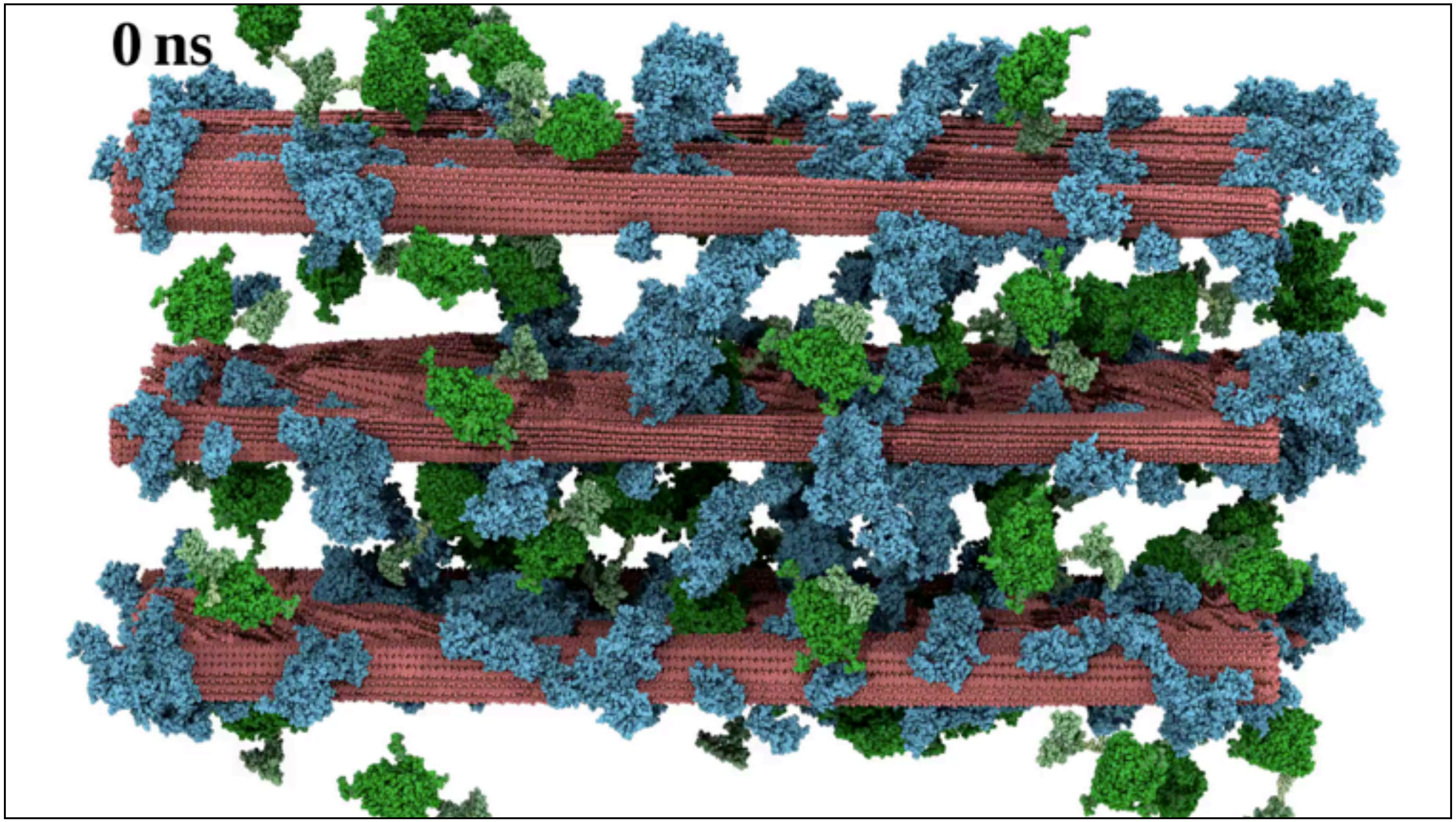
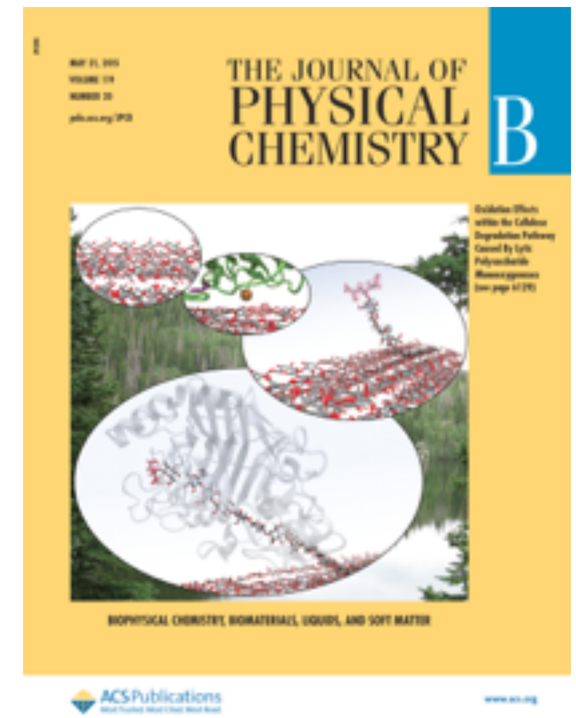
Exploring Biomass Recalcitrance at the Petascale with Molecular Simulation





Josh Vermaas

CSGF Annual Program Review

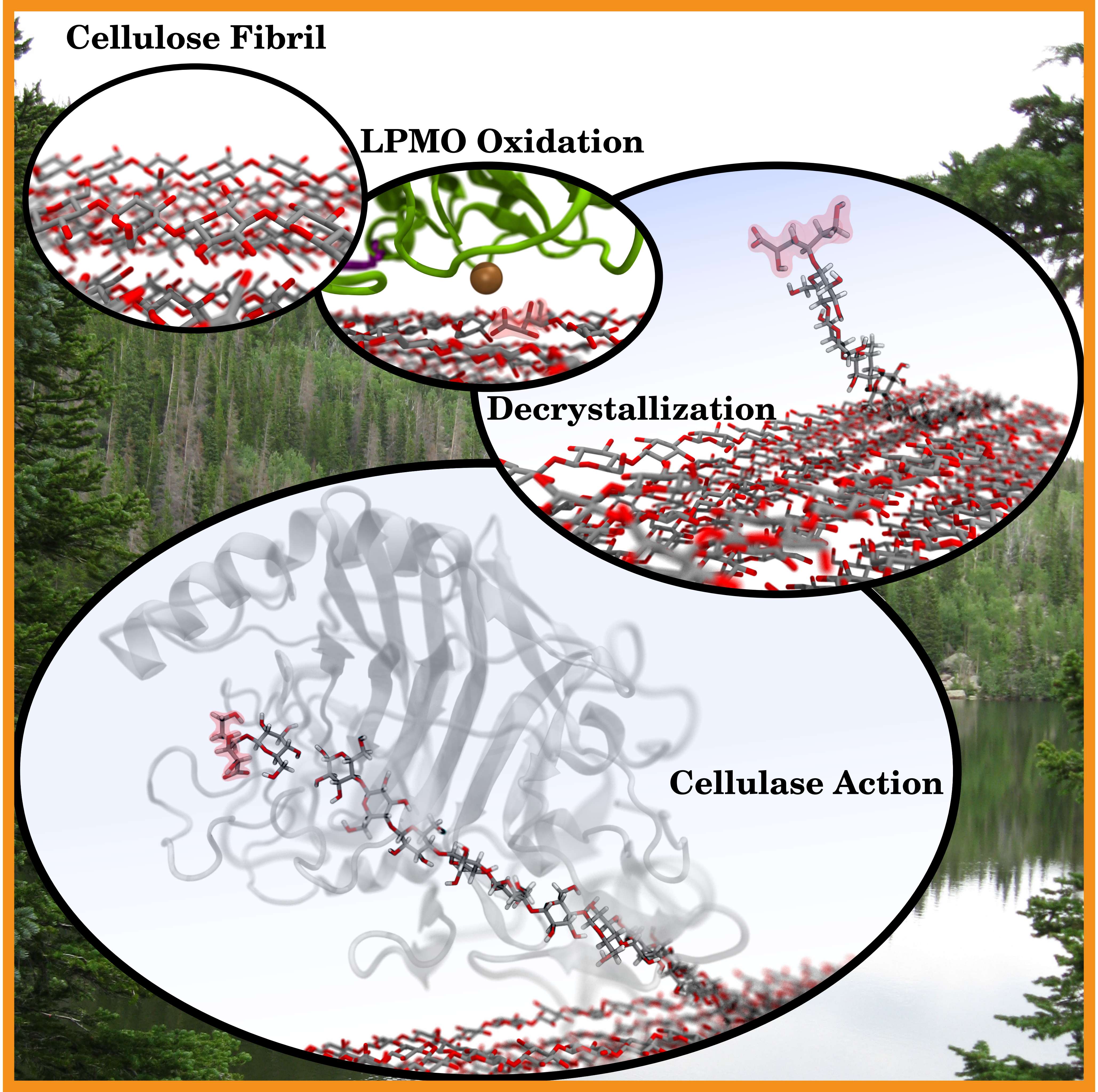
July 28th, 2015

DOE CSGF

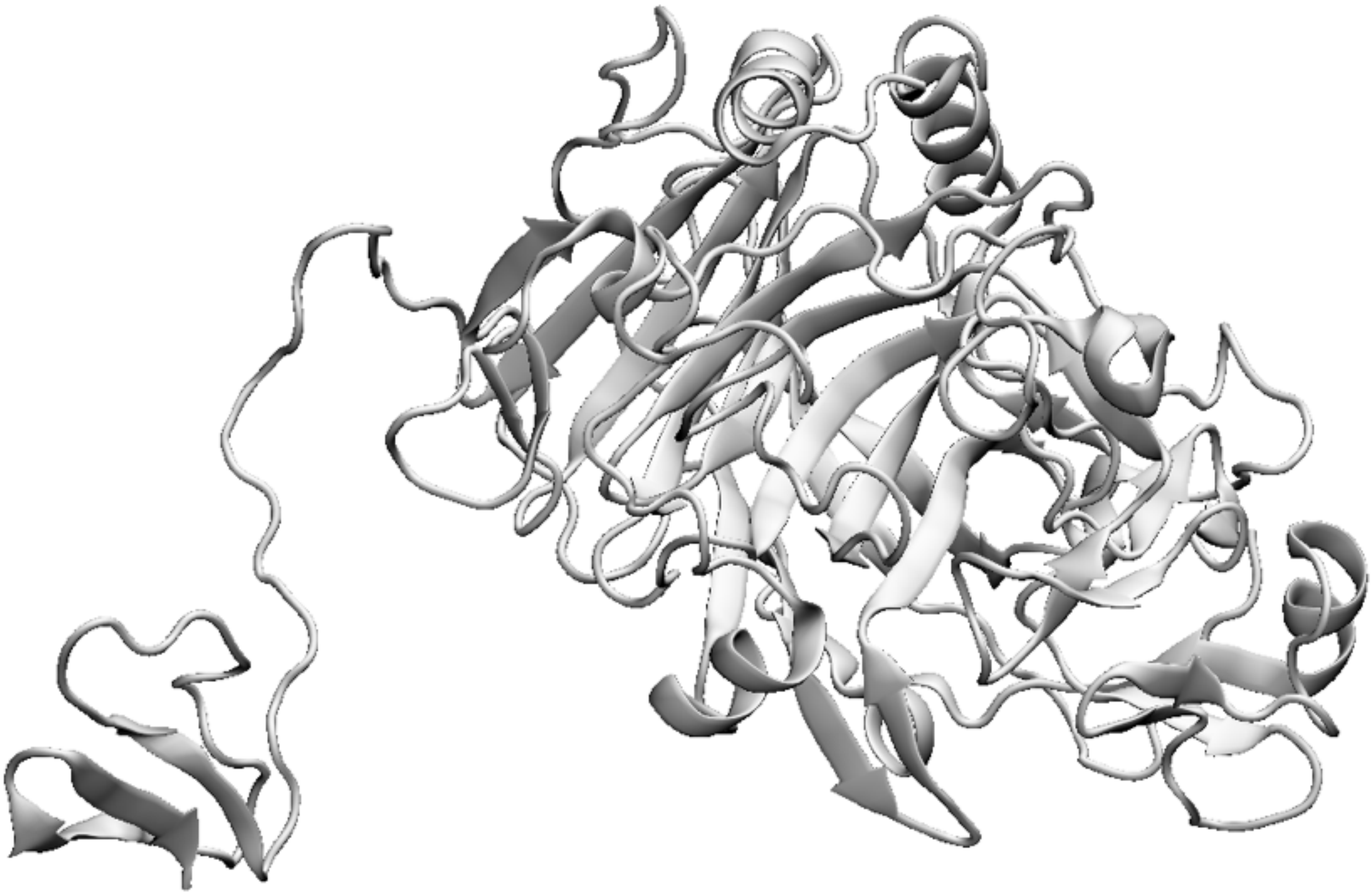
OAK RIDGE National Laboratory

NREL NATIONAL RENEWABLE ENERGY LABORATORY

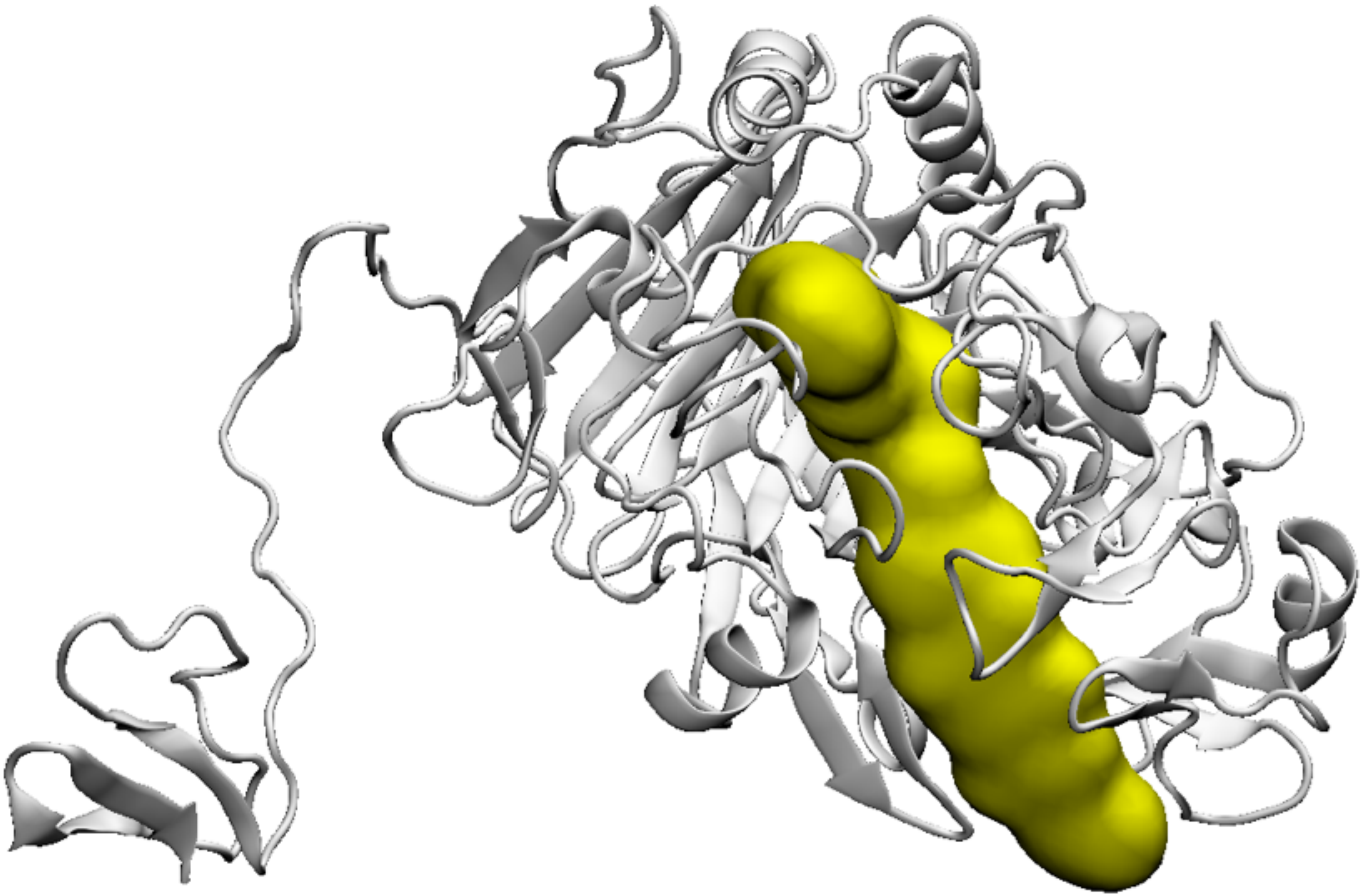
ILLINOIS UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN


Cellulose Fibril
LPMO Oxidation
Decrystallization
Cellulase Action

Anatomy of TrCel7A

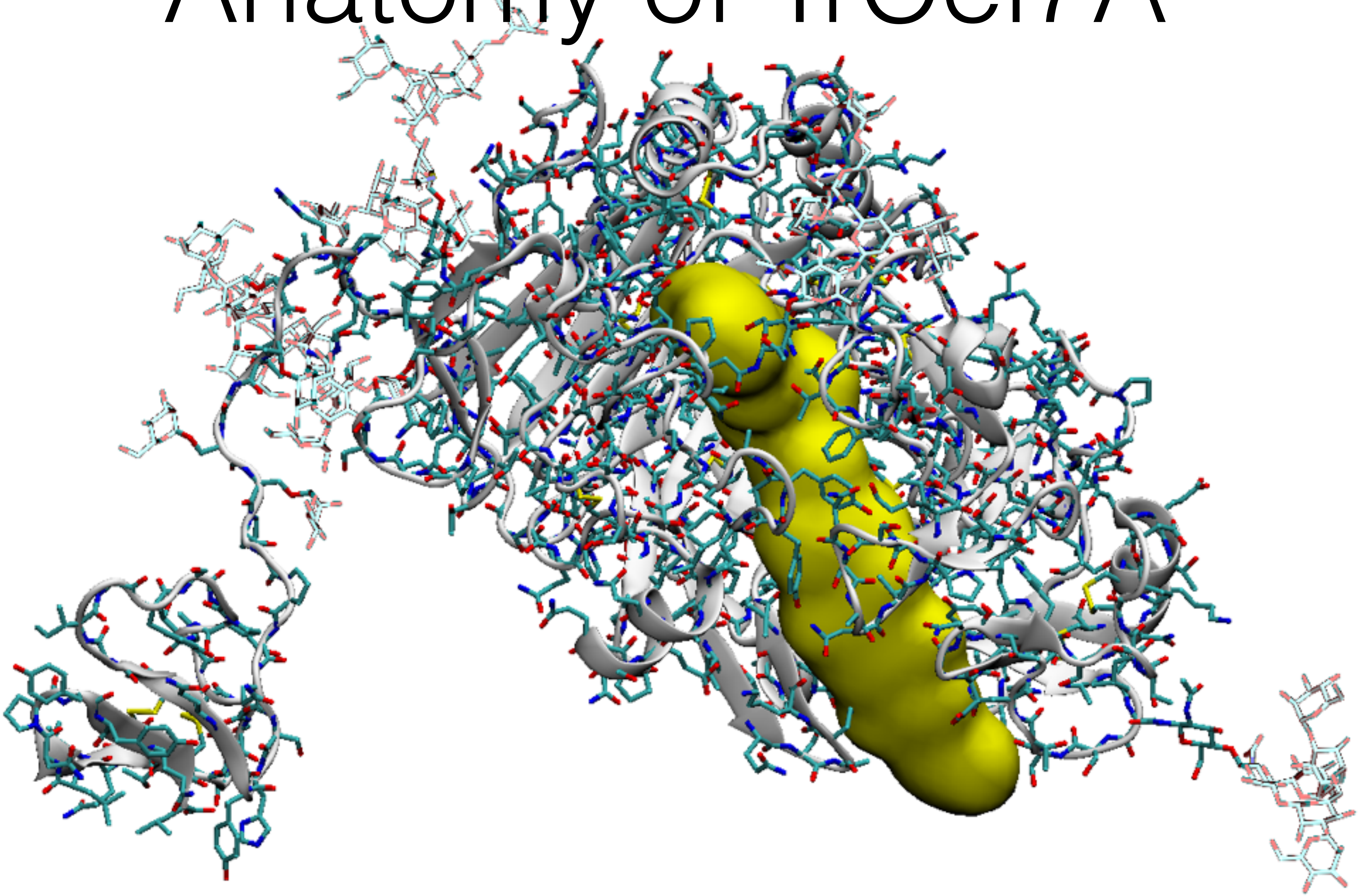


Anatomy of TrCel7A



Cellulose binding tunnel

Anatomy of TrCel7A



Glycosylations abound, and strengthen cellulose binding

The Basics of Classical Molecular Dynamics

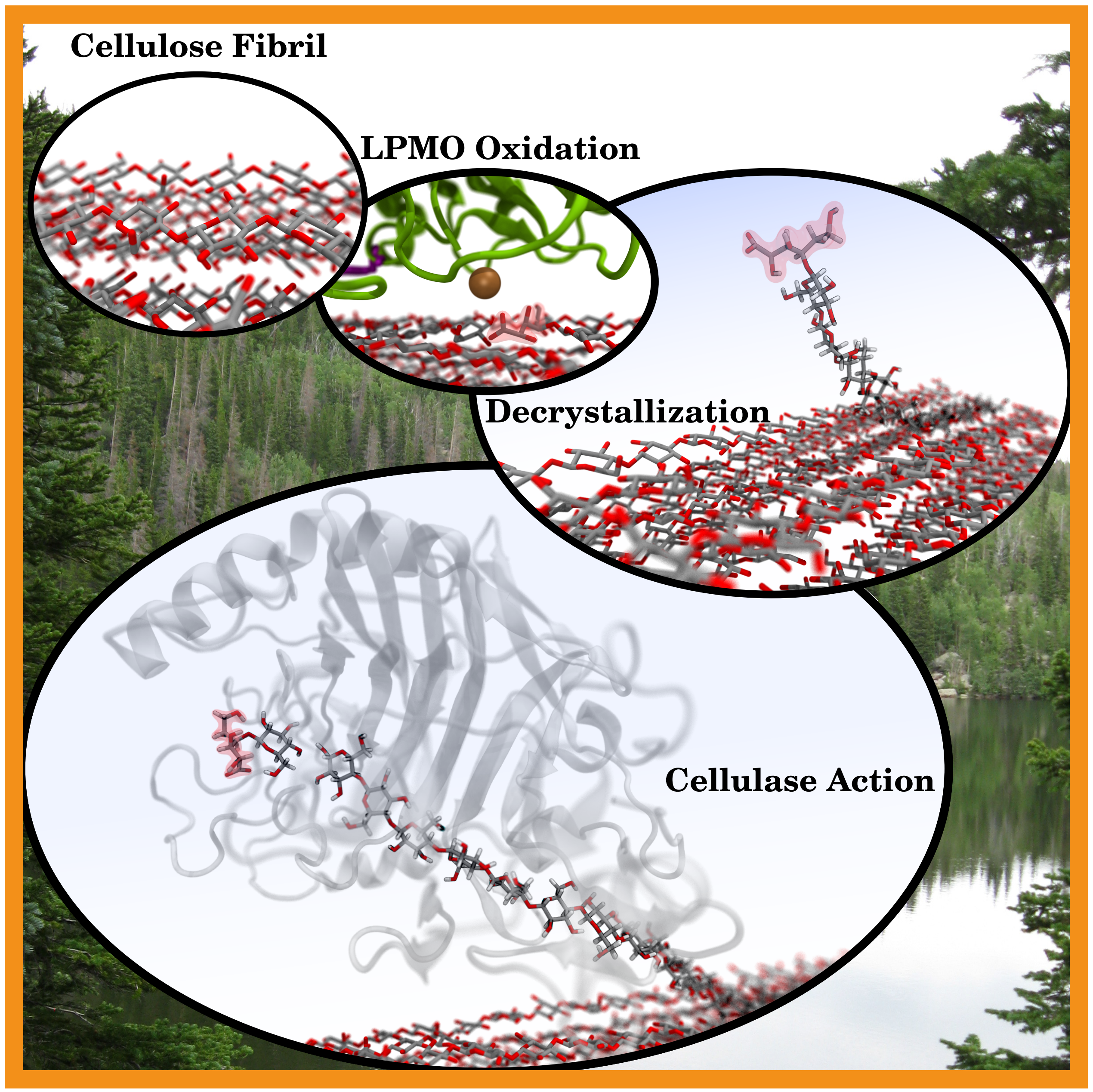
$$F = ma$$

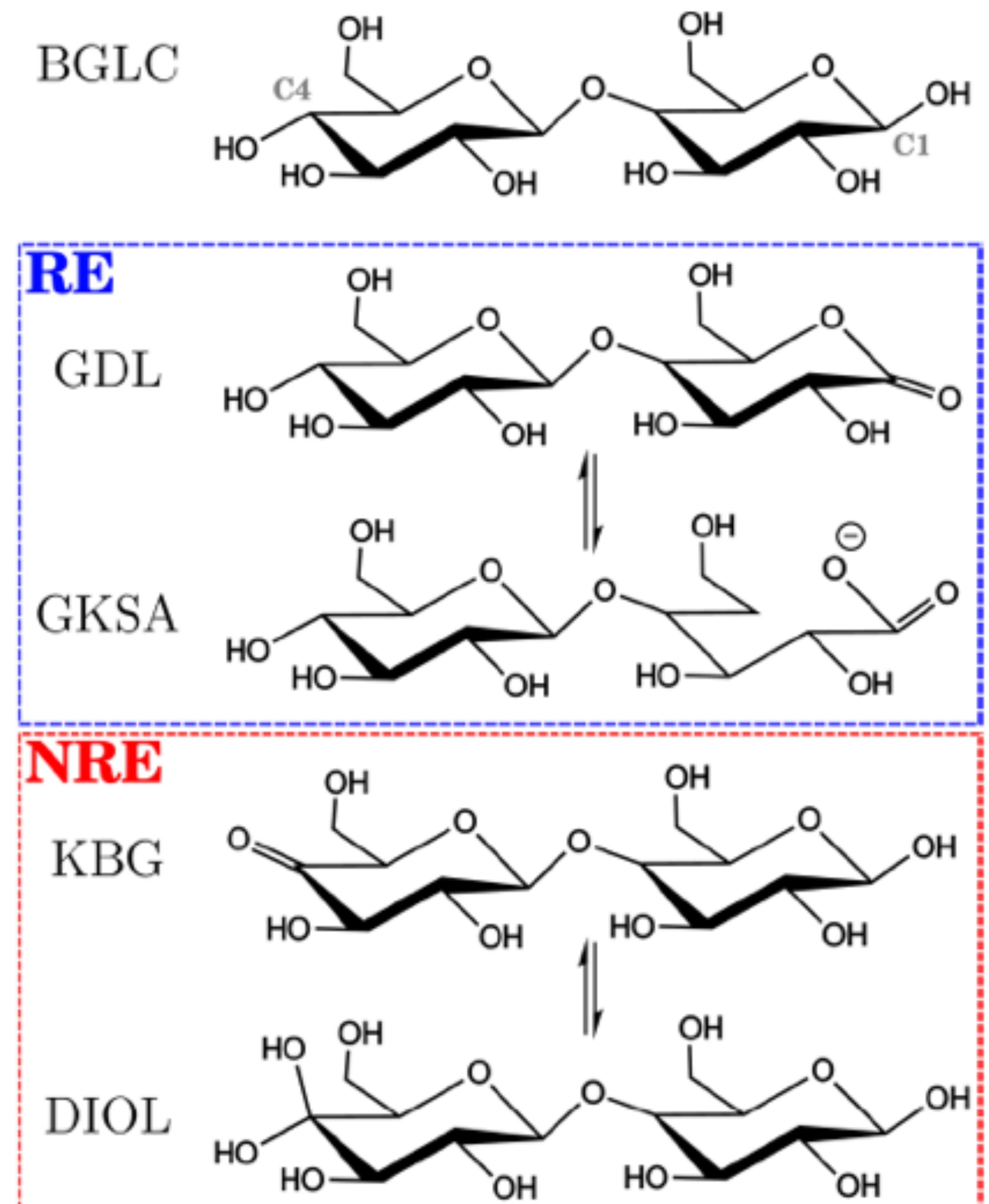
$$U_{total} = U_{bonded} + U_{nonbonded}$$

$$= \sum_{bonds} k_b (d - d_0)^2 + \sum_{angles} k_a (\theta - \theta_0)^2 + \sum_{dihedrals} k_d (1 + \cos(n\phi + \delta))$$

$$+ \sum_i \sum_j \left(\epsilon_{ij} \left[\left(\frac{r_m}{r_{ij}} \right)^{12} - 2 \left(\frac{r_m}{r_{ij}} \right)^6 \right] + \frac{k q_i q_j}{r_{ij}^2} \right)$$

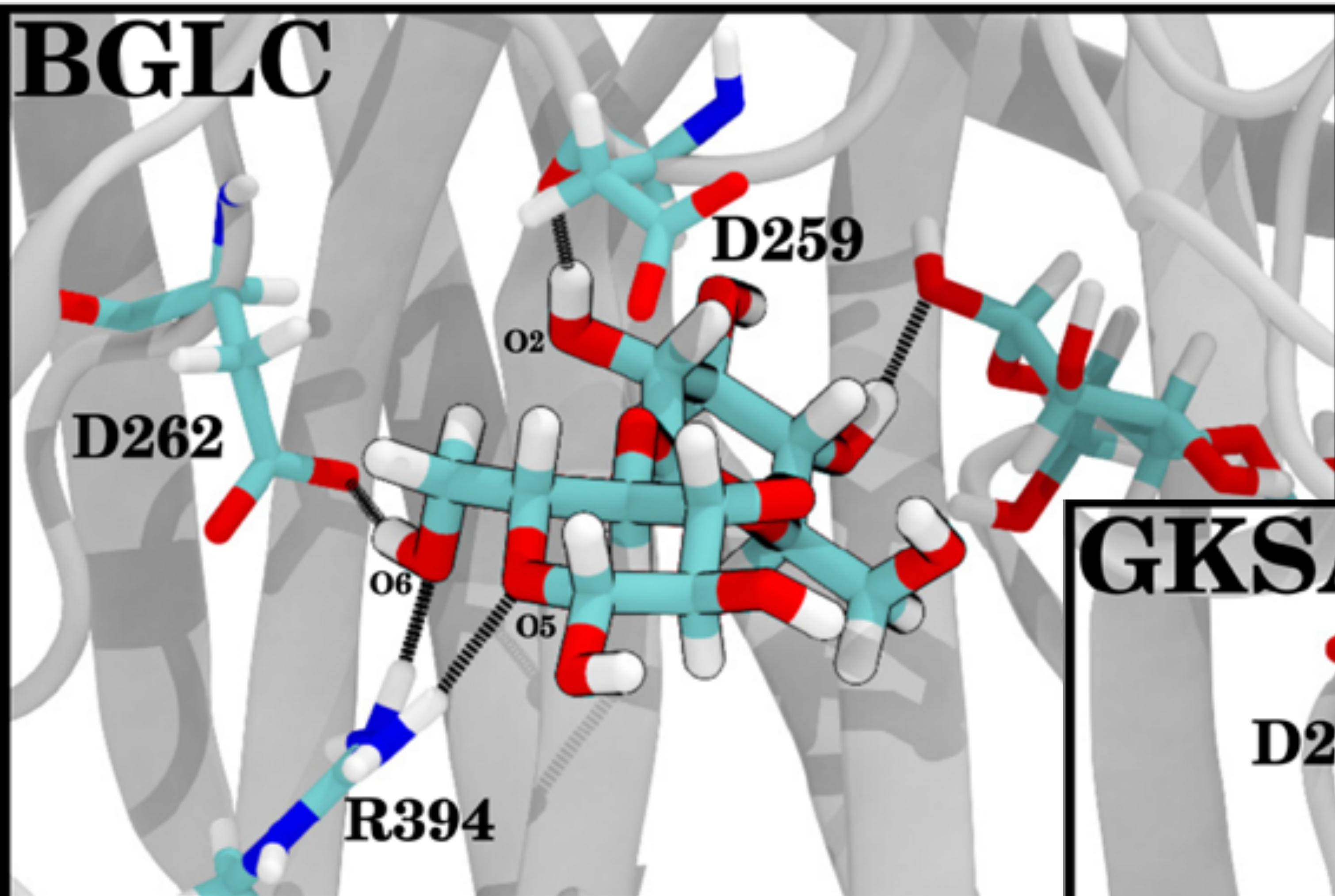
What if the Cellulose Substrate is Oxidized?

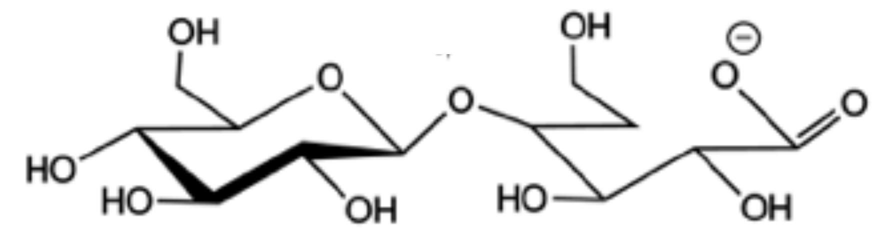


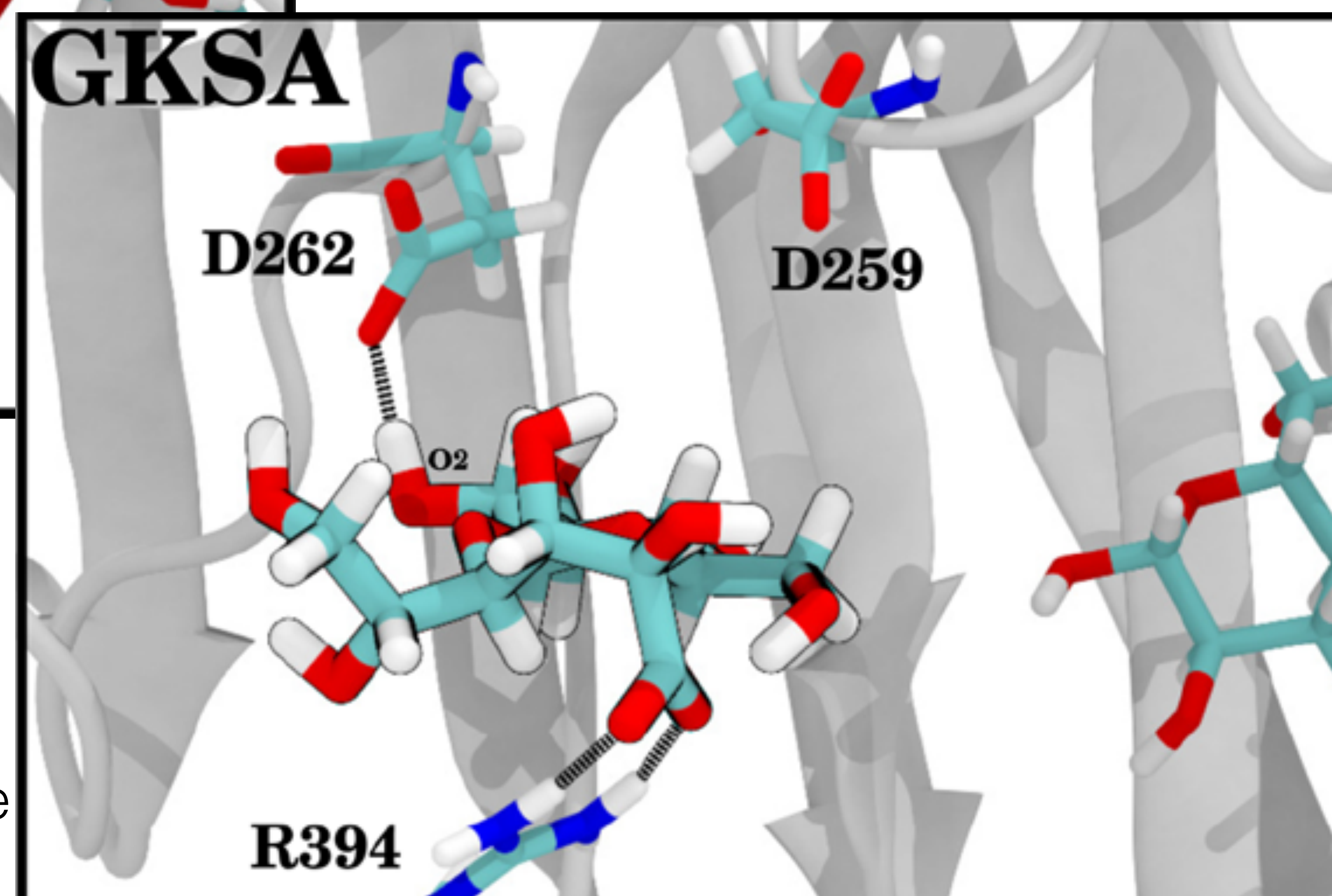


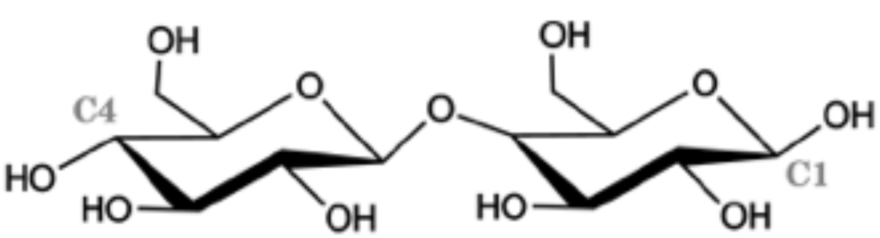
Vermaas, Crowley, Beckham, and Payne,
Journal of Physical Chemistry B 2015

Hydrogen Bonding Patterns Shift upon Oxidation









Vermaas, Crowley, Beckham, and Payne
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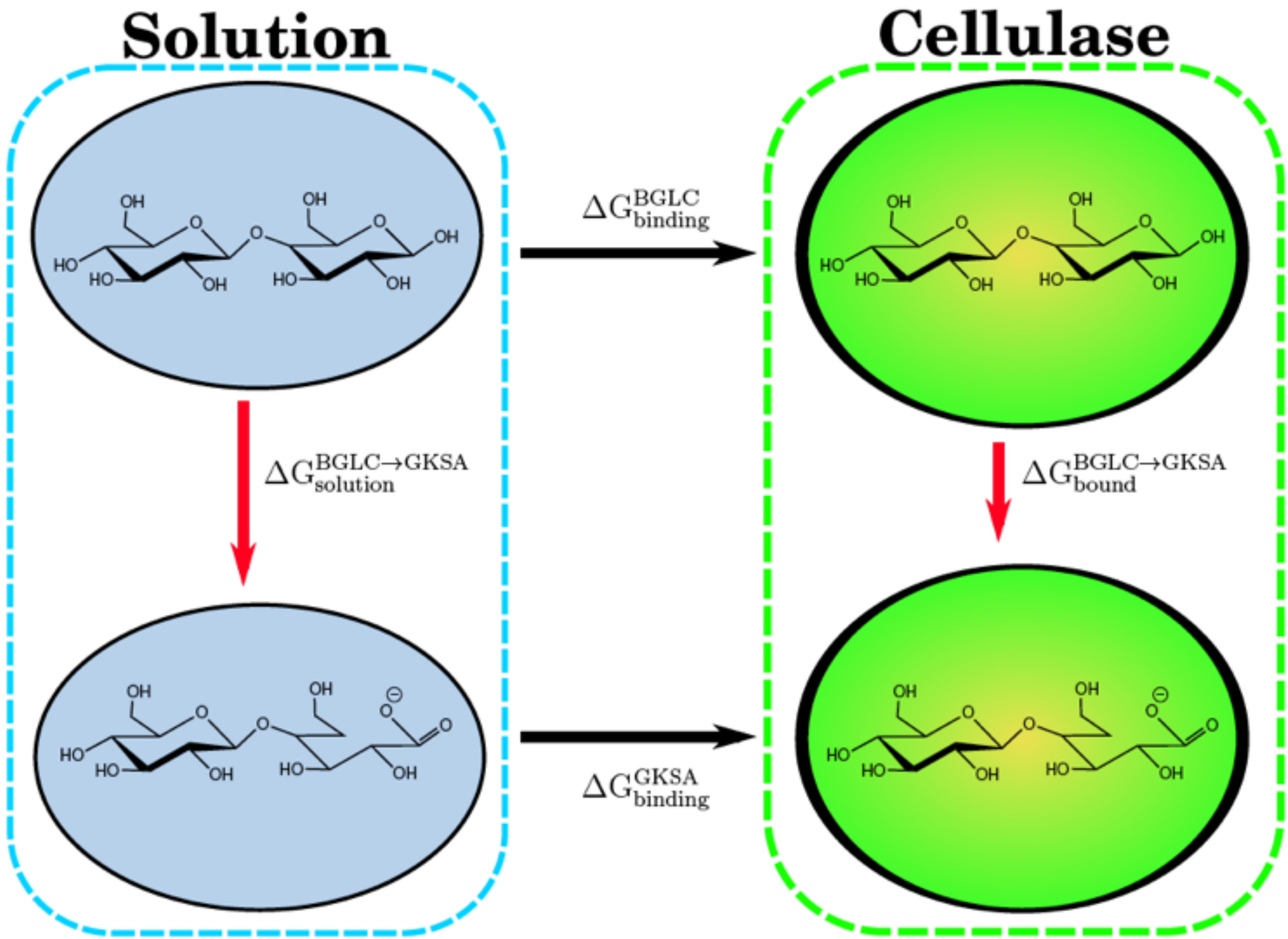
Quantitation through Thermodynamic Integration

- Compute the relative binding free energies of the oxidized vs unoxidized species
- Alchemical changes are be made *in silico*
- Form a complete thermodynamic cycle with binding transition



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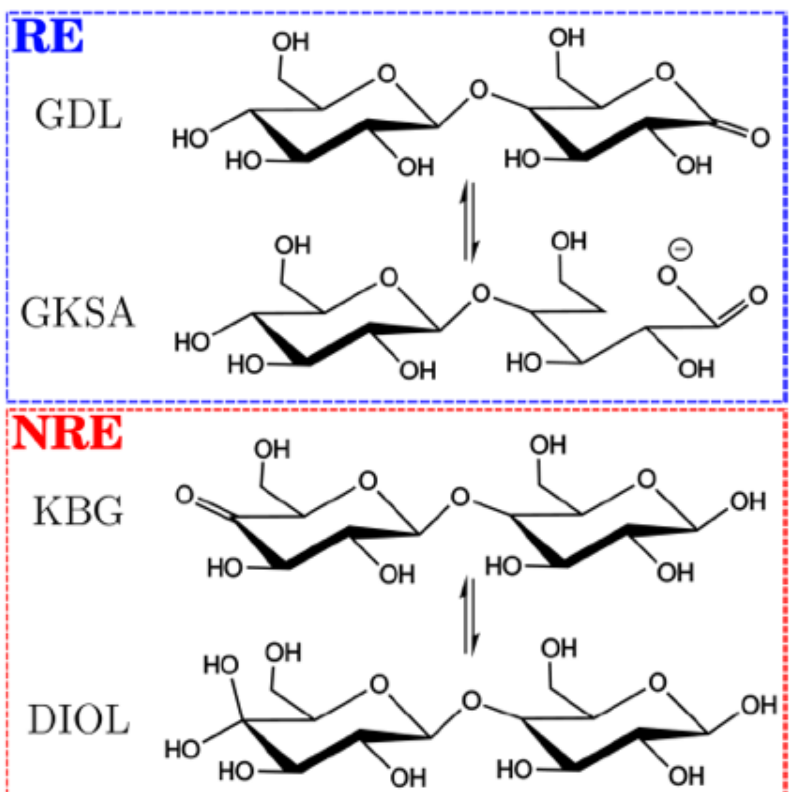
Oxidized Products Bind Tighter in the Presence of Substrate



*Tr*Cel7A	*Tr*Cel7A w/S
0.51 ± 0.18	1.96 ± 0.17
0.05 ± 0.22	−3.23 ± 0.20
1.88 ± 0.20	−0.85 ± 0.22
0.03 ± 0.22	−0.29 ± 0.25

Δ Δ*G* in kcal/mol

Large and negative = potentially inbititory binding

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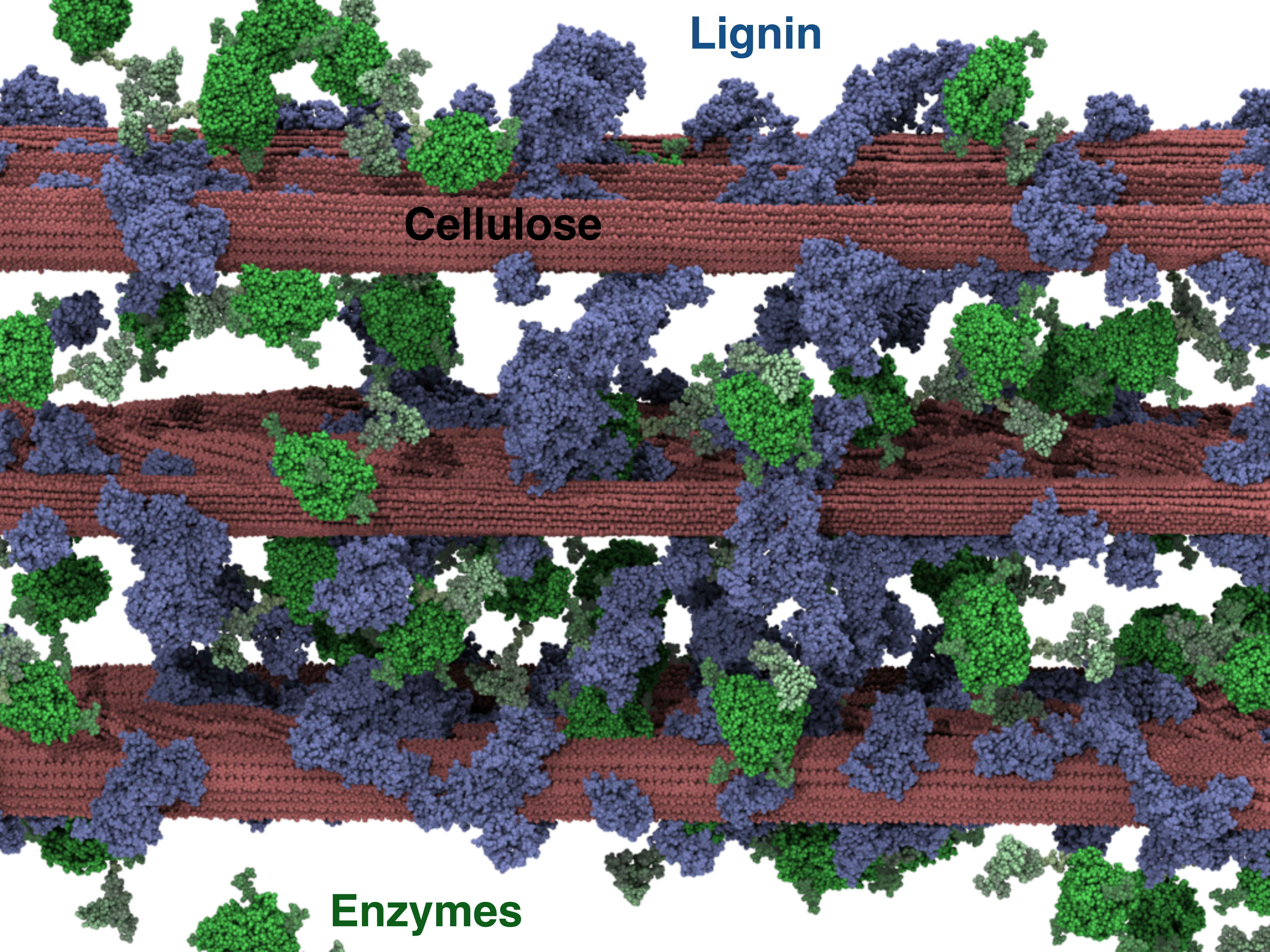
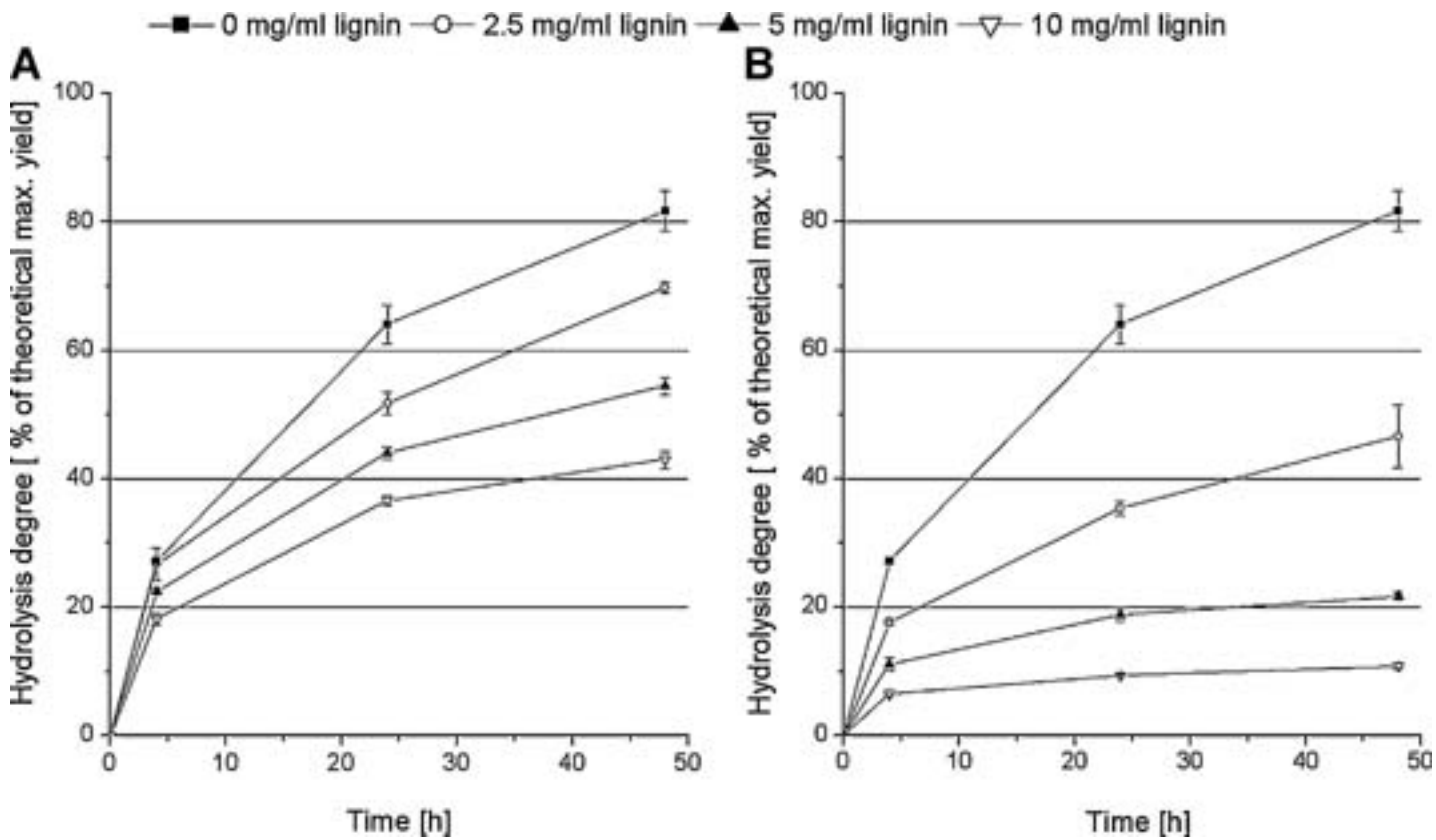
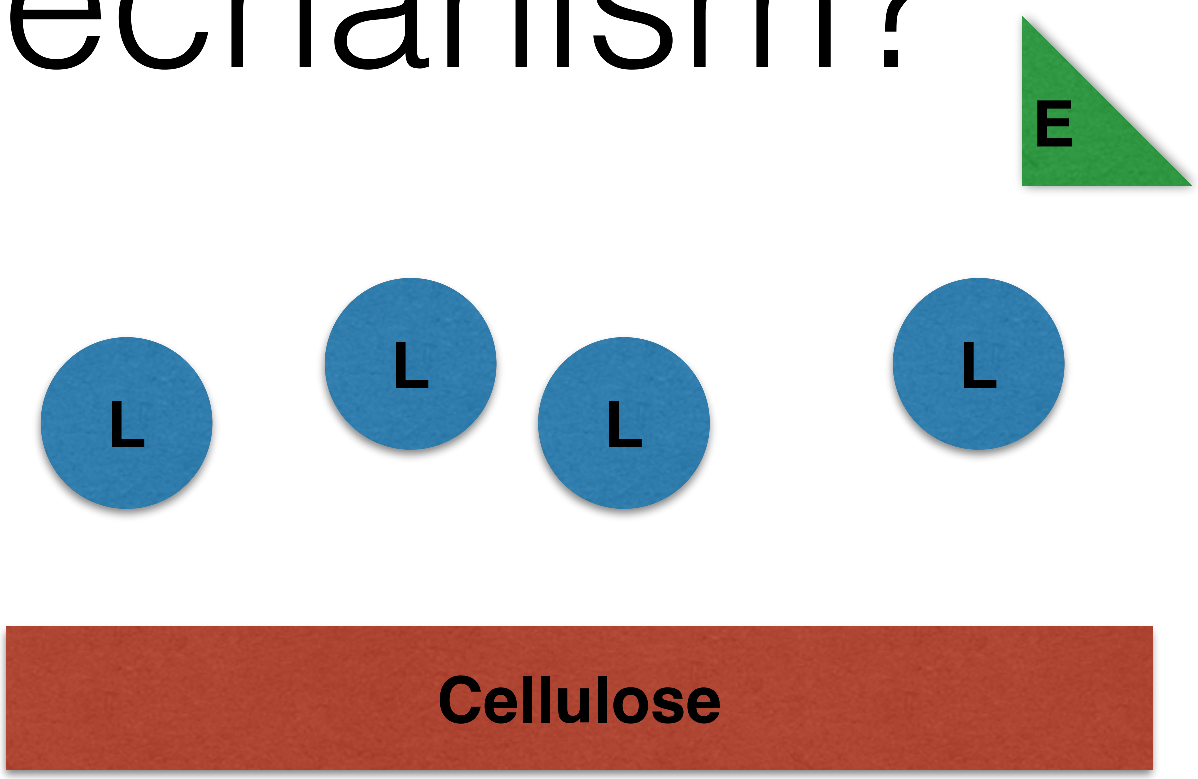

Lignin
Cellulose
Enzymes

Lignin reduces the yield from pretreated biofuel feedstocks

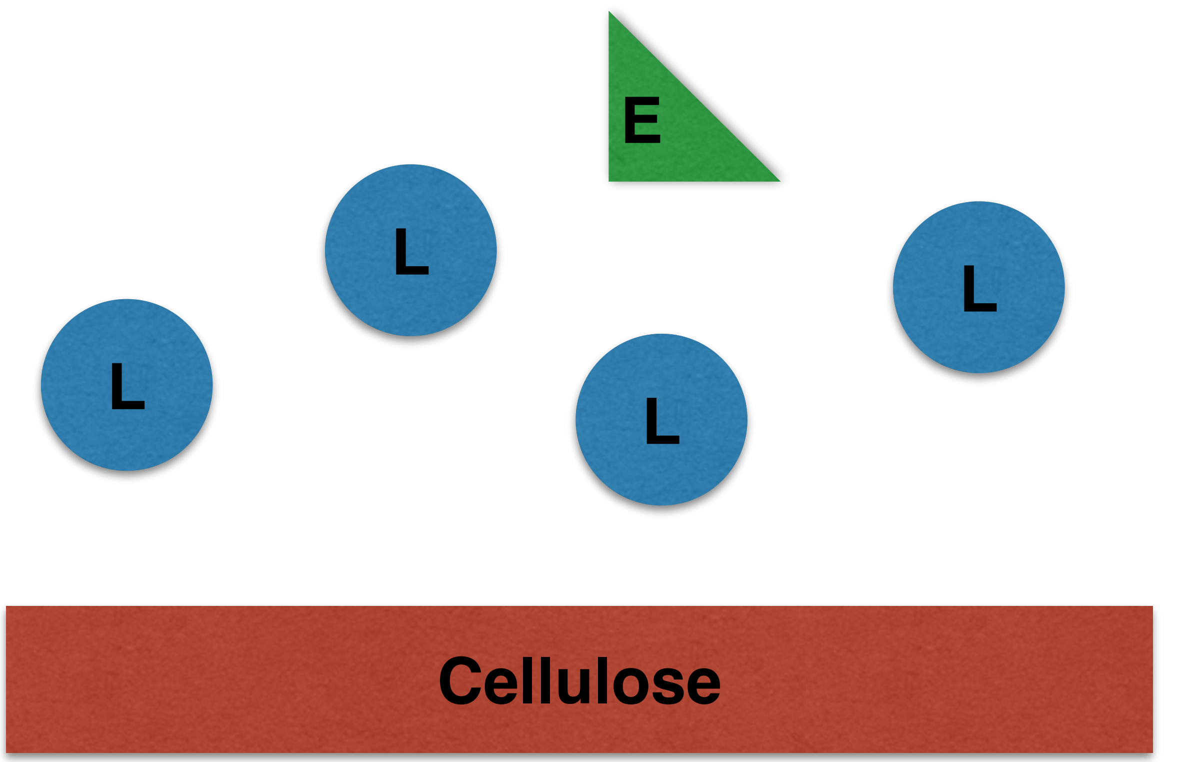


Rahikainen, J., Mikander, S., Marjamaa, K., Tamminen, T., Lappas, A., Viikari, L. and Kruus, K. (2011), Inhibition of enzymatic hydrolysis by residual lignins from softwood—study of enzyme binding and inactivation on lignin-rich surface. Biotechnol. Bioeng., 108: 2823–2834. doi: 10.1002/bit.23242

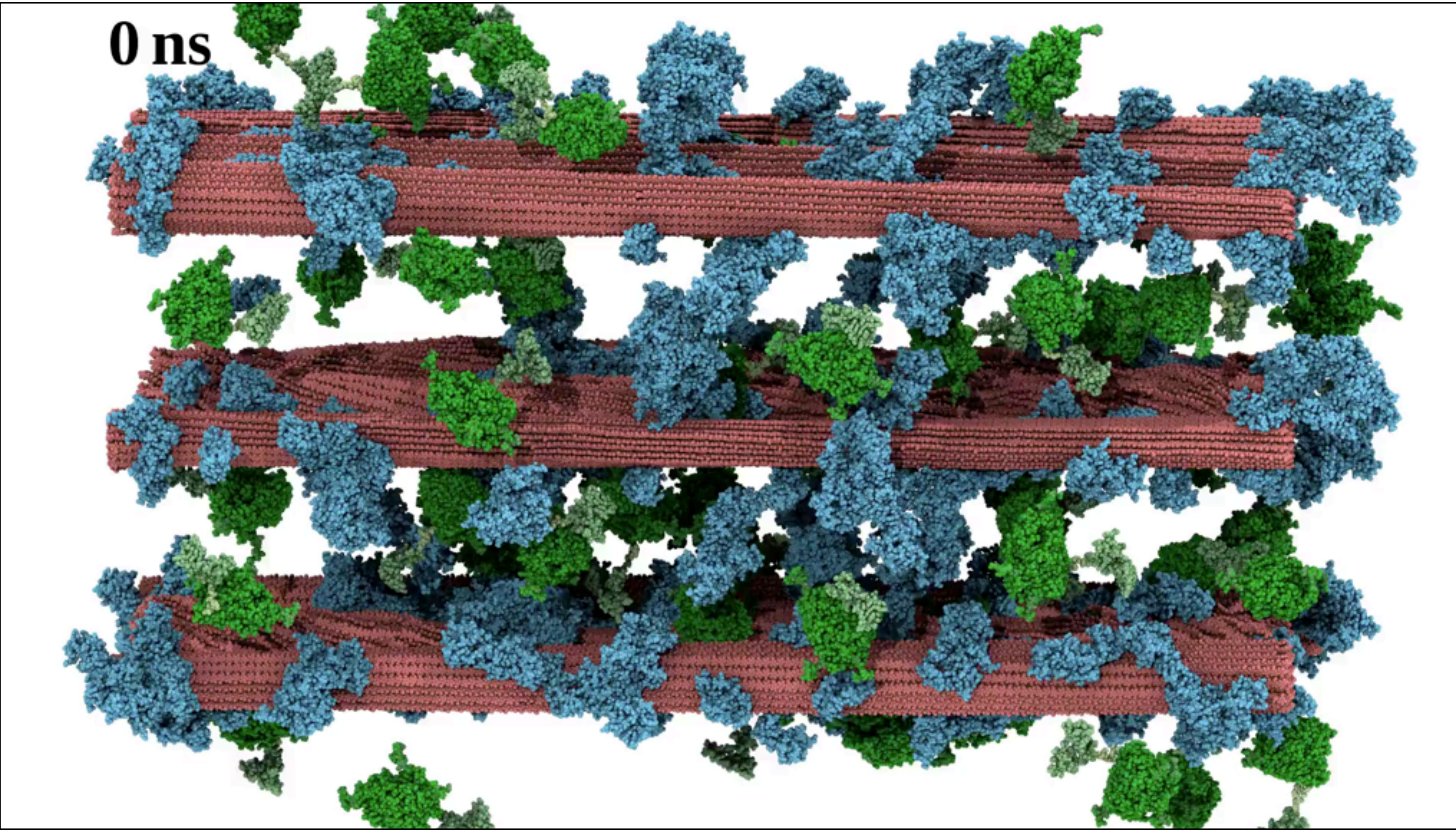
What is the mechanism?



- In the literature, two main mechanisms have been proposed
    - Lignin binds to cellulose, blocking cellulase access
    - Lignin binds to cellulases, preventing their productive association to cellulose
- Through petascale atomic simulation, we investigate each of these hypotheses



The Complete Trajectory



Vermaas, Petridis, Schultz, Qi, Lindner, and Smith *Under Review*

Hidden Lessons

1. Lignin binds to cellulose, particularly to the hydrophobic face
2. Lignin binds to cellulases, particularly to tyrosine residues on the carbohydrate binding module
3. The lignocellulosic mesh network formed hinders enzyme diffusion

Hidden Lessons

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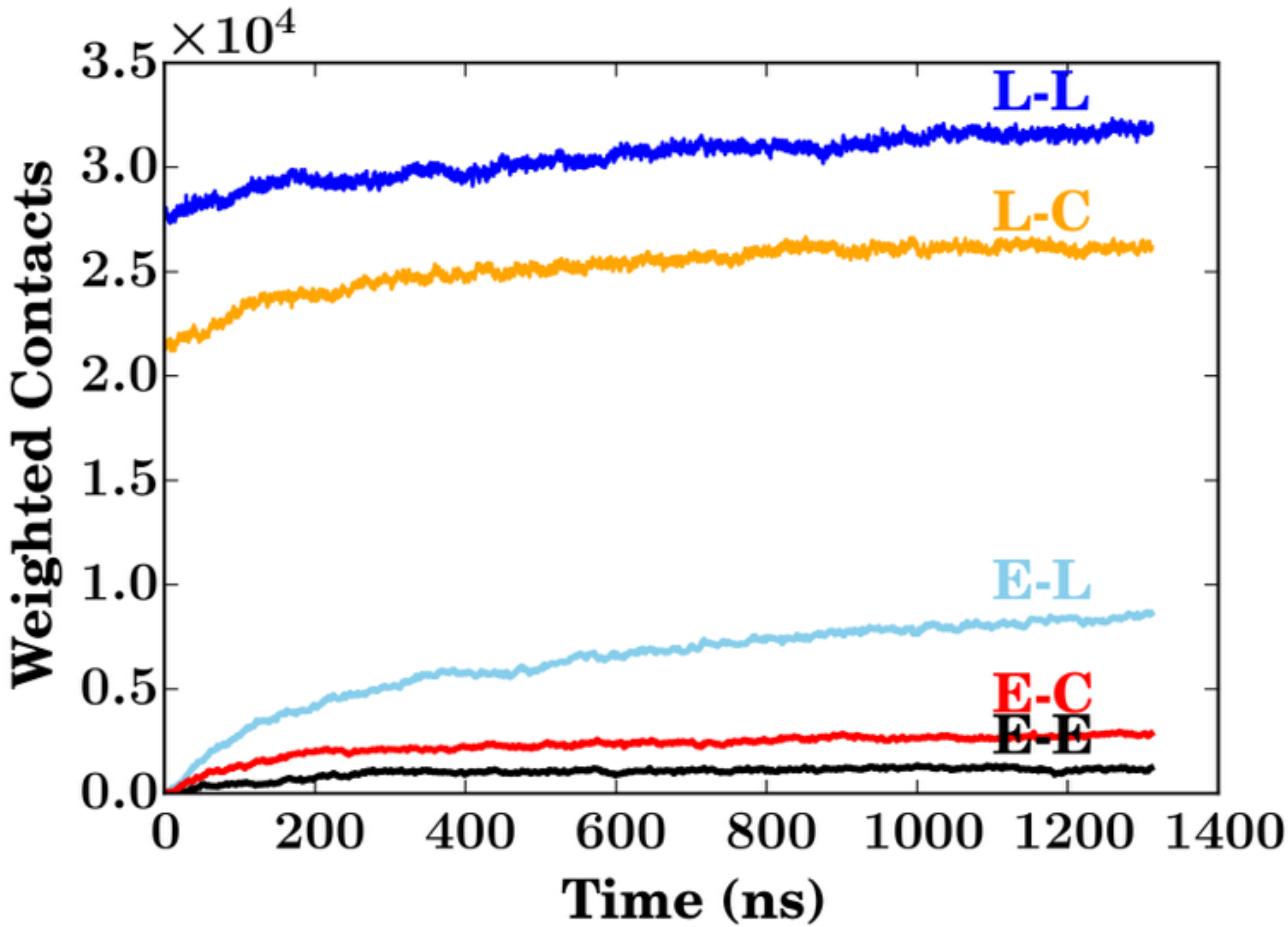
Lignins form many cellulose contacts



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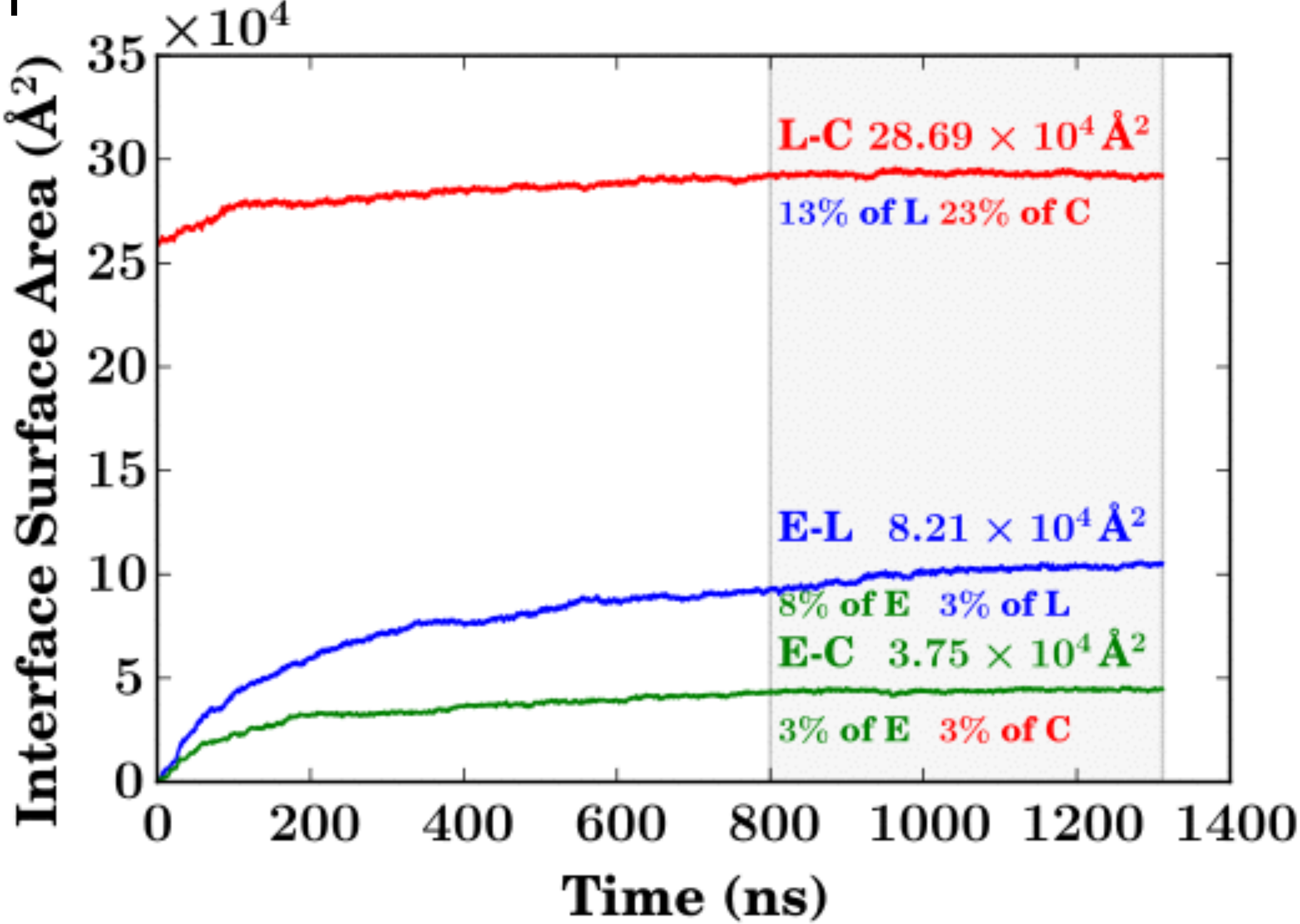
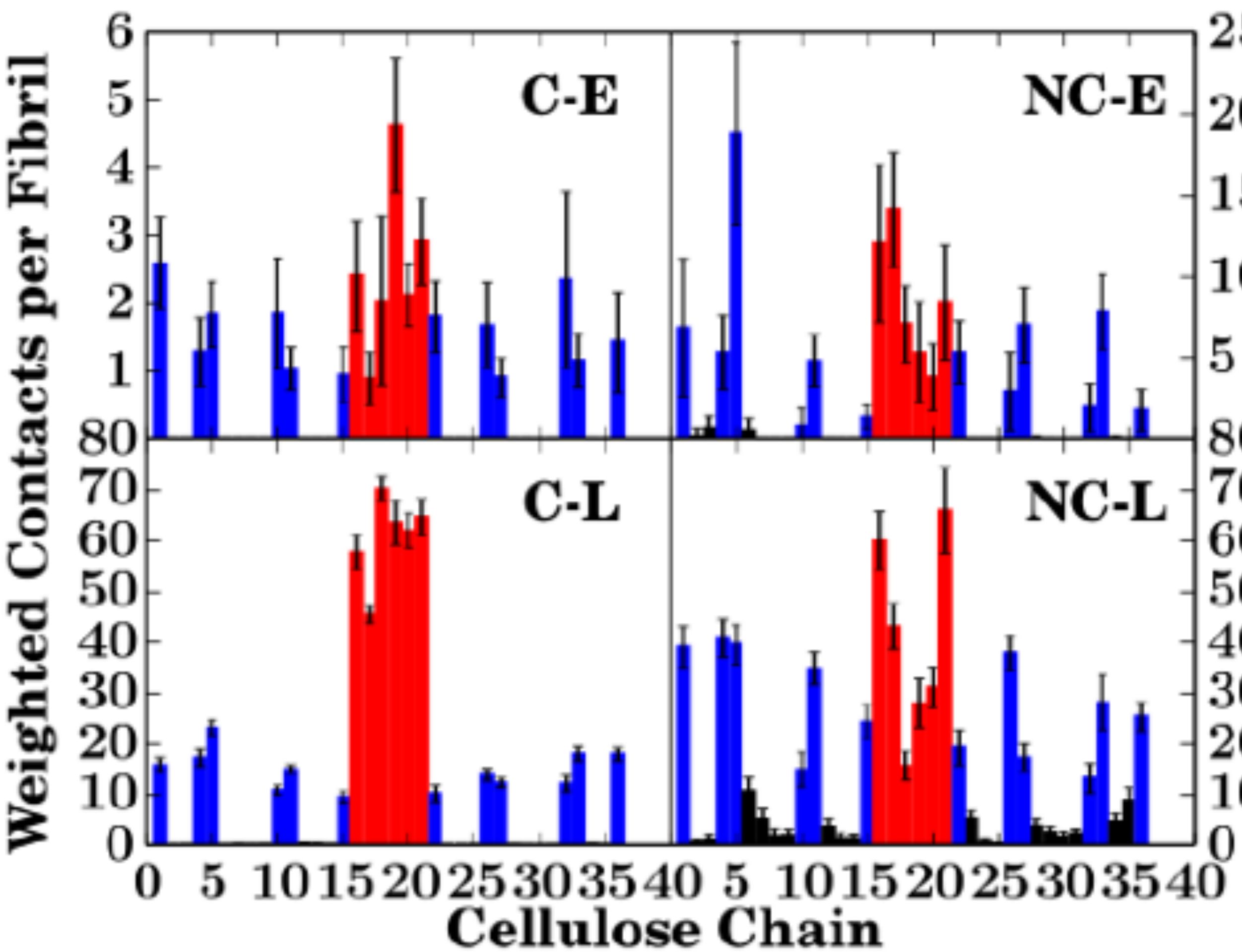
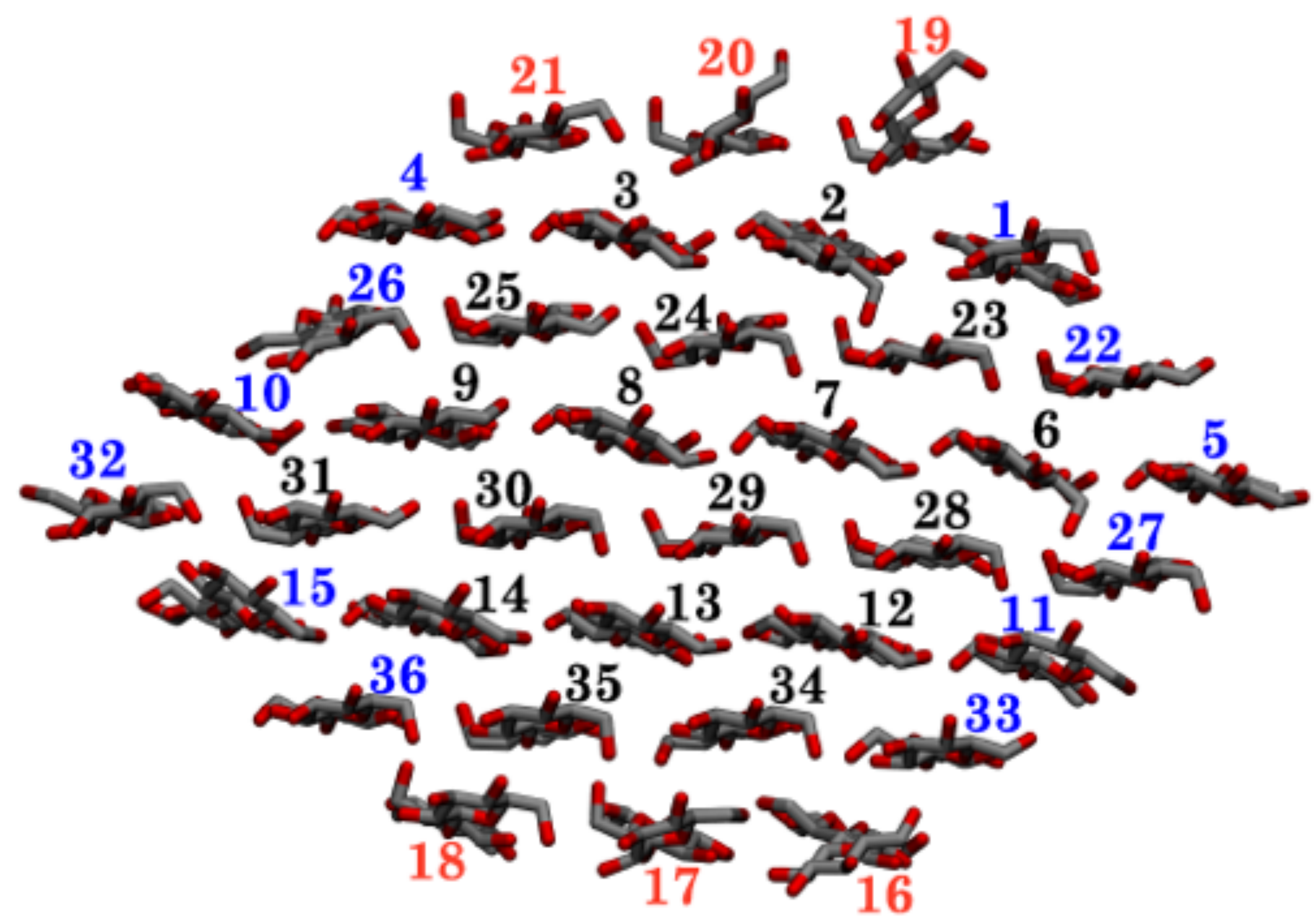
Lignin occludes nearly a quarter of the cellulose surface



Vermaas, Petridis, Schultz, Qi, Lindner, and Smith *Under Review*

This is localized to the hydrophobic surfaces





Vermaas, Petridis, Schultz, Qi, Lindner, and Smith *Under Review*

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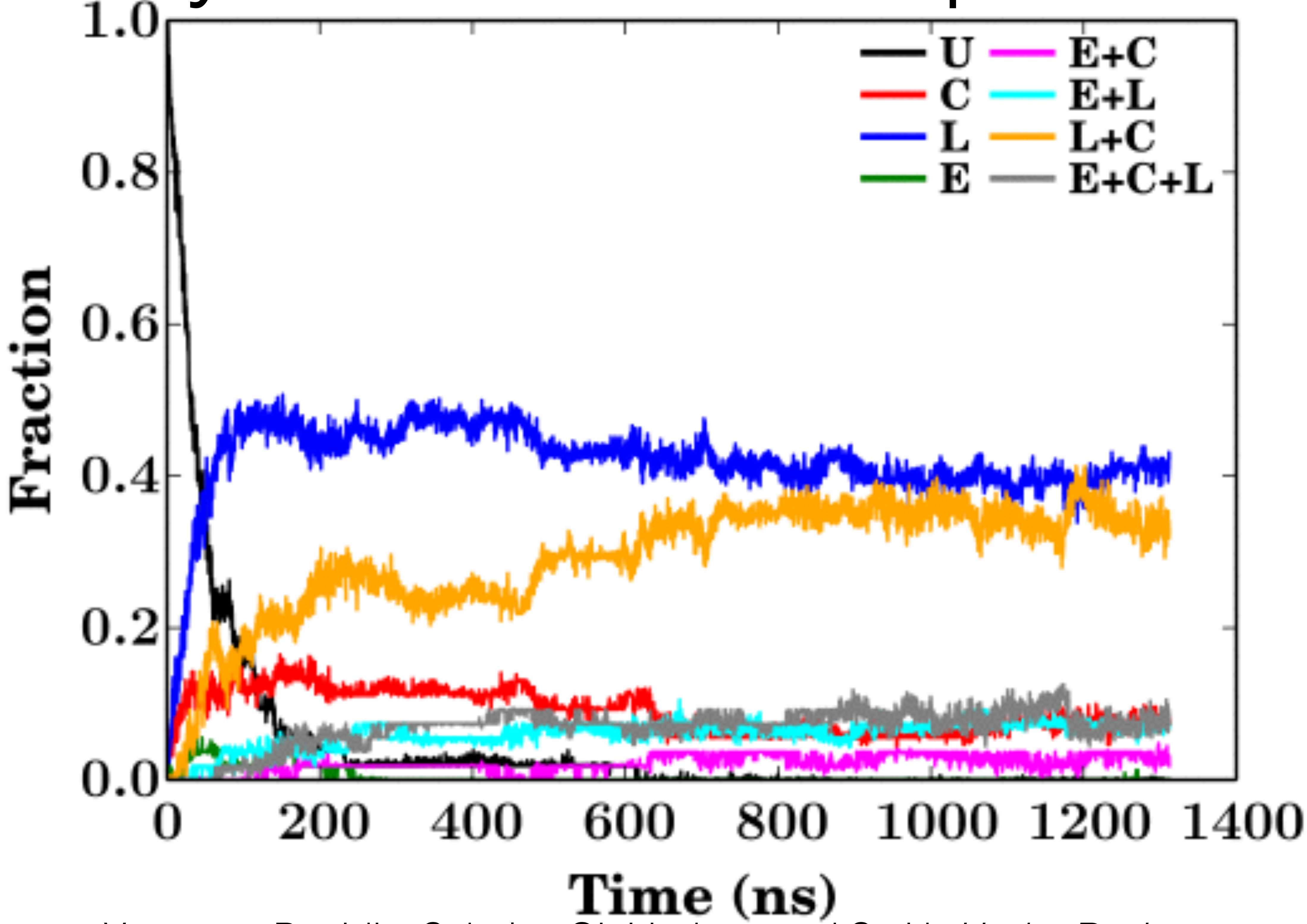
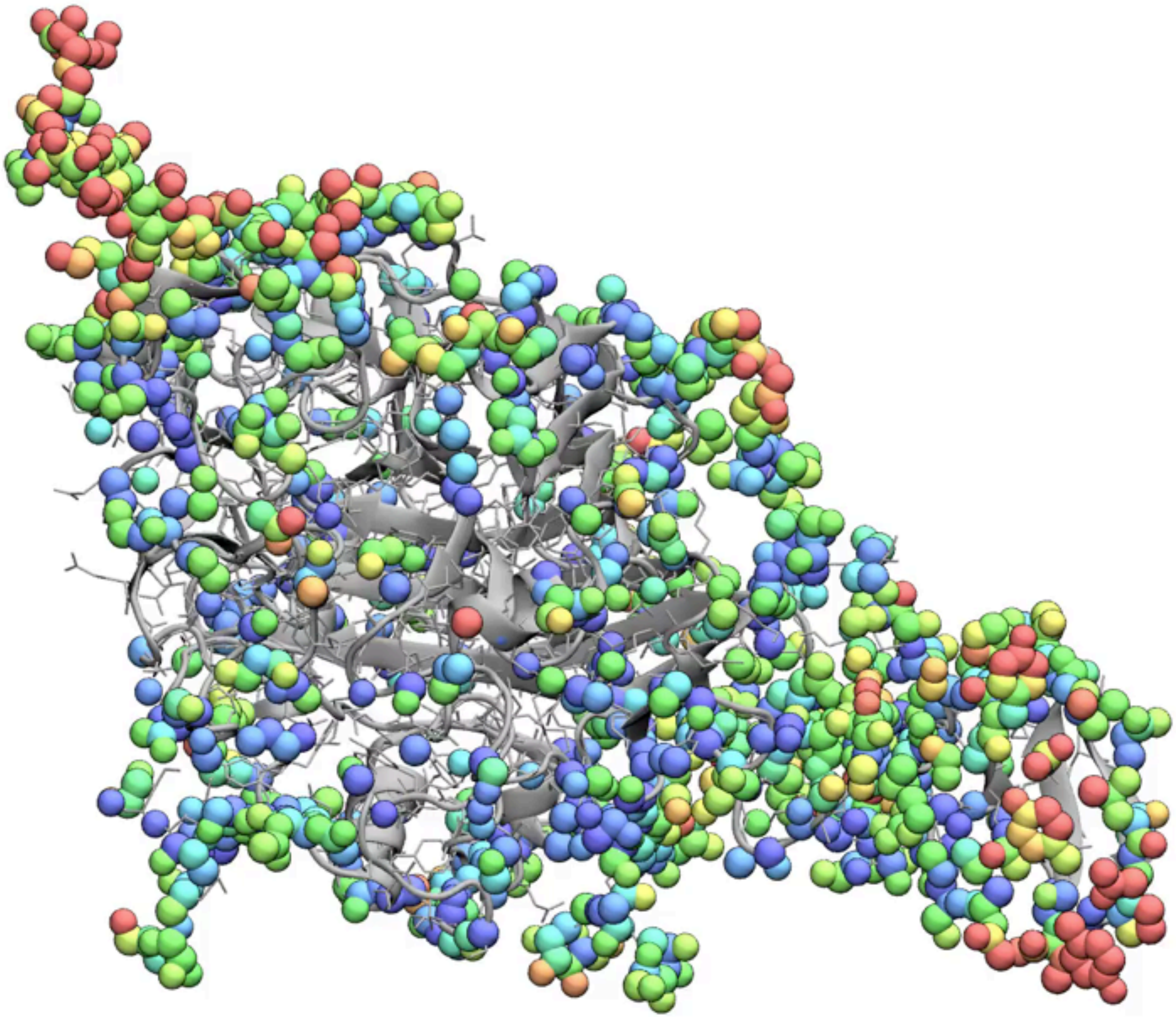
Lignin is the most common enzyme interaction partner



Vermaas, Petridis, Schultz, Qi, Lindner, and Smith *Under Review*



Vermaas, Petridis, Schultz, Qi, Lindner, and Smith *Under Review*

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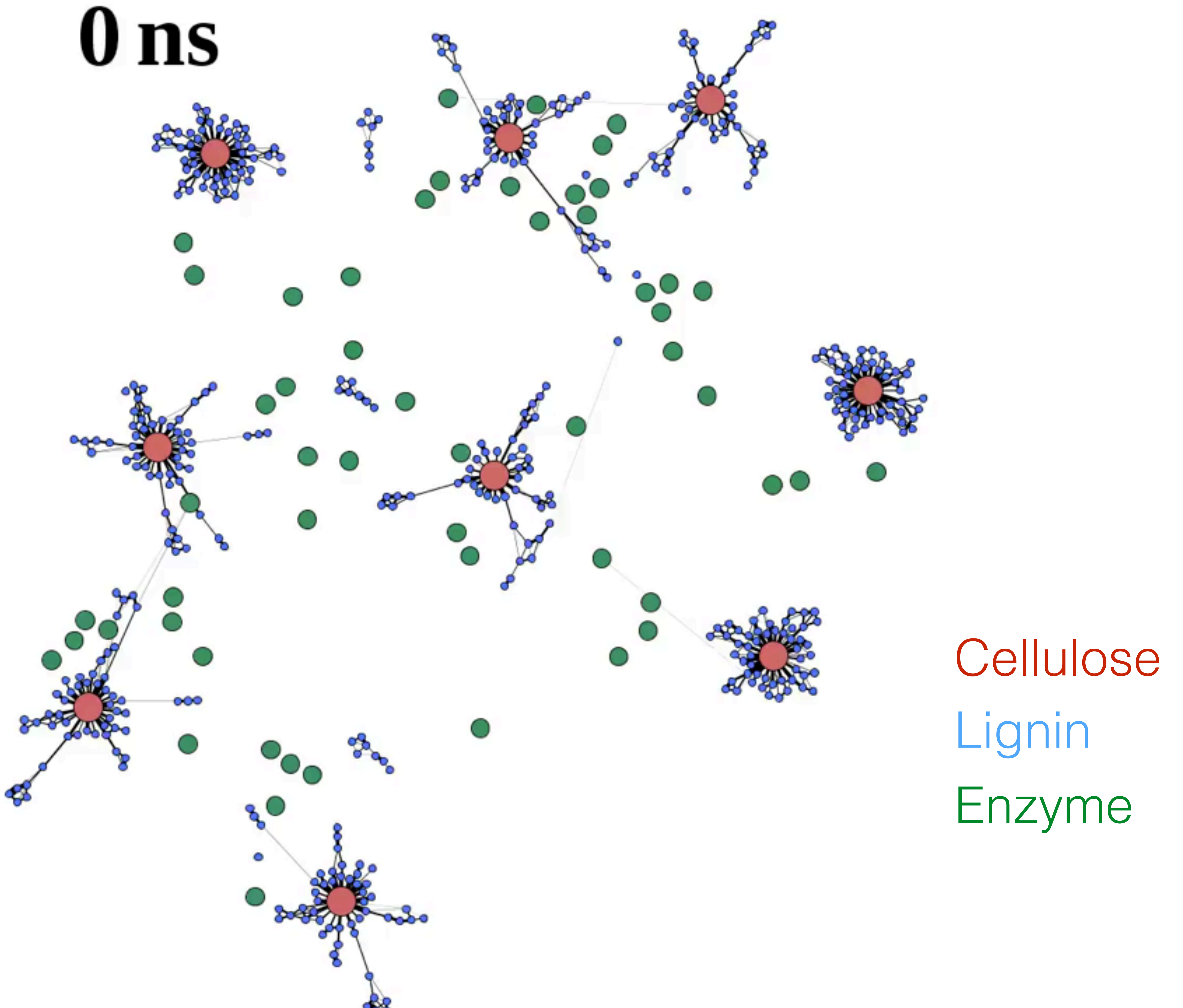

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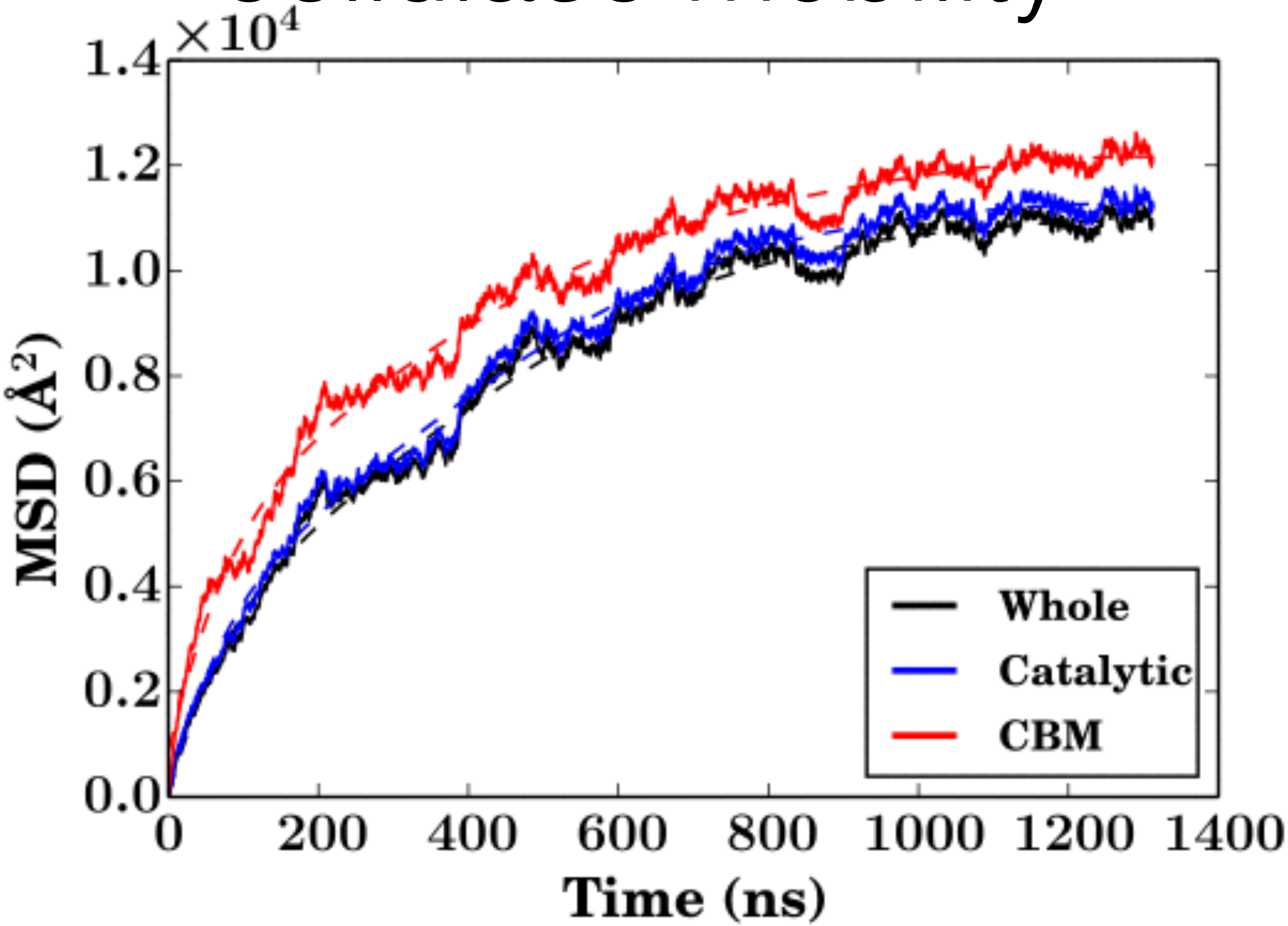
Network formation impedes cellulase mobility



Vermaas, Petridis, Schultz, Qi, Lindner, and Smith *Under Review*

Lessons Revealed

1. Lignin binds to cellulose, particularly to the hydrophobic face

2. Lignin binds to cellulases, particularly to tyrosine residues on the carbohydrate binding module

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Acknowledgements

DOE CSGF

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Jeremy Smith

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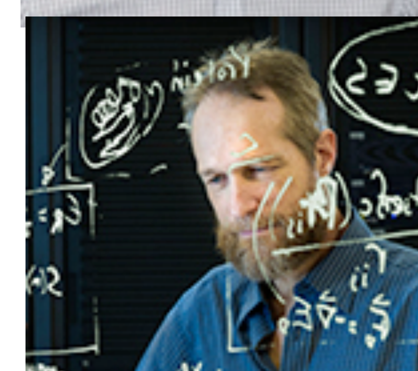

Emad Tajkhorshid

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Questions?