Topological States in Out-of-Equilibrium Allosteric Assemblies

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Stochastic systems are key to many areas of biophysics as much of living matter takes place in a highly noisy environment. However, despite this noisiness, many biological systems show a high degree or robustness. A recent new direction in understanding this apparent paradox is the study of topology of stochastic systems[1–3]. Topological states can effectively reduce the dimensionality of the configurational space and thus can explain robustness without making specific assumptions about the mechanics of a system, while themselves being robust to local changes. In this study we look for topological features in a non-equilibrium, thermodynamically consistent stochastic model of an allosteric assembly where each unit can change conformation and (de)phosphorylate. The system is driven out of equilibrium by the inclusion of two different phosphorylation reactions: a direct reaction by (de)binding a phosphate group and one driven by ATP to ADP conversion. We allow these to couple differently depending on subunit conformation as this is to only way for an isolated subunit to favour undergoing a futile cycle of phosphorylating, changing conformation, dephosphorylating and changing conformation back. Such futile cycles are common in biological settings[4, 5] and give rise to topological currents when imposed artificially[1]. We find that even without explicitly favouring futile cycles in the assembly, adding a nearest neighbour interaction results in a directed probability currents in the steady state.

References

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[3]C. Zheng and E. Tang, "A topological mechanism for robust and efficient global oscillations in biological networks", Nature Communications **15**, 6453 (2024).

[4]A. K. Sharma, R. Khandelwal, and C. Wolfrum, "Futile cycles: Emerging utility from apparent futility", Cell Metabolism **36**, 1184–1203 (2024).

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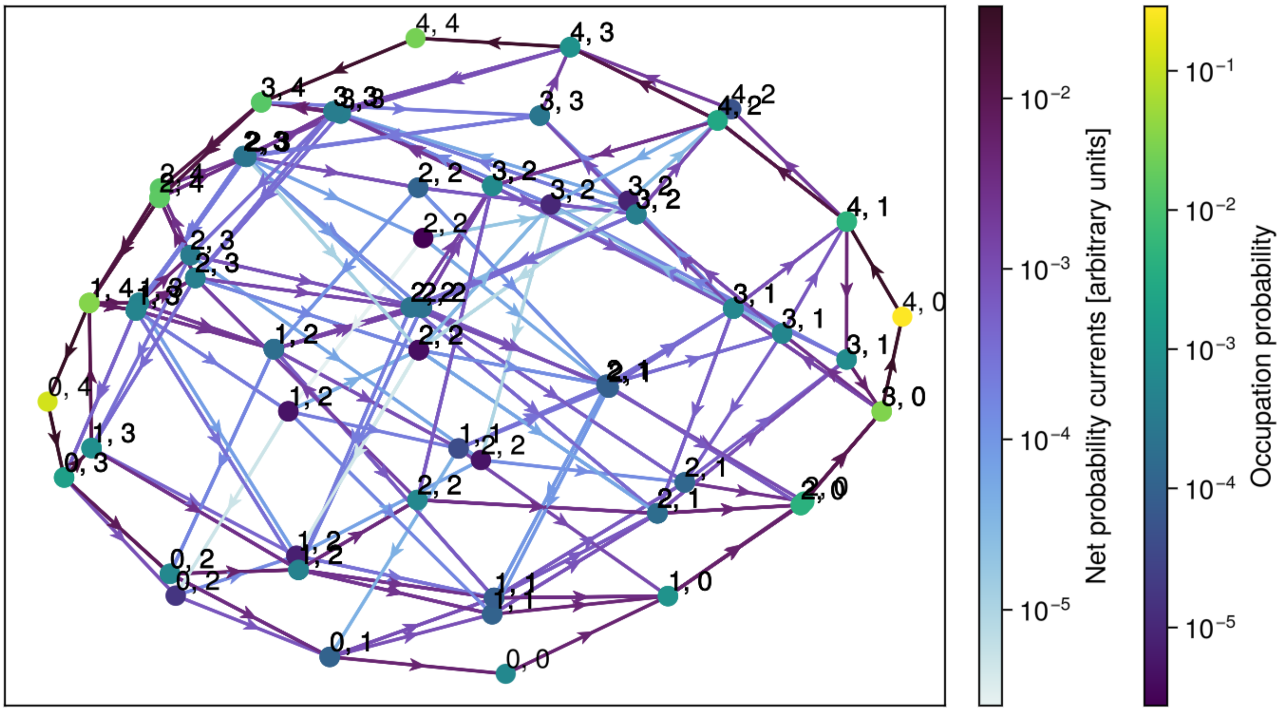

Net probability currents [arbitrary units]
10^{-2}
10^{-3}
10^{-4}
10^{-5}
Occupation probability
10^{-1}
10^{-2}
10^{-3}
10^{-4}
10^{-5}

1 Notes

1.1 Key points

- 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

1.2 Topic?

- 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

1.3 "Formula"

Title/Topic

Motivation Topological phases have been a hot topic in physics ever since the quantum hall effect. Recently their study has been extended to non-Hermitian systems such as a non-reciprocal stochastic processes.

Problem Idrk?

Study design

Predictions and results

Conclusions