IN5100:
Modeling and Analyzing Protein Aggregation in the Brain

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Curriculum

The curriculum is the paper

> Lucian Bentea, Peter Csaba Ölveczky, and Eduard Bentea: *Using Probabilistic Strategies to Formalize and Compare α-Synuclein Aggregation and Propagation under Different Scenarios.* In Proc. CMSB 2013. In volume 8130 of Springer's Lecture Notes in Computer Science. Available at `https://link.springer.com/chapter/10.1007%2F978-3-642-40708-6_8`.

What to Know?

I do not expect students to have much knowledge of the brain, proteins, etc. Furthermore, I do not expect you to know the language *PSMaude* in detail. The point is that in PSMaude you have a "base" Maude/rewriting logic model, which may not be probabilistic, of a system. To add probabilities to such a Maude model, in PSMaude you can add "weights" to the different rewrite rules (so that a rule with larger weight has a greater probability of being applied to a state than a rule with less weight), and also to *how* that rule is executed (i.e., where in a term should the rewrite take place, etc). These weights are then used to probabilistically select *which* rule to apply, and *how* to apply it.

You should do well on this stuff if you can answer (and understand) the following questions:

- What does the paper want to do, and why? (What is the point? Why is this potentially important/useful?)
- What are the different "settings" being analyzed?
- (Section 2) What "causes" Parkinson's Disease (PD) according to the paper?
- The paper talks about different (3–4?) "kinds" of protein aggregates. Which ones? Which is the one you absolutely do not want to have in your brain?
- Very roughly, how can these proteins spread?
- (Section 3) Roughly, how are brains modeled in Maude in this paper?
- What happens in the five equations on page 97?

- What happens in the four rewrite rules `oligomerElongation`, `oligomerDissociation`, `aggNucleusFragmentation`, and `lysosomalAutophagy`?
- (Section 4) Consider the large chunk of "code" on page 100.
  - In a healthy 40-year-old person, how much more likely is it that rule `oligomerElongation` (bad rule, I guess) is applied instead of the rule `oligomerDissociation` (good rule, I think) being applied?
  - How do the "rule weights" capture the fact that things get shittier the older we get?
- (I would not worry about the top half of page 101.)
- How are weights changed to model different kinds of persons (predisposed and predisposed taking rapamycin)?
- (Section 5) What kind(s?) of analysis is performed?
- What are the "outcomes" (results?) of these analyses?
- (Think for yourself) What could be some weaknesses with this work and method?