Lateral organization of a non-equilibrium membrane model with quenched random impurities

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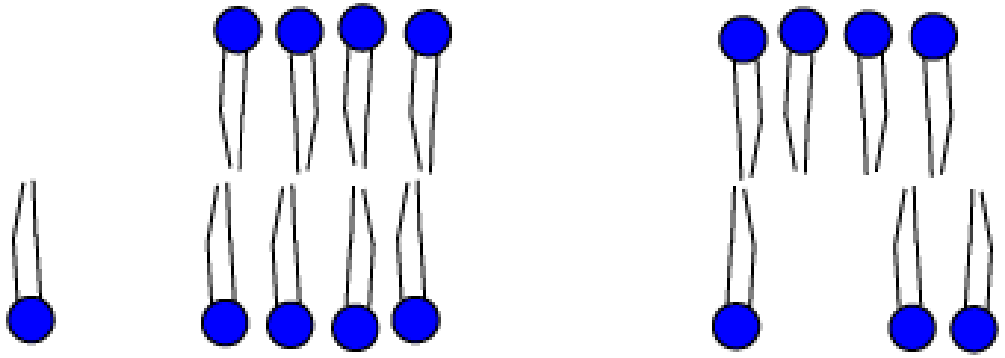
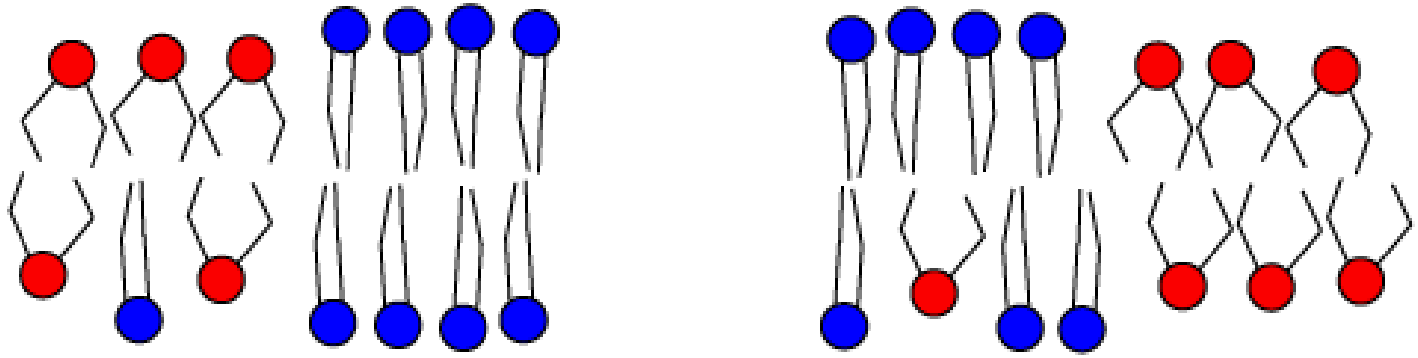
Cell Membrane Composition



We wish to simulate an active, dynamic membrane.

We begin with saturated lipids (s)...

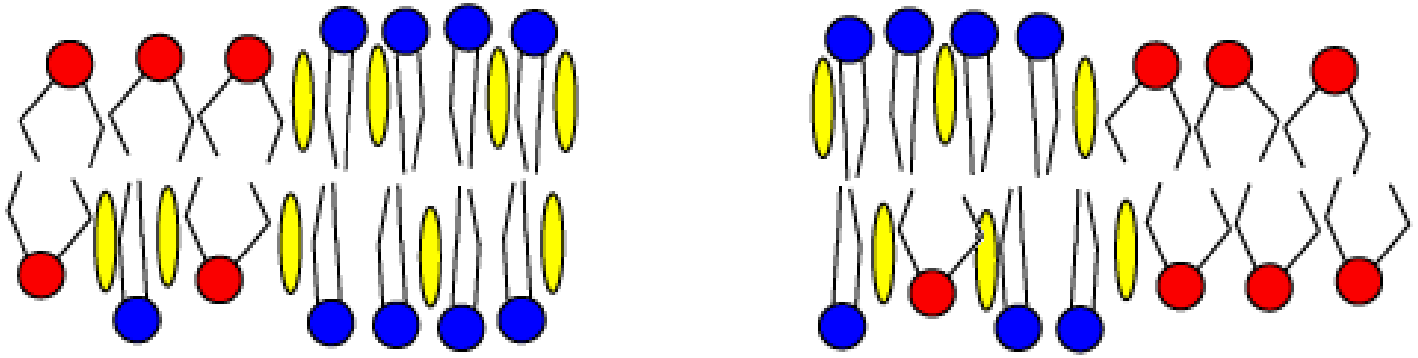
Cell Membrane Composition



We wish to simulate an active, dynamic membrane.

... and add some unsaturated lipids (u)...

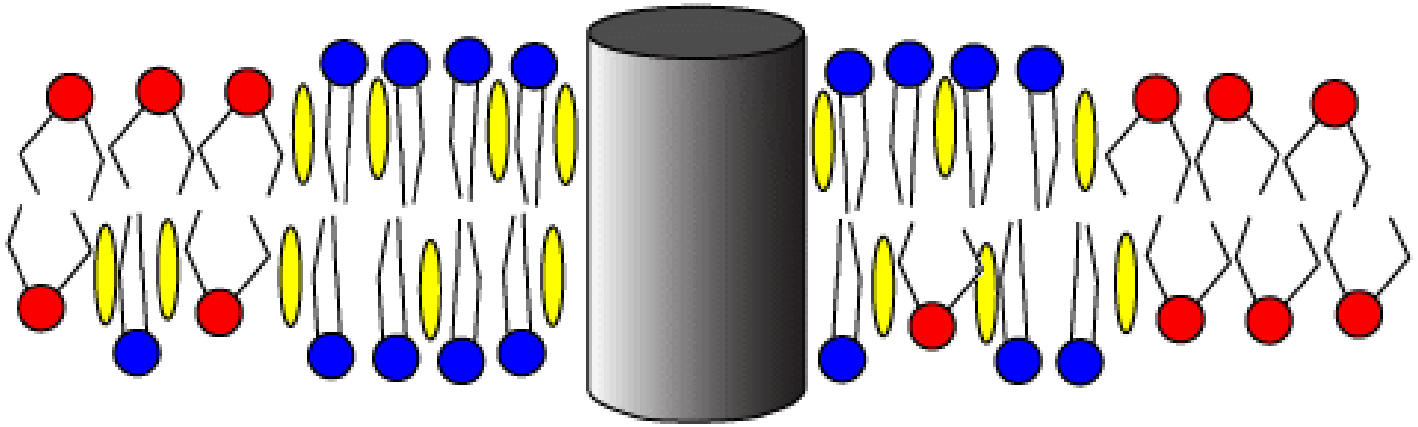
Cell Membrane Composition



We wish to simulate an active, dynamic membrane.

... then some cholesterol (c)...

Cell Membrane Composition



We wish to simulate an active, dynamic membrane.

... and finally add protein (p).

Hydrophobic Forces Drive Lateral Organization

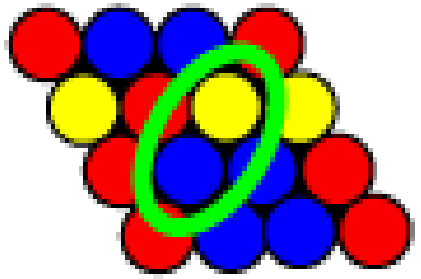
We encapsulate this process in an **interaction matrix**

J_o	s	u	c
s	-1.0	1.0	-1.0
u	1.0	-0.5	-0.5
c	-1.0	-0.5	0.2

and set the species on a fixed triangular lattice, where they interact at the nearest-neighbor level.

Nearest-Neighbor Monte Carlo

Should these two lipids swap locations? (top view)

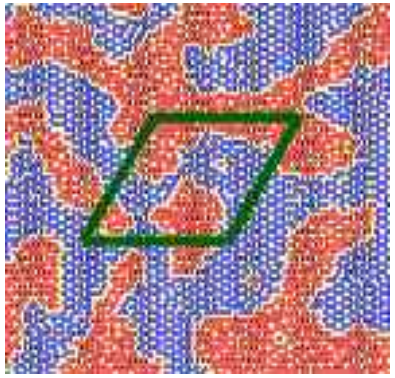
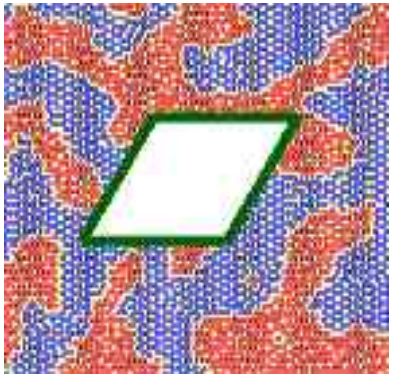
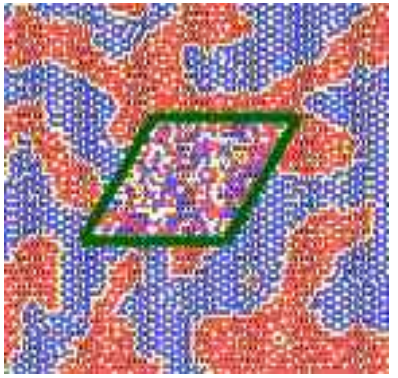


Lateral organization evolves via the Metropolis algorithm, using the total local interactions, *U*.

$$U - \frac{1}{2}\left[N_{ss}e_{ss} + N_{uu}e_{uu} + N_{cc}e_{cc} + N_{su}e_{su} + N_{sc}e_{sc} + N_{uc}e_{uc}\right]$$

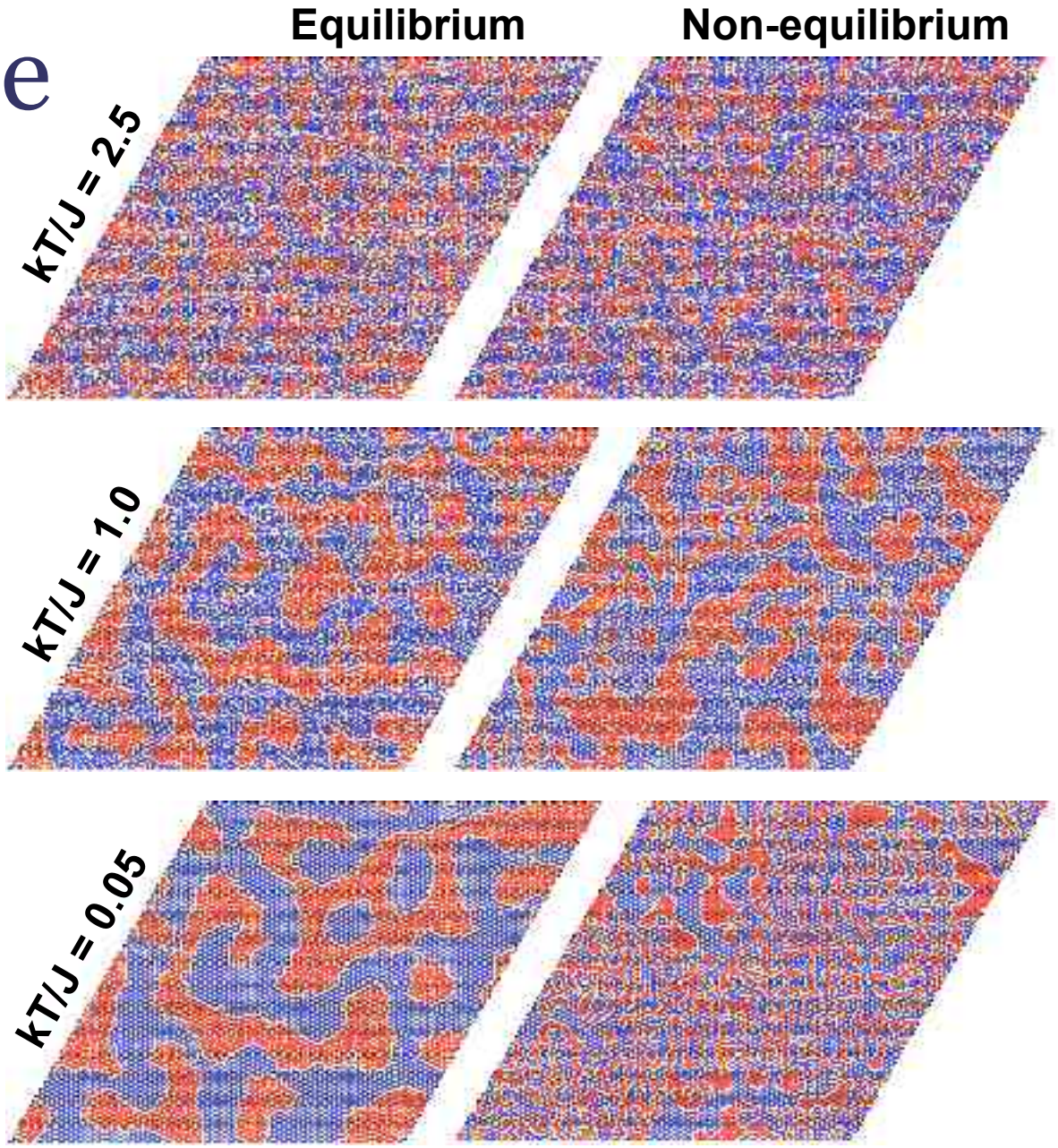
Incorporating Non-Equilibrium Behavior

Most past studies considered the membrane as an equilibrium system. But this is not realistic.

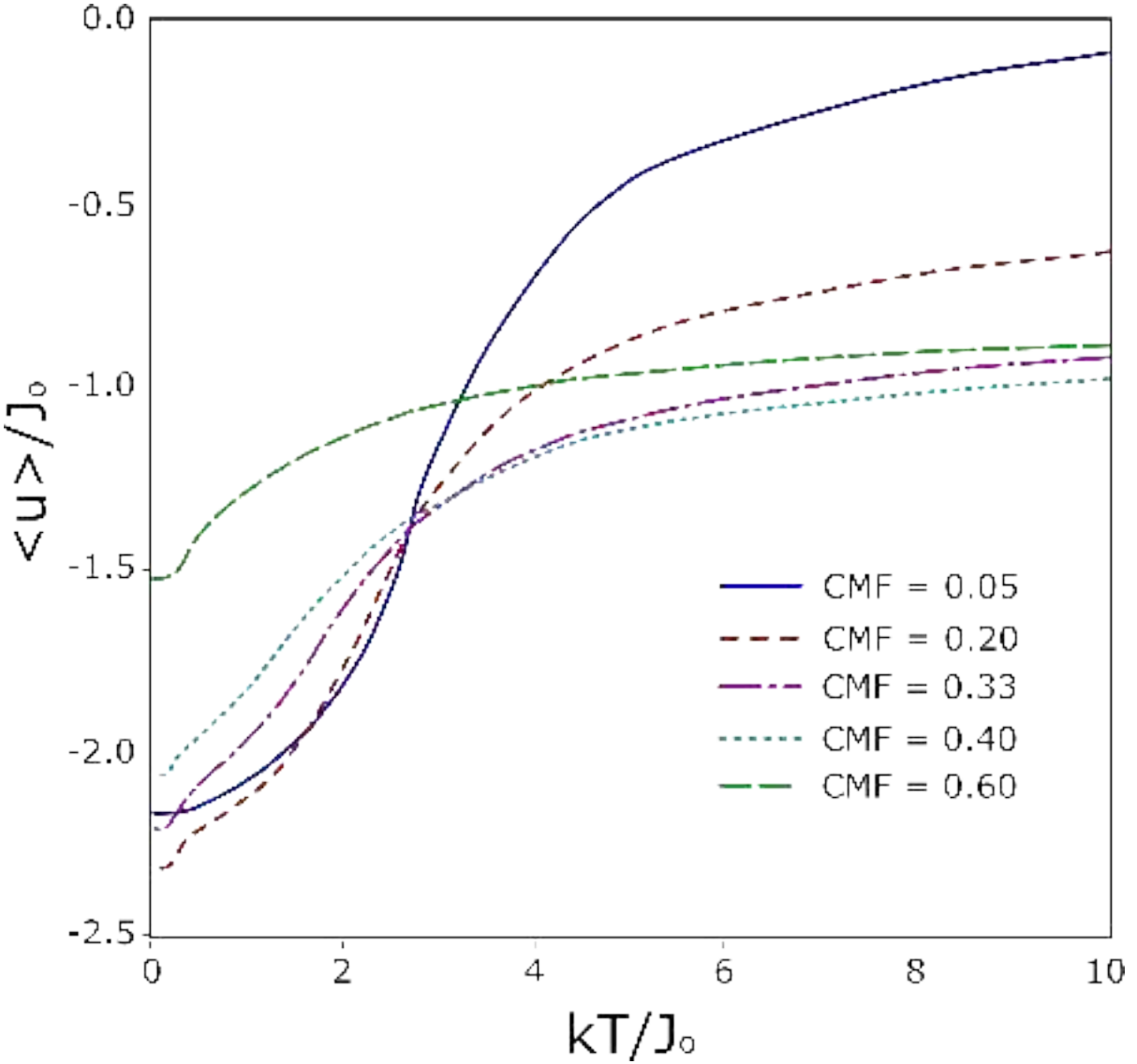
We use **simulated endo- and exocytosis** events to keep the system out of equilibrium.

Results: 1) Large Variety of Domain Sizes

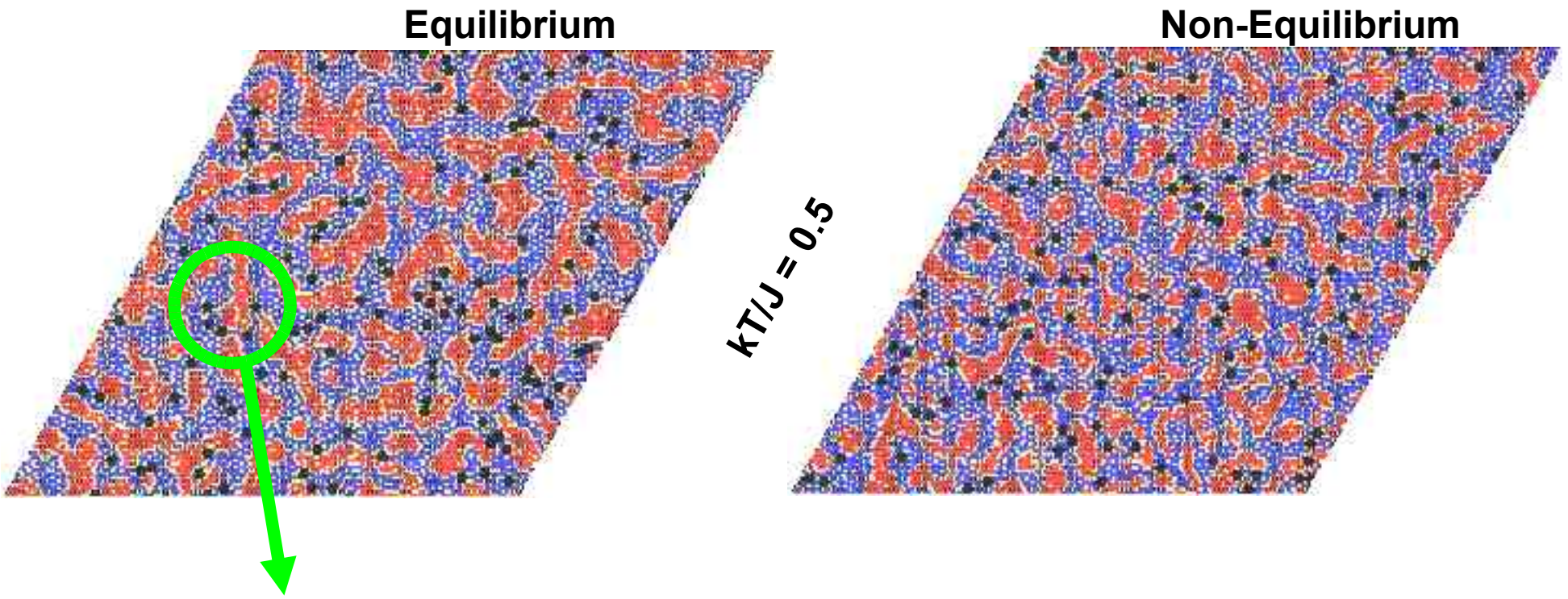


Incorporating only nearest neighbor interactions and simulated endo- and exocytosis, we can show nice variety in domain size and in cholesterol's mediating effects on unfavorable saturated-unsaturated interactions.

Results: 2) Adjusting Cholesterol Mole Fraction Alters Membrane T Response



Results: 3) Proteins Influence Lateral Organization on Several Scales



In particular, note the “smile” of protein that shepherds the unsaturated lipids to take the same fundamental shape.

Conclusions

Cholesterol mediates heterogeneity by reducing disorder of the biomembrane at high temperatures, and by enhancing disorder at low temperatures.

Simulated endo- and exocytosis lead to larger range of domain sizes and elevated values of internal energy per site.

The presence of **protein lays a fundamental road map** for lipid lateral organization.