Possible Extensions to Minimal Lipid Protein Model

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The lipid protein model as simulated in the computer (Webb, 2004), demonstrates one possible mechanism of protein sorting in the Golgi complex. The initial or minimal version of this model is only intended as a prototype, a foundation that can subsequently be extended in numerous ways. At this point it is very much a work in progress that requires critical input from the biochemistry community.

Some of the many possible fixes and extensions include:

1. Add additional 2D lattices to model multiple membranes in parallel (ER, Golgi, Plasma membrane), along with vesicle traffic between membranes. This cannot be (easily) done in NetLogo. C or C++ might be a good choice. Repast might be possible, but Repast applications use Java and may not have the required performance.
2. Develop a better measure of sorting than the one currently used and graphed.
3. Allow for any number of protein TMD lengths (2, 6, or whatever), although 6 may be all that is needed.
4. Allow for any number of lipid types. For example, an extended version could have Sphingolipid (or combinations of this with the other two types) as a third type in addition to Sopc and CholSopc (Lundbaeck, 2003).
5. The "Future Work" section of the paper mentions two additional independent variables that could be added in a future version. (1) Some finite probability ($0.0 < p <= 1.0$) that the movement of a lipid patch will also move any given protein embedded within that patch. (2) Lipids and proteins arriving in vesicles from the ER could already be somewhat clustered and pre-sorted.
6. Examine in the model how "cholesterol-induced changes in … material properties … can effect protein sorting" (Lundbaeck, 2003, p.2081).
7. Handle other aspects mentioned by Lundbaeck (2003), and by other authors. Should energetics be included in the model?
8. Add membrane curvature as a way to get lipid thickness. This was to have been an important part of the initial minimal model.
9. Add specific details contained in the biochemistry literature.
10. Add back those elements dropped from a slightly more complex version, when the minimal version was created.
11. Add genetic algorithms or some other appropriate approach, to optimize the lipid and protein movement parameters.
12. Set up a proper experimental design, run experiments using the model, and examine the results statistically.
13. Use the model to make testable predictions, or alter it so that it can make testable predictions.
14. Add details of mechanisms that facilitate vesicle budding and docking.

15. Add support for *kin recognition*. "Aggregation of proteins that function in the same compartment – called *kin recognition* – is a general mechanism that compartments use to organize and retain their residual proteins. Golgi enzymes that function together, for example, also bind to each other and are thereby restrained from entering transport vesicles." (Alberts, p.731)
16. Get the current version to work in NetLogo 2. The results when run with this newly-released version are different. The NetLogo 2 documentation mentions a number of changes that have been made, any of which could be causing the problem.
17. Fix bugs mentioned at the end of the paper (Webb, 2004).
18. Possibly submit the model to the NetLogo web site.

Alberts, B., et al. (2002). Molecular Biology of the Cell, 4th ed. New York: Garland Science.

Lundbæck, J., et al. (2003). *Cholesterol-induced protein sorting: An analysis of energetic feasibility*. Biophysical Journal 84: 2080-2089.

Webb, K. (2004). ALife – Project Report. Brighton: University of Sussex Artificial Life course.