Non-equilibrium Protein Complexes as Molecular Automata

Considerable effort is being put into understanding how biological and biomimetic systems store and process information, a field known as molecular computation. Here we build a thermodynamically consistent kinetic model of a molecular complex made of identical subunits which can be in one of two states (e.g., phosphorylated or not). We then analyse the dynamics of the complex when each subunit can be modified by driven enzymes which act conditionally based on the state of its neighbours. For strongly driven enzymes we identify a one-to-one mapping to elementary cellular automata rules, each rule corresponding to a set of up to eight enzymes. Among these rules we find a rich set of behaviours, including multistability and dynamical steady states. Finally, we show how to deterministically manipulate the state of the complex by sequentially changing the rule (i.e. which enzymes are present).

1 New Notes/Outline/Points to mention

- describe the model
  - Identical subunits
  - Out-of-equilibrium + kinetic model
  - Rates depend on nearest neighbors
  - Thermodynamically consistent, but maximally driven
- what we find
  - connection to cellular automata (classic model of computation)
  - rich set of behaviours
  - identify analyze attracting components (attractors) which include
    - multistability and dynamical steady states
    - individual states (with basins of attraction)
    - loops (directed or not), single state or branching, of either travelling waves or transitioning between all 0s and all 1s
    - more complex components, including plane/2D like structures
  - we look at
  - can provide insights on the "error correction" ideas of Crick and others - can have a rule that error corrects but nothing else and can put limits on it from the nearest neighbour limit (no global counting)

- context/significance
  - Molecular computation? It is relevant, worth noting that MC is generally on DNA so this is perhaps a new perspective?
  - Allostery? it is related but not sure what

2 Old New Notes

2.1 Questions and things to discuss

- Title! Right now it is very clunky. Should it include "thermodynamically consistent"?
- Conclusion bit! Very much not sure about it as it is – is it too short? Should I specifically cite the paper I do there as that really proposes a similar but different model for it, or should I instead highlight the locality difference we add to it? Not sure
- In order to expand the conclusion I need to slightly cut down something.
- Should I reference the figure from the abstract?
- Little Things
  - Should I explicitly list what our futile cycle is? It's a bit long and perhaps obvious but I think it's nice to give a concrete, simple thing to visualize.
  - I should probably check that using "artificially" where I do is appropriate.
  - "this robustness" $\rightarrow$ "biological robustness"?
  - Is "We consider" acceptable language?

2.2 General

- So going for **Clocks, timers and cell cycle dynamics** topic
- Can I squeeze in "non-Hermitian topology" somewhere (I have some references for it, and it is relevant)?

3 Old Notes

Format For POL2025 (the one due on the 6th) it should be 250 words, include references and up to 1 figure.

Topic I need to choose one of a list of topics. Perhaps the closest might be: **"Biomolecular assemblies and condensates"** given that the main model is of an allosteric assembly? Others that may be relevant:

- "Patterns, waves, transport, collective phenomena, and microswimmers" – there's collective phenomena! but idk about microswimmers
- "Clocks, timers and cell cycle dynamics" – if we lean into KaiABC then maybe
- "Protein structure, dynamics and interactions" – cause I guess the polymer as I've been calling it would realistically be a protein?
- "Emerging Areas in the Physics of Life" – idk what this is but probably not

3.1 Questions

- Approach to talk about a project that has only just started?
- Should I be talking about allostery or not so much? It seems relevant and as an interesting topic but it's not really a core ingredient in it.
- I'm a bit worried that the only "result" is a bit obvious once you think about it. If we add a penalty for NN having different conformation then of course the ones with all the same conformation will be preferred. Then if all are in conformation 1 (tense) then they are ATP driven to bind ligands so they do so. After that they are by our choice of parameters not favoured to debind hence the only thing they can do is change conformation. The same sort of reasoning then completes the cycle.
- Is an ArXiV citation admissible here?

3.2 Key points to cover

- stochastic systems
- futile cycles
- non-equilibrium dynamics
- allostery
- system features
  - complex – high dimensional network, not pen-and-paper tractable
  - locality – unlike the previous models, have NNs, can model waves along the polymer
  - discrete configurational space
  - Thermodynamically consistent? idk if this is the right wording

- Search for topological states/patterns in realistic systems (this means starting from the ground up with (non-equilibrium) statphys, LDB, no arbitrary choices) with futile cycles
- the futile cycle is implemented via physical parameters by coupling to two physically reasonable asymmetrical processes