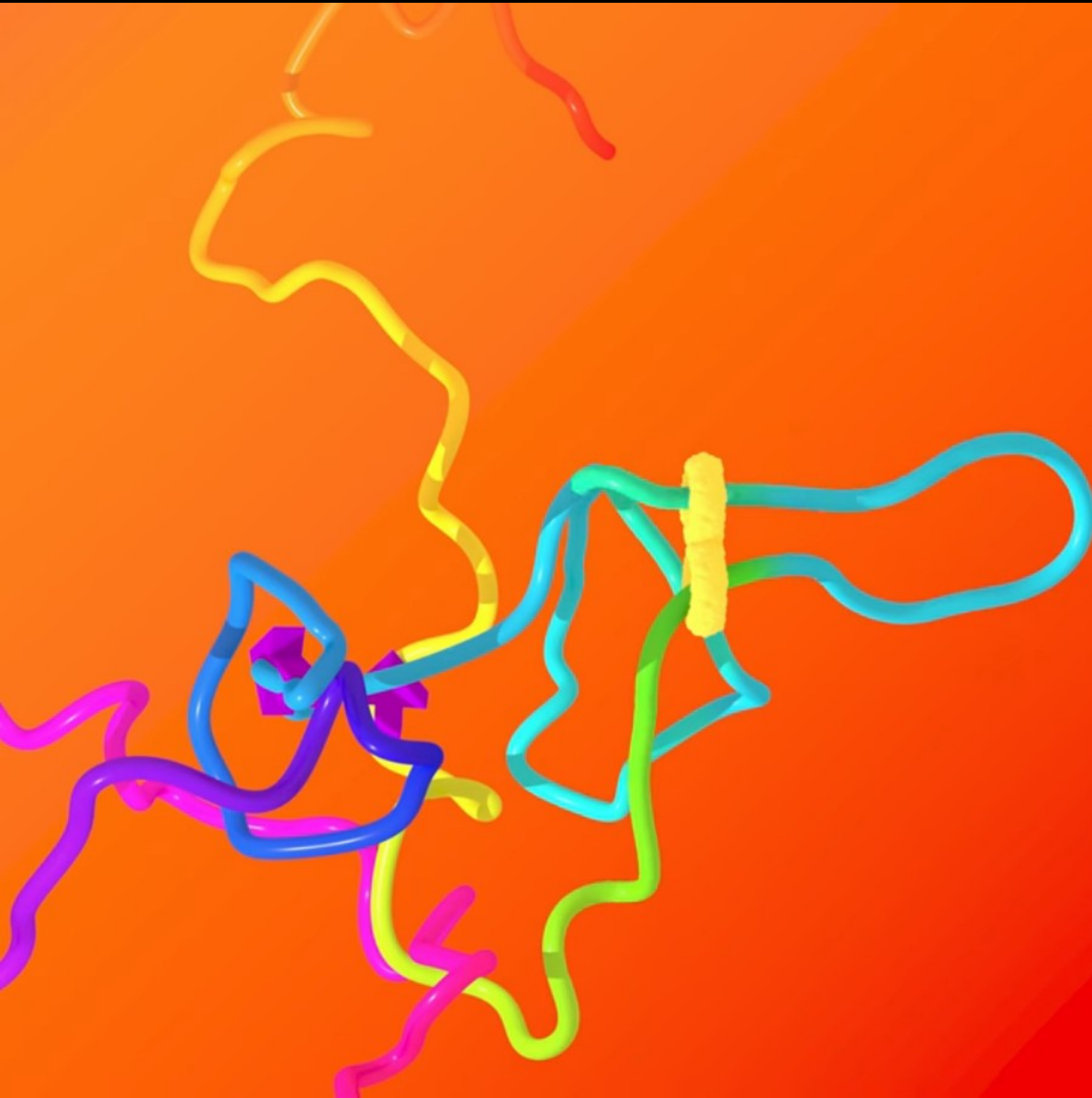in wild-type and engineered genomes

Adrian L. Sanborn*, Suhas S. P. Rao*, Su-Chen Huang, Neva C. Durand,
Miriam H. Huntley, Andrew I. Jewett, Ivan D. Bochkov, Dharmaraj Chinnappan,
Ashok Cutkosky, Jian Li, Kristopher P. Geeting, Andreas Gnirke, Alexandre Melnikov,
Doug McKenna, Elena K. Stamenova, Eric S. Lander, Erez Lieberman Aiden
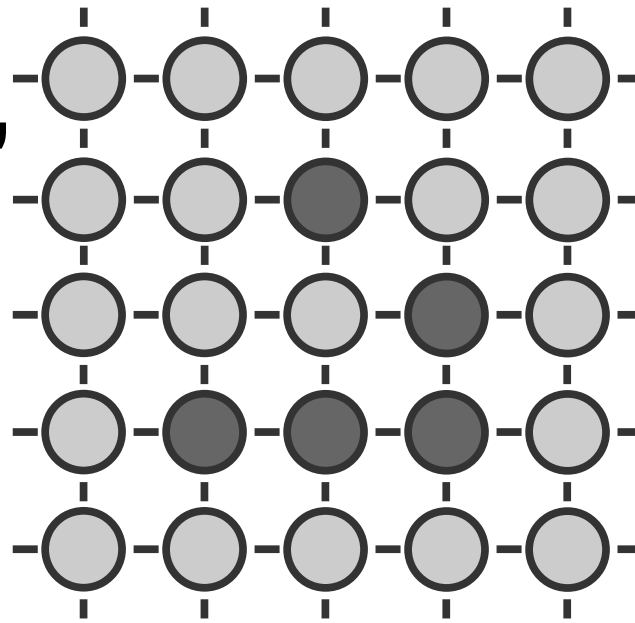
- MCA can simulate "Cellular Automata"

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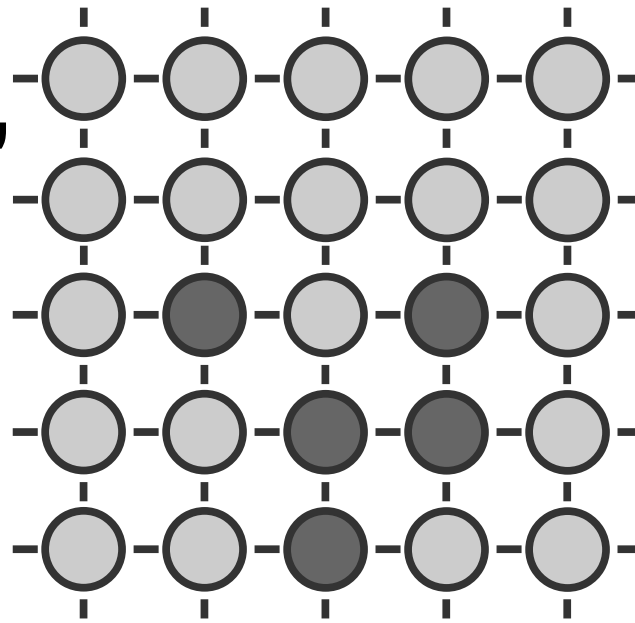
# Definition: cellular automaton

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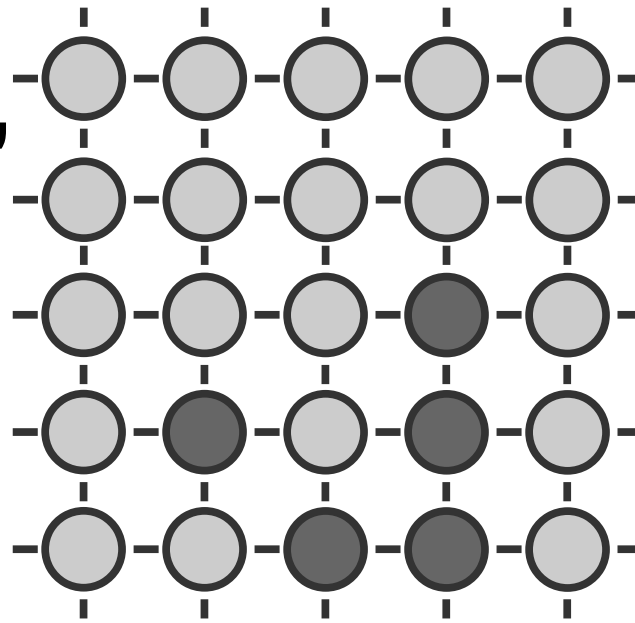
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- Cellular Automata can simulate Turing Machines

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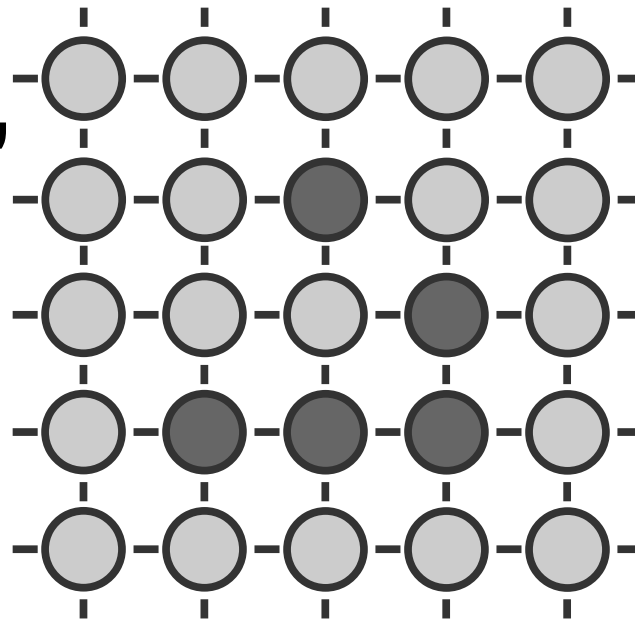
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Example: Conway's Game of Life

# Conway's Game of Life



1) Any live cell with fewer than two live neighbours dies (underpopulation)
2) Any live cell with two or three live neighbours lives
3) Any live cell with more than three live neighbours dies (overpopulation)
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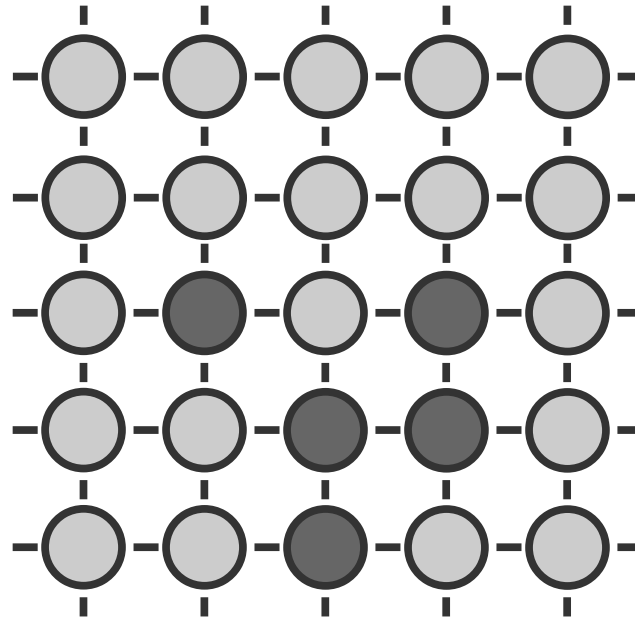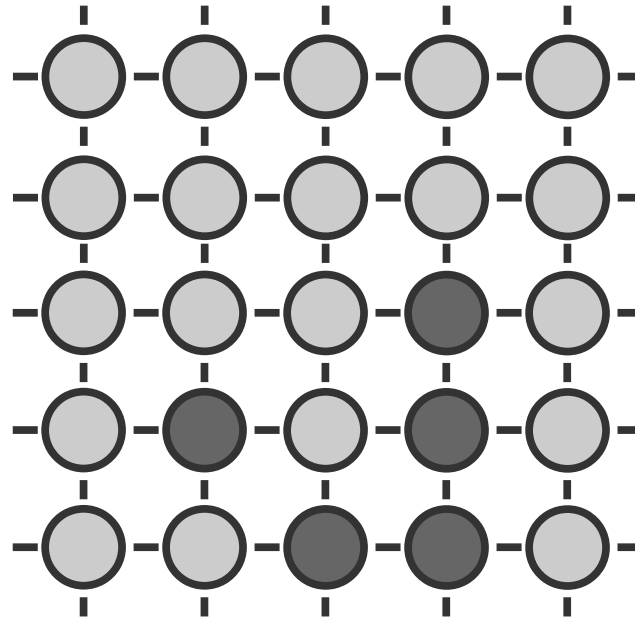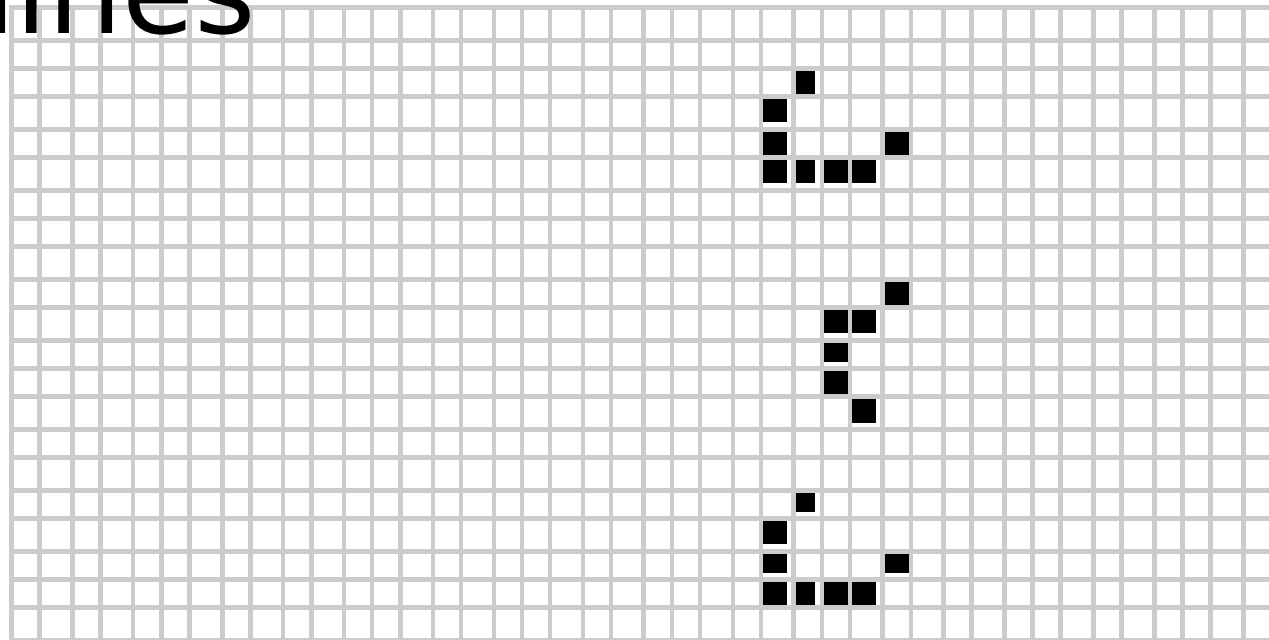# Cellular Automata can simulate Turing Machines

# Conways Game of Life in LAMMPS

```
if   atoms @atom:C0  @atom:Live and bond @bond:NeighborUnread
then atoms @atom:C1  @atom:Dead and bond @bond:NeighborRead

if   atoms @atom:C1  @atom:Live and bond @bond:NeighborUnread
then atoms @atom:C2  @atom:Dead and bond @bond:NeighborRead

if   atoms @atom:C2  @atom:Live and bond @bond:NeighborUnread
then atoms @atom:C3  @atom:Dead and bond @bond:NeighborRead

if   atoms @atom:C3  @atom:Live and bond @bond:NeighborUnread
then atoms @atom:C4  @atom:Dead and bond @bond:NeighborRead


if   bond @bond:NeighborRead
then bond @bond:NeighborUnread

if   atoms @atom:Live @{atom:C0}*@{atom:C1}  and  bond @bond:SendTotal
then atoms @atom:Dead SAME

#   Overpopulation:  Any live cell with 4 living neighbors dies
if   atoms @atom:Live @atom:C4  and  bond @bond:SendTotal
then atoms @atom:Dead SAME

#   Birth:          Any dead cell with exactly 3 living neighbors lives
if   atoms @atom:Dead @atom:C3 and  bond @bond:SendTotal
then atoms @atom:Live SAME

#   Reset counters:
if   atom *
then atom @atom:C0
```
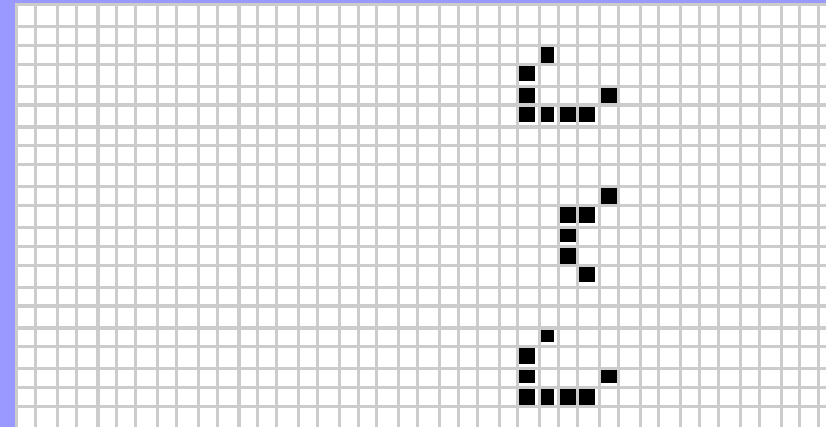
*Note: Syntax may change in the future...*

# Universality of cellular automaton

1) LAMMPS (now) can simulate cellular automata.

2) Cellular automata (such as Conway's game of life), can be used to simulate a (universal) Turing machine

3) A Turing machine can simulate anything going on in a living cell (ignoring quantum mechanics).

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→ LAMMPS can now simulate the machinery of life.

(...Moreover, it typically only takes a few of these LAMMPS commands to simulate processes in the cell that biologist care about. *See earlier examples.*)

# Comparison with *fix bond/react*

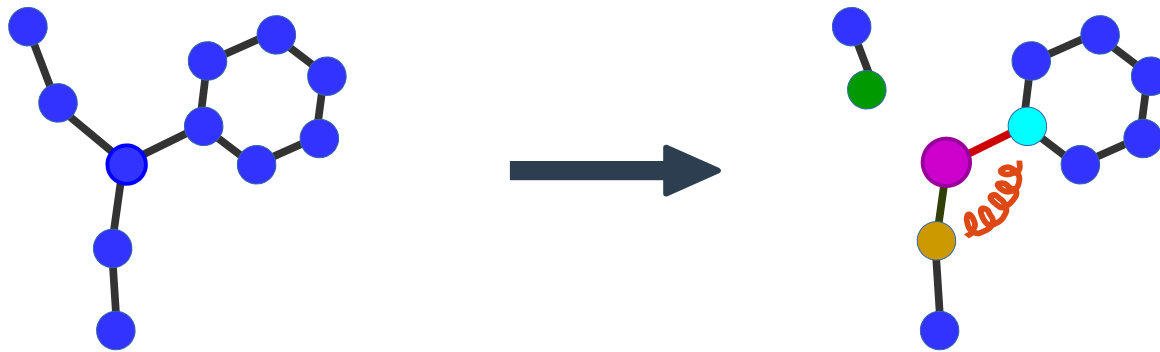| *fix bond/react* | *fix bond/modify* |
|---|---|
| consider atoms an arbitrary number of bonds from the central atom | considers only atoms directly bonded to the central atom |
| can modify **multiple bonds** in a single reaction step | can modify **only one bond** at a time |
| requires creating separate molecule **template files** for each reaction step. | Each step is a **single line command**. |
| applies optional **relaxation** (minimization) to nearby atoms for numeric stability | *This feature is currently planned.* |
| does not (yet) consider bond types. *(Easy feature to add.)* | considers bonded types as well as atom types when deciding. |

**Both are equivalent. Both are Turing-complete.**
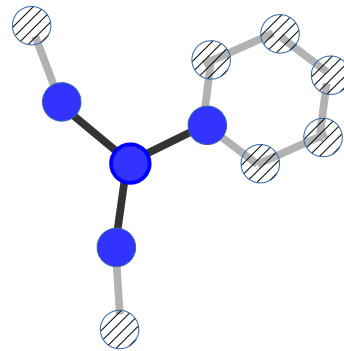
# Comparison: *fix bond/react*



This is a single step using fix bond/react

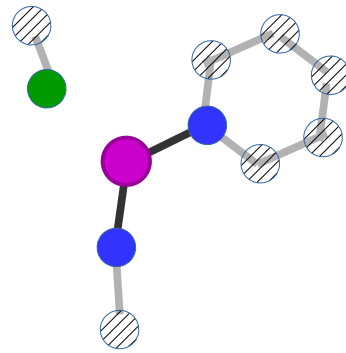(fix bond/modify requires 3 steps to modify 3 bonds)

# Comparison: *fix bond/modify*

*(Multiple steps are required with fix bond/modify to accomplish the same thing)*
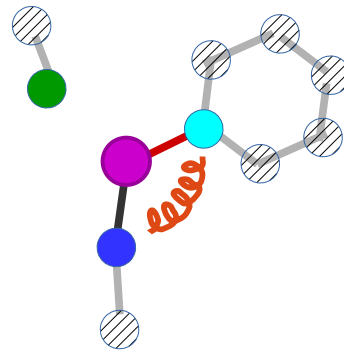
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