YASARA - Yet Another Scientific Artificial Reality Application

File Edit Simulation Analyze View Effects Options Window Help

ATOM PROPERTIES

```
Number:
Name:
Element:
Occupancy:    % BFactor:
Residue:
Object:

Position: X = 000000.00000 Å
          Y = 000000.00000 Å
          Z = 000000.00000 Å

Speed: X = 0000000000 m/s
       Y = 0000000000 m/s
       Z = 0000000000 m/s
   Total = 0000000000 m/s

Active X = 0000000000 fN
Forces:Y = 0000000000 fN
       Z = 0000000000 fN
   Total = 0000000000 fN

Bonds:
1) Type   to ----(---------)
   Length --.--- Å
2) Type   to ----(---------)
   Length --.--- Å
3) Type   to ----(---------)
   Length --.--- Å
4) Type   to ----(---------)
   Length --.--- Å

Marked Distance: -----.--- Å
Marked Angle:    -----.--- o
Marked Dihedral: -----.--- o
```

SCENE CONTENT

Obj	Name	Vis	Act	Atom
1	----------	No	No	------
2	----------	No	No	------
3	----------	No	No	------
4	----------	No	No	------
5	----------	No	No	------
6	----------	No	No	------
7	----------	No	No	------
8	----------	No	No	------
9	----------	No	No	------
10	----------	No	No	------

Molecular Dynamics Simulations in YASARA Software

Jhelaine Palo
Eduard Bitto Ph.D.

60 Hz | Mem100 | Sys L | YASARA Structure | Sim Off | Obj all | 0 Atoms

What is Molecular Dynamics (MD)

Introduction

Simplified schematic of the molecular dynamics algorithm

Give atoms initial $\boldsymbol{r}^{(i=0)}$ and $\boldsymbol{v}^{(i=0)}$, set $\boldsymbol{a} = 0.0$, $t = 0.0$, $i = 0$, choose short Δt

↓

Predictor stage: predict next atom positions:
Move atoms: $\boldsymbol{r}^{p} = \boldsymbol{r}^{(i)} + \boldsymbol{v}^{(i)}\,\Delta t + {}^{1}/_{2}\,\boldsymbol{a}\,\Delta\, t^{2}$ + more accurate terms
Update velocities: $\boldsymbol{v}^{p} = \boldsymbol{v}^{(i)} + \boldsymbol{a}\,\Delta t$ + more accurate terms

↓

Get forces $\boldsymbol{F} = -\nabla V(\boldsymbol{r}^{p})$ or $\boldsymbol{F} = \boldsymbol{F}(\Psi(\boldsymbol{r}^{p}))$ and $\boldsymbol{a} = \boldsymbol{F}/m$

↓

Corrector stage: adjust atom positions based on new $\boldsymbol{a}$:
Move atoms: $\boldsymbol{r}^{(i+1)} = \boldsymbol{r}^{p}$ + *some function of* $(\boldsymbol{a}, \Delta t)$
Update velocities: $\boldsymbol{v}^{(i+1)} = \boldsymbol{v}^{p}$ + *some function of* $(\boldsymbol{a}, \Delta t)$

↓

Apply boundary conditions, temperature and pressure control as needed

↓

Calculate and output physical quantities of interest

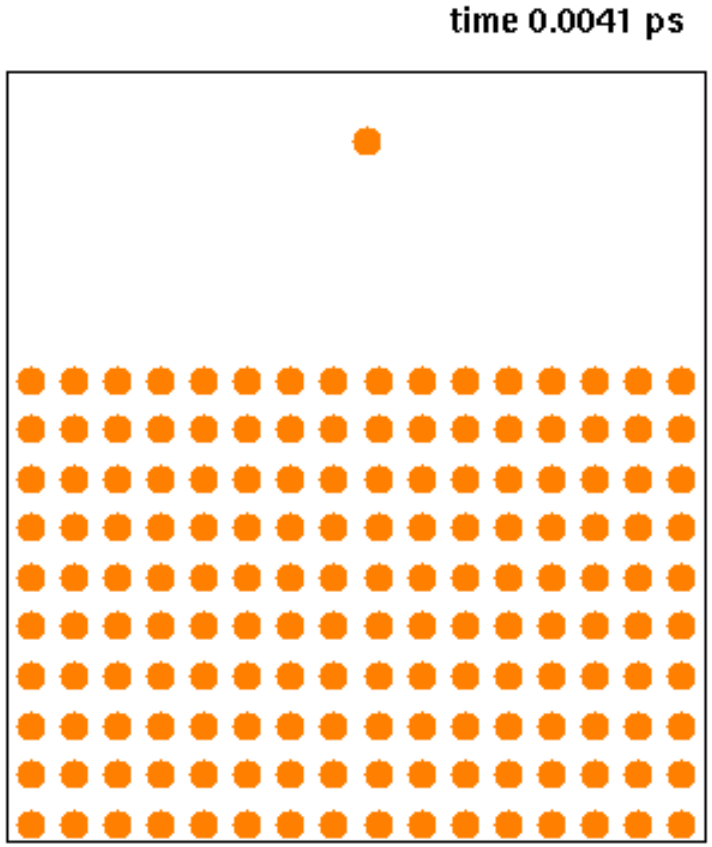
↓

Move time and iteration step forward: $t = t + \Delta t$, $i = i + 1$

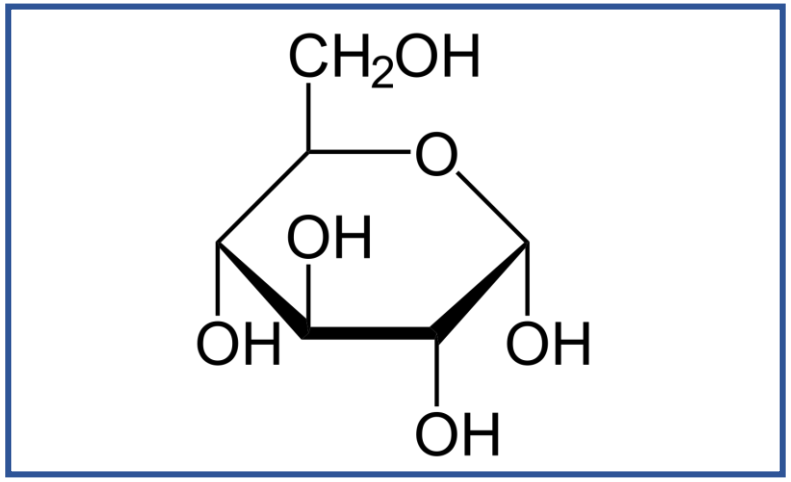
↓

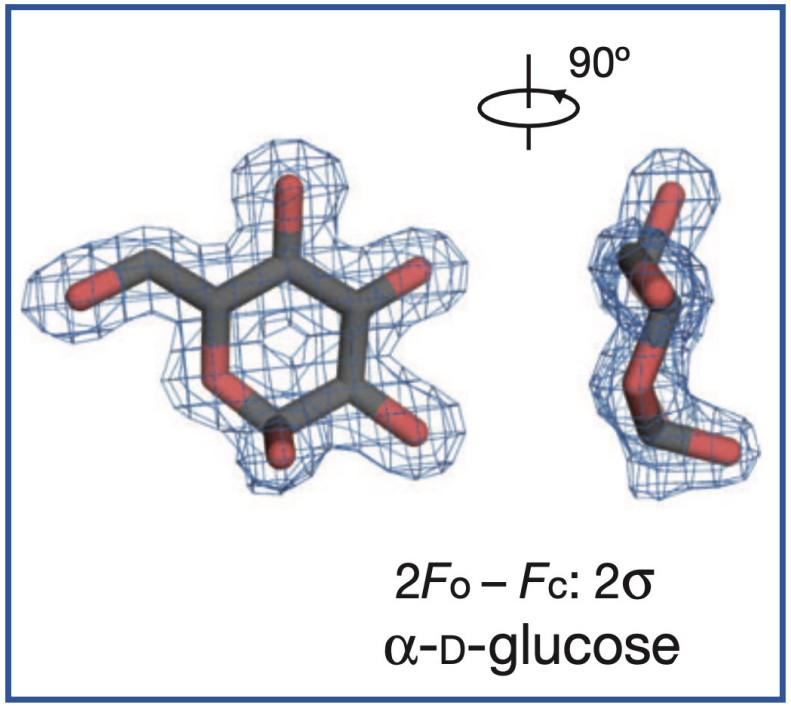
Repeat as long as you need

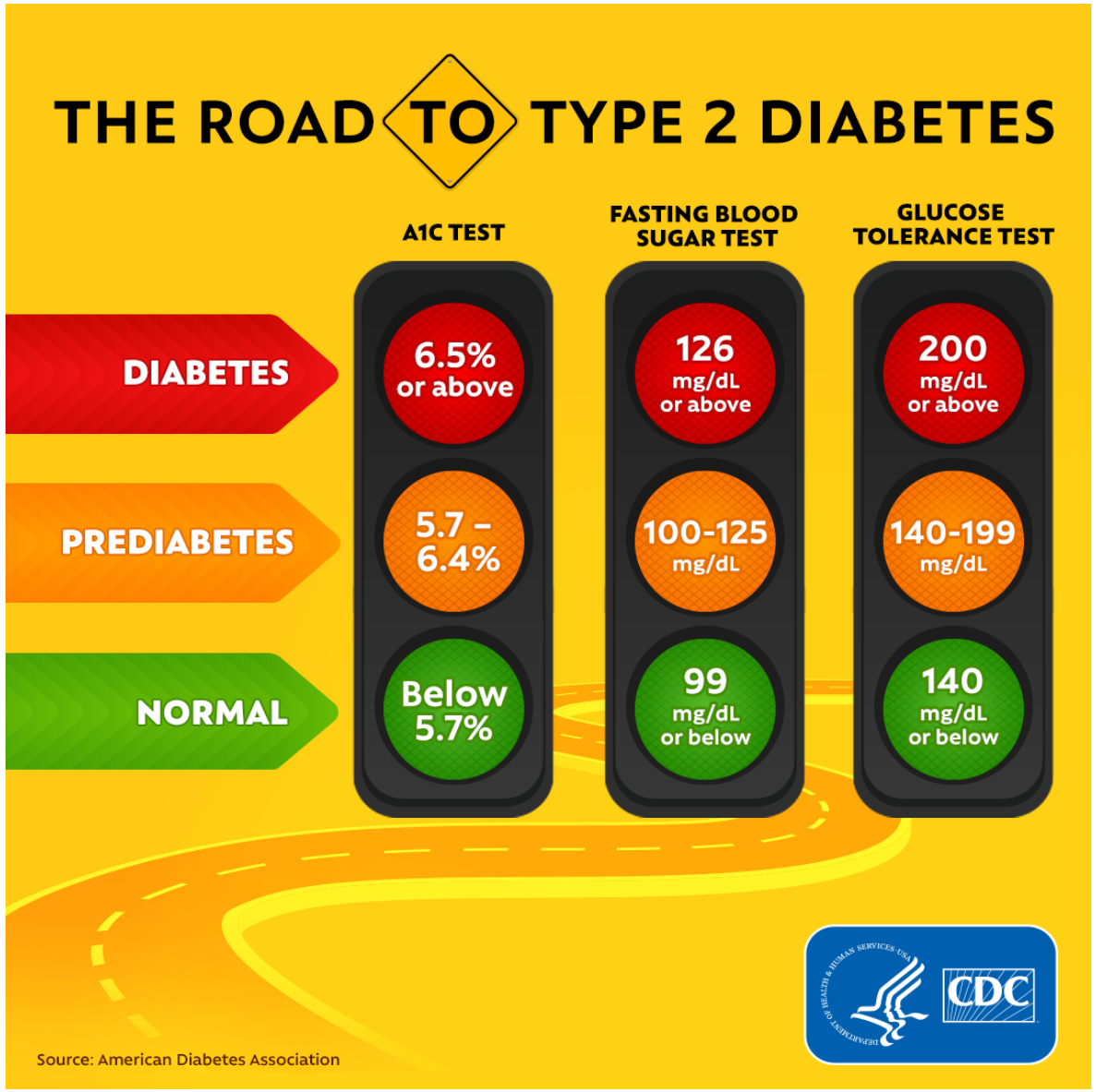
It is a computer simulation technique that uses Newton's equations of motion to solve molecular system mechanics in an electrostatic force field (Meller 2001)



Relevance


CH2OH
O
OH
OH
OH
OH


90°
2Fo – Fc: 2σ
α-D-glucose


THE ROAD TO TYPE 2 DIABETES
A1C TEST
FASTING BLOOD SUGAR TEST
GLUCOSE TOLERANCE TEST
DIABETES
PREDIABETES
NORMAL
6.5% or above
5.7 – 6.4%
Below 5.7%
126 mg/dL or above
100-125 mg/dL
99 mg/dL or below
200 mg/dL or above
140-199 mg/dL
140 mg/dL or below
Source: American Diabetes Association
CDC

Purpose

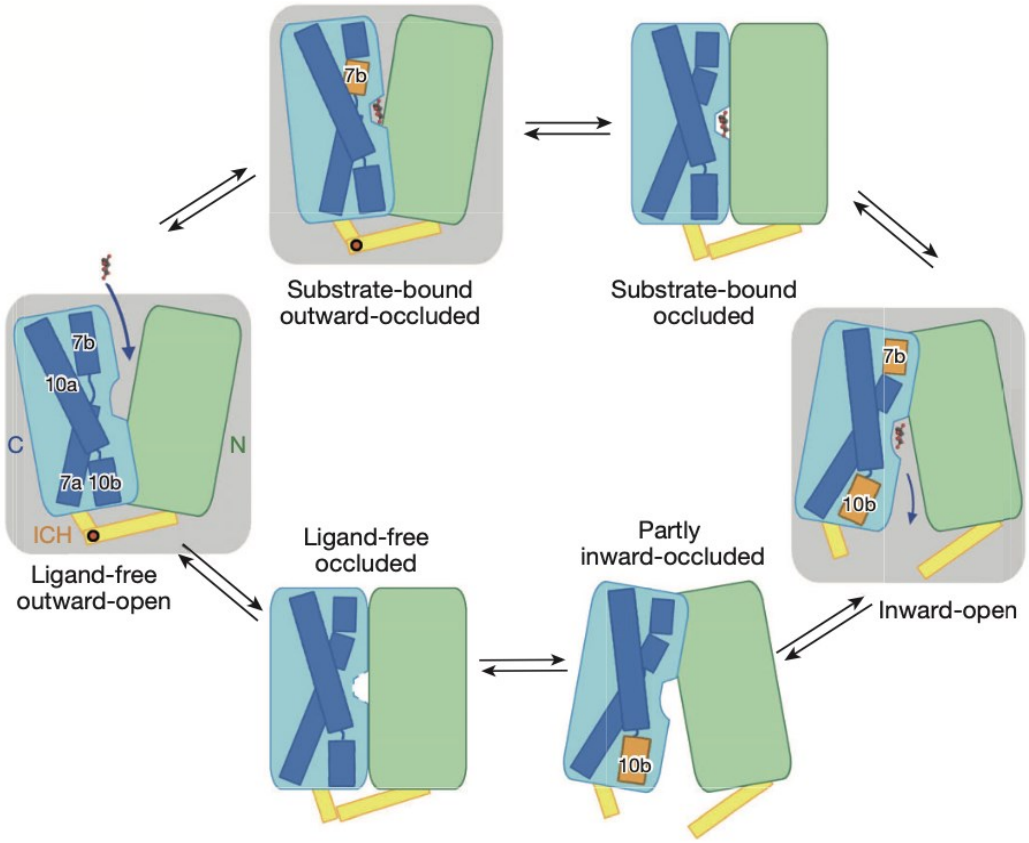
ARTICLE

doi:10.1038/nature14655

Molecular basis of ligand recognition and transport by glucose transporters

Dong Deng[1,2,3]*, Pengcheng Sun[1,2,3]*, Chuangye Yan[1,2,3], Meng Ke[1,2,3], Xin Jiang[1,2], Lei Xiong[3], Wenlin Ren[1,2], Kunio Hirata[4,5], Masaki Yamamoto[4], Shilong Fan[2] & Nieng Yan[1,2,3]

The major facilitator superfamily glucose transporters, exemplified by human GLUT1–4, have been central to the study of solute transport. Using lipidic cubic phase crystallization and microfocus X-ray diffraction, we determined the structure of human GLUT3 in complex with D-glucose at 1.5 Å resolution in an outward-occluded conformation. The high-resolution structure allows discrimination of both α- and β-anomers of D-glucose. Two additional structures of GLUT3 bound to the exofacial inhibitor maltose were obtained at 2.6 Å in the outward-open and 2.4 Å in the outward-occluded states. In all three structures, the ligands are predominantly coordinated by polar residues from the carboxy terminal domain. Conformational transition from outward-open to outward-occluded entails a prominent local rearrangement of the extracellular part of transmembrane segment TM7. Comparison of the outward-facing GLUT3 structures with the inward-open GLUT1 provides insights into the alternating access cycle for GLUTs, whereby the C-terminal domain provides the primary substrate-binding site and the amino-terminal domain undergoes rigid-body rotation with respect to the C-terminal domain. Our studies provide an important framework for the mechanistic and kinetic understanding of GLUTs and shed light on structure-guided ligand design.



OM PROPERTIES

SCENE CONTE

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       Y = 000000.00000 Å
       Z = 000000.00000 Å

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    Y = 0000000000 m/s
    Z = 0000000000 m/s
Total = 0000000000 m/s

ive X = 0000000000 fN
ces:Y = 0000000000 fN
    Z = 0000000000 fN
Total = 0000000000 fN

ds:
Type   to ----(---------)
Length --.--- Å
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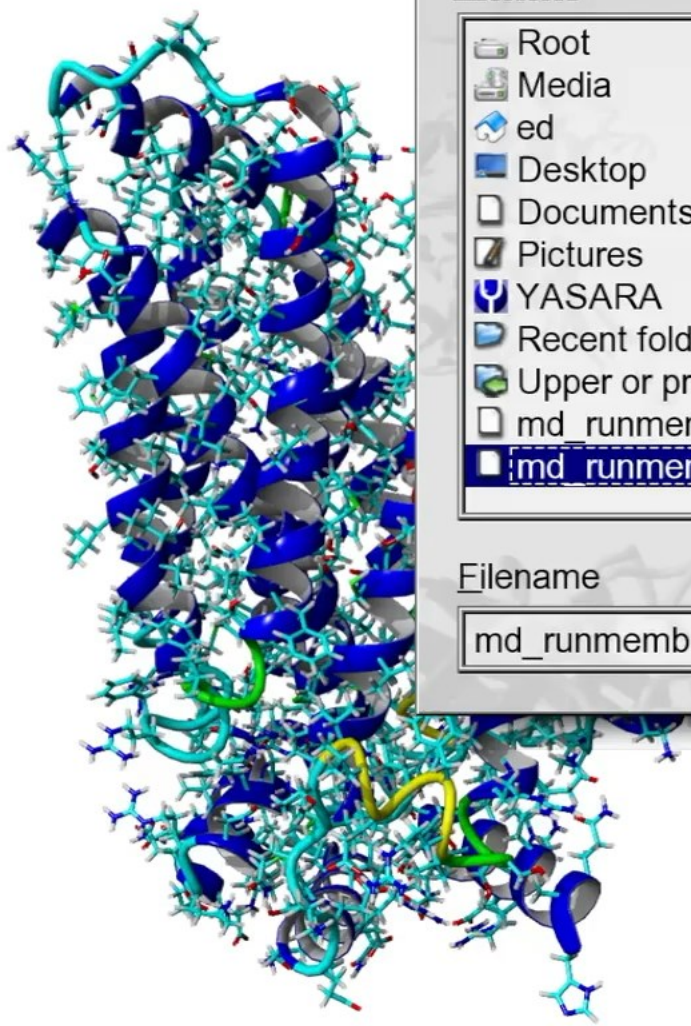
Length --.--- Å

ked Distance: -----.--- Å
ked Angle:    -----.--- o
ked Dihedral: -----.--- o
```

Obj| Name |Vis|Act| At



Select YASARA macro to play

Browse

- Root
- Media
- ed
- Desktop
- Documents
- Pictures
- YASARA
- Recent folders
- Upper or previous folder (+Ctrl)
- md_runmembrane.mcr
- md_runmembranefast.mcr

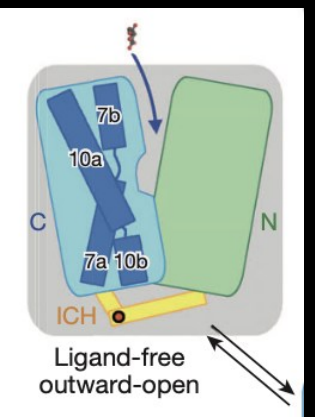
Yanaconda

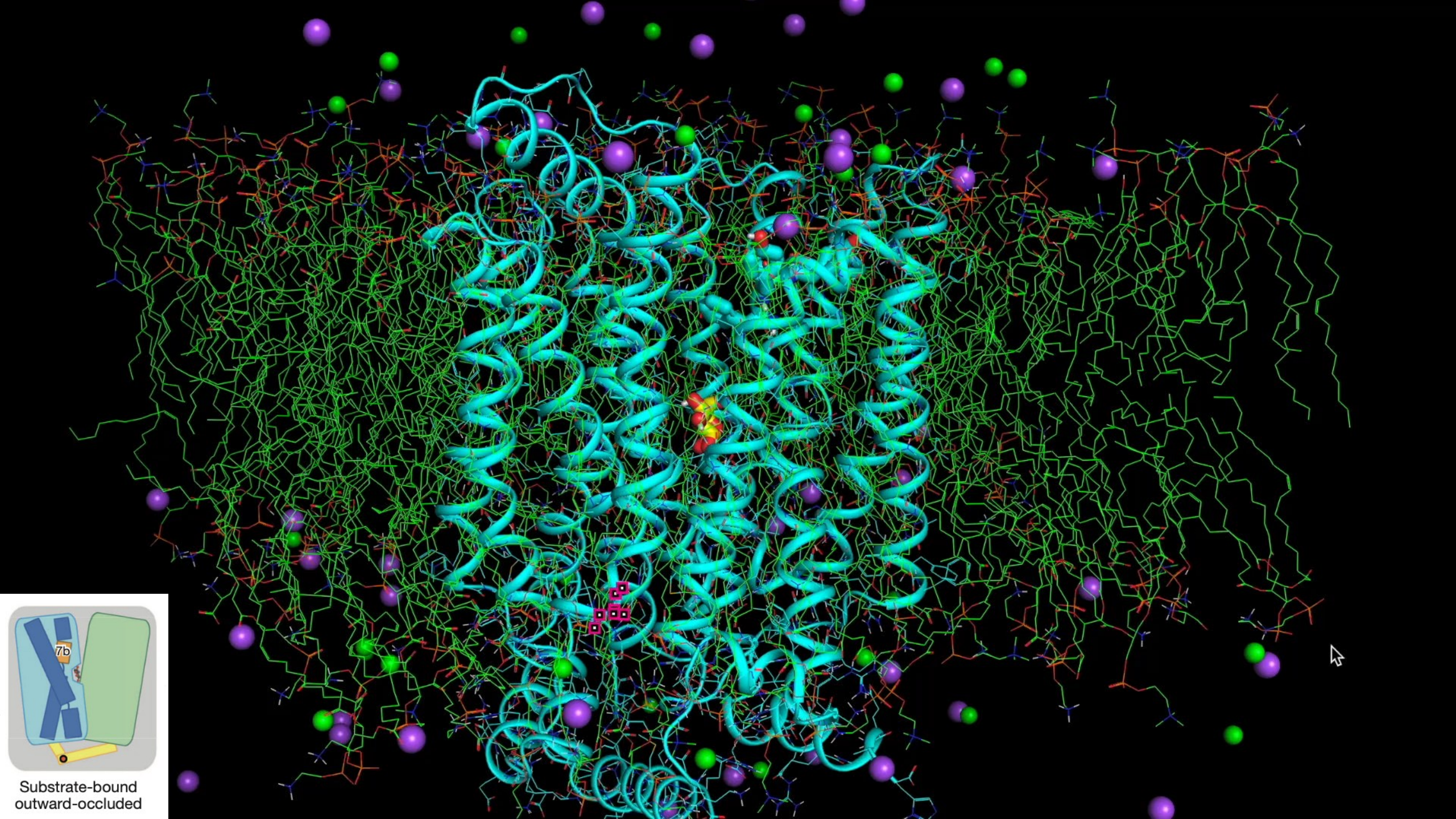
Always on startup

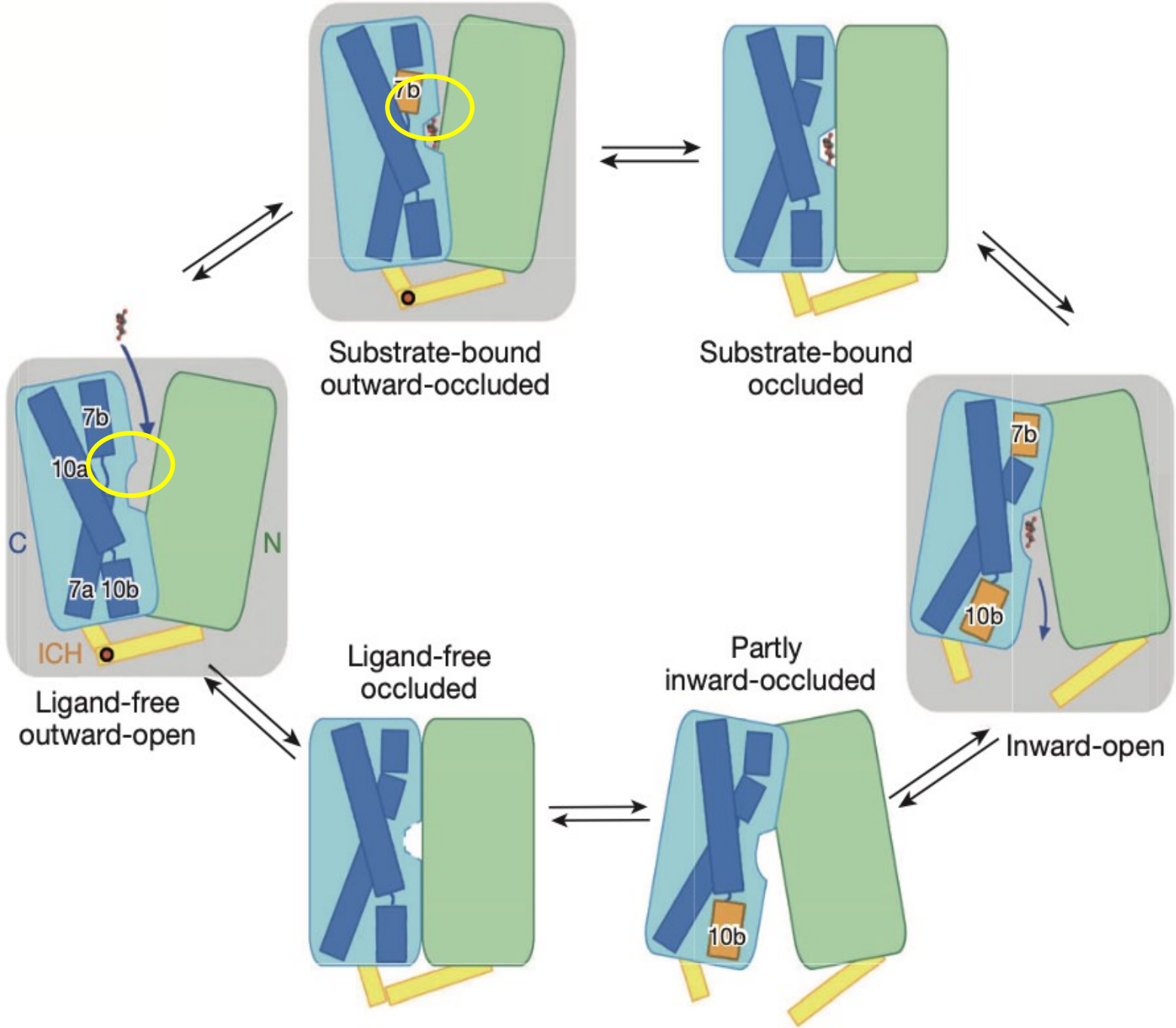
Filename

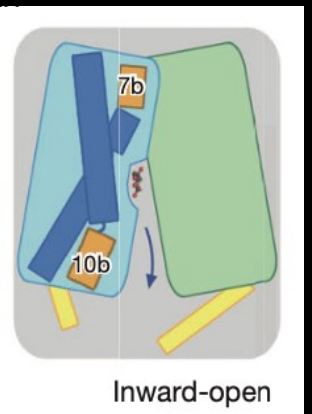
md_runmembranefast.mcr

OK

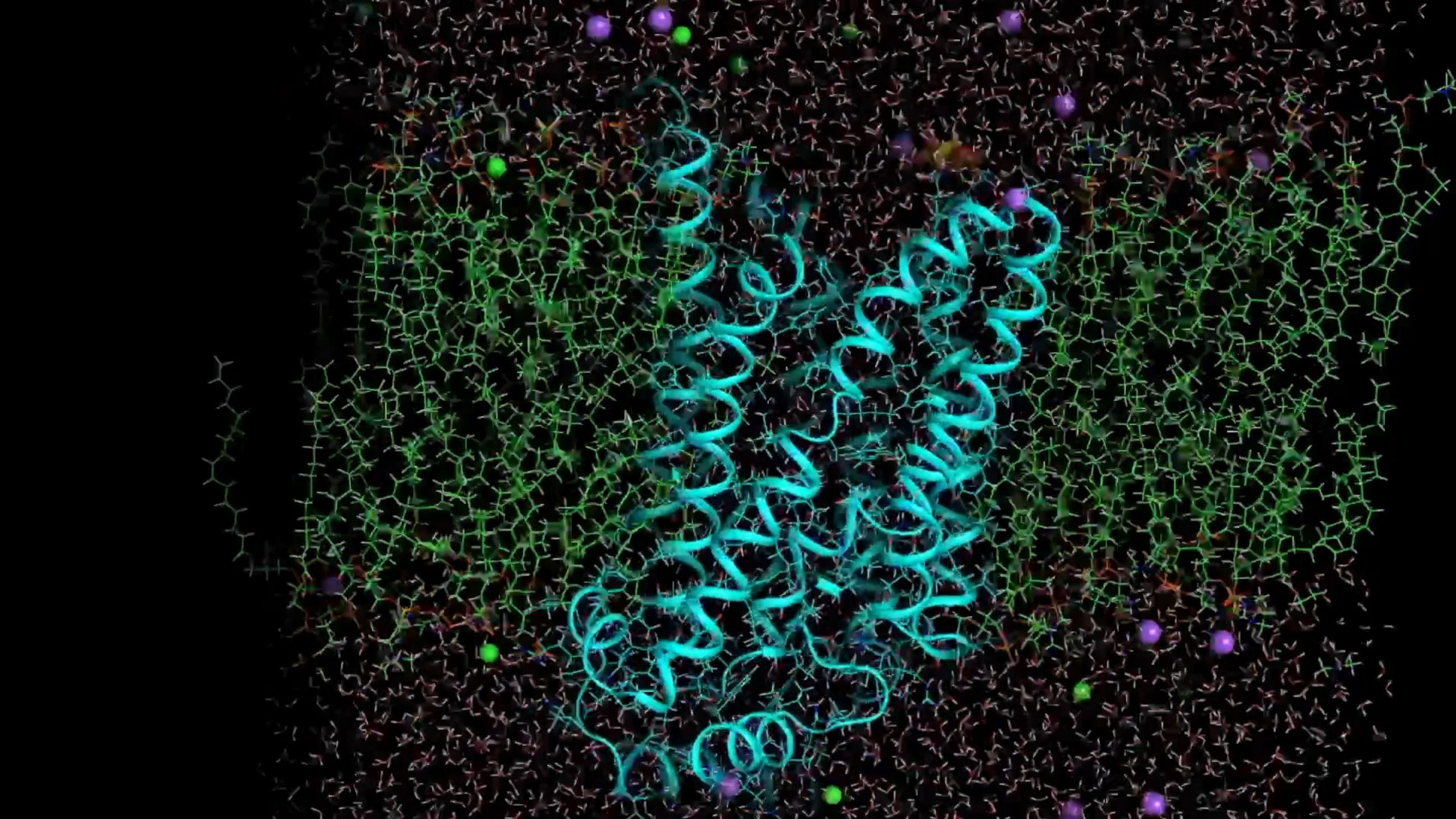

7b
10a
C
N
7a
10b
ICH
Ligand-free
outward-open


7b
Substrate-bound
outward-occluded


7b
Substrate-bound
outward-occluded
Substrate-bound
occluded
7b
10a
C
N
7a 10b
ICH
Ligand-free
outward-open
Ligand-free
occluded
Partly
inward-occluded
7b
10b
Inward-open
10b



Inward-open



Acknowledgements

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References

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Dong, D., Sun, P., Yan, C., Ke, M., Jiang, X., Xiong, L., Ren, W., Hirata, K., Yamamoto, M., Fan, S., Yan, N. (2015). Molecular basis of ligand recognition and transport by glucose transporters. *Nature*, 521(391-396). https://doi.org/10.1038/nature14655

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