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NITMB MathBio Convergence Conference
National Institute for Theory and Mathematics in Biology
Funded by the U.S. National Science Foundation and the Simons Foundation

How does the cell stay mechanically rigid even when its architecture constantly changes?

Rigidity homeostasis of the actin cortex emerging from mechano-sensitive filament and crosslinker dynamics

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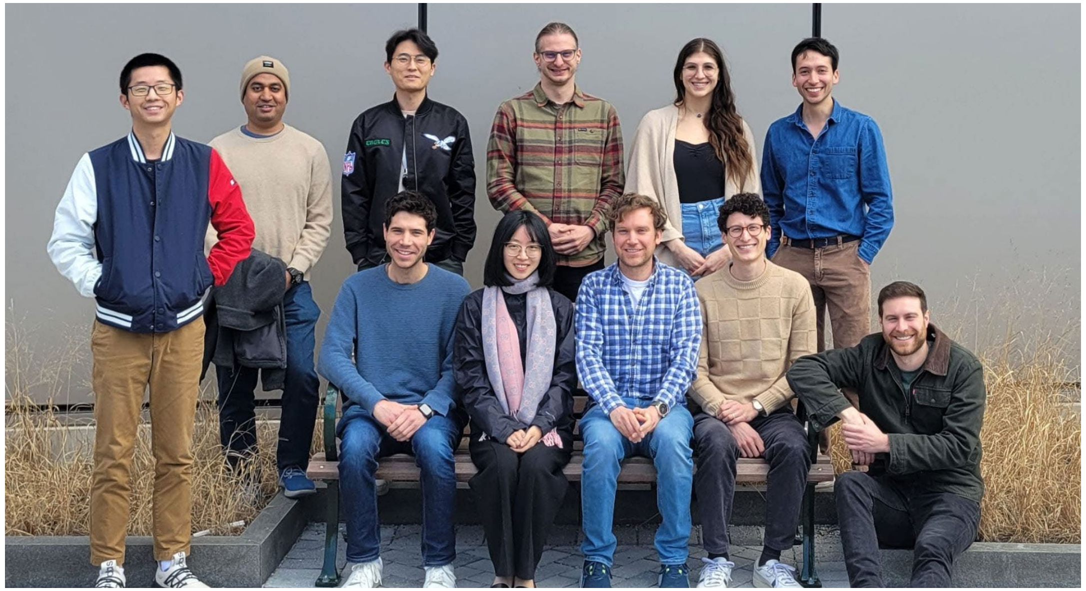
NITMB MathBio Convergence Conference

Chicago, August 2025

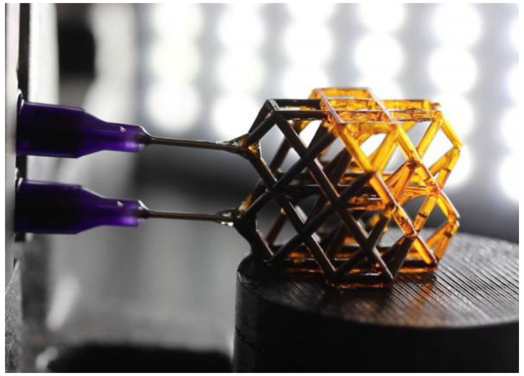
About me

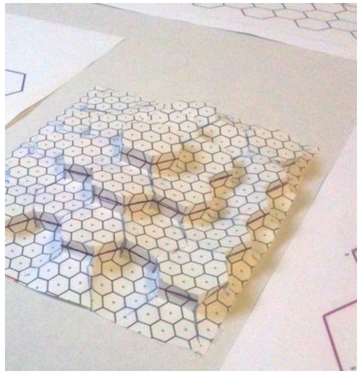
- Postdoc fellow at Center for Soft and Living Matter @ Penn
- Princeton *24 – Sal Torquato group
  - Statistical mechanics, chemical physics, metamaterials design
- Penn – Biophysics & systems biology via computational modeling
  - “Algorithms that cells live by”

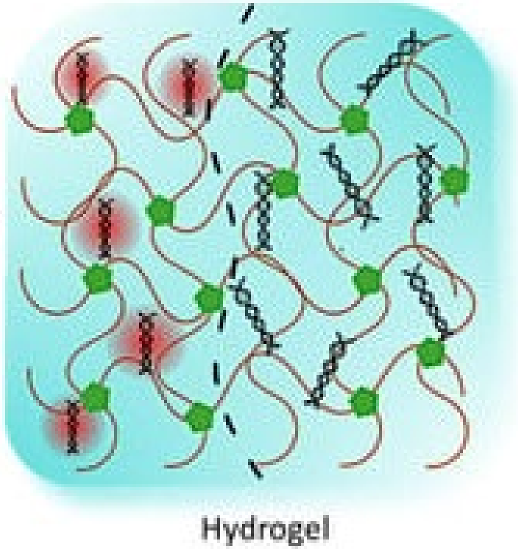


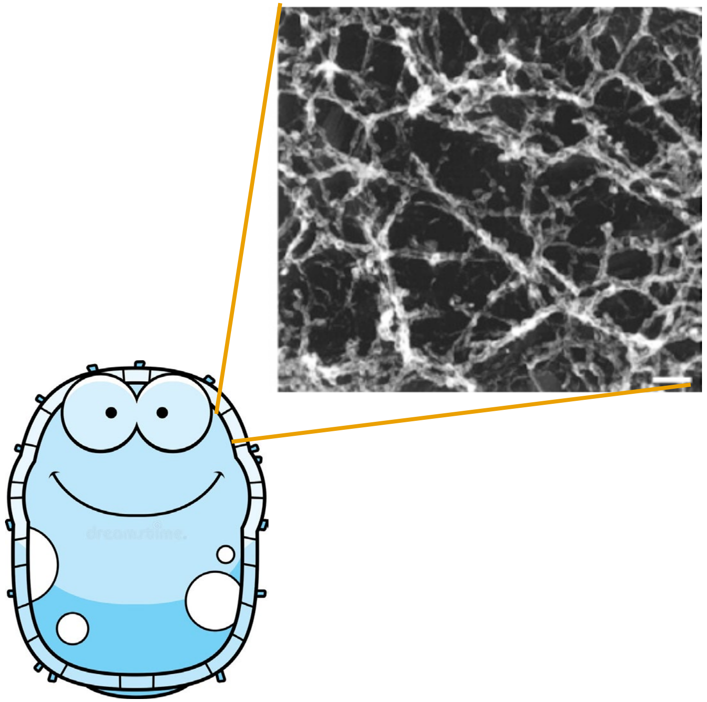
The cell as a **mechanical** engineer

- **Metamaterials** are natural or engineered materials whose properties arise from meso- or macro-scale structure—not just chemical composition on the molecular level
  - 3D printed structures
  - Knitted fabrics
  - Origami/Kirigami
  - Hydrogels
- **Actin cortex**, a network made of actin filaments.
  - Located beneath the cell membrane, it supports cell shape and regulates mechanic responses.

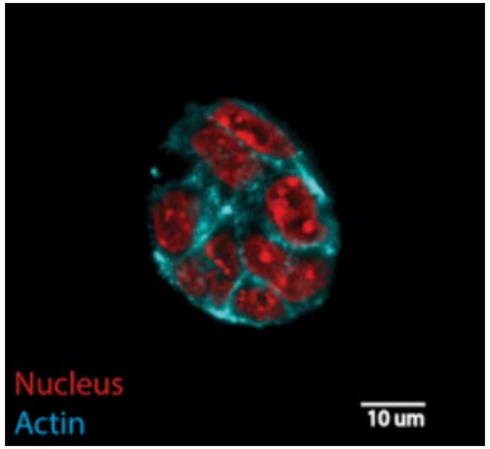




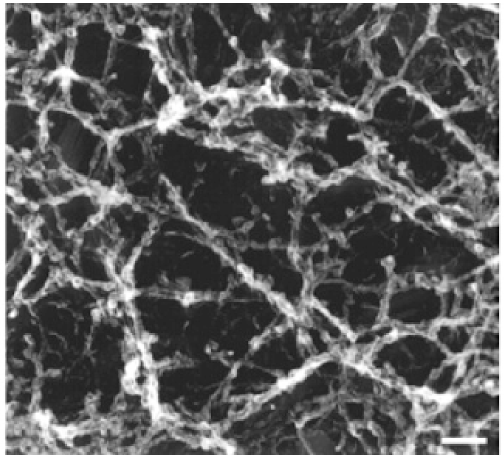




The actin cortex is both rigid and highly dynamic

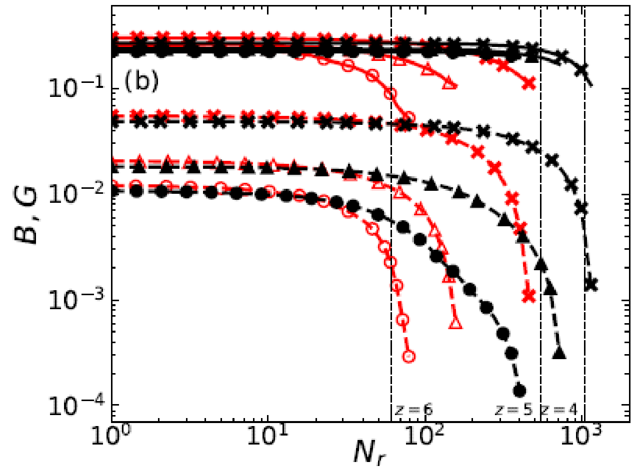


Chalut & Paluch 2016

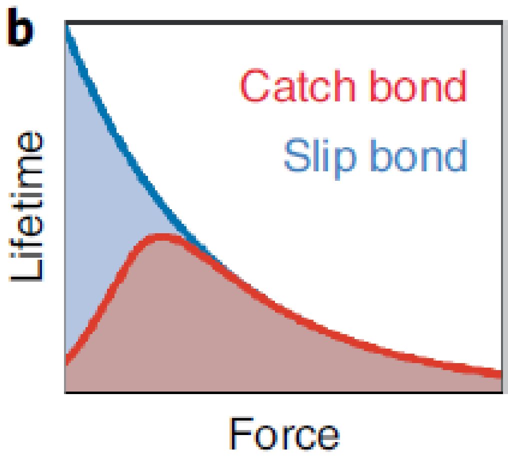

Stossel et al. 2001

- **Tensional rigidity:**
  - Average coordination number $3 < \bar{z} < 4$ is below Maxwellian isostaticity $\bar{z} = 6$
  - Prestressed filaments shifts the floppy-rigid phase transition to smaller $\bar{z}$
- Filaments and crosslinkers undergo **fast turnover**; $\tau \sim 30$ seconds (Fritzsche 2013)
  - Regulated by actin-binding proteins: motors, severing proteins and crosslinkers
  - Can take up to 50% of ATP hydrolysis!
- Why and how?

Mechano-sensitive dynamics: "use it or lose it"



Galvani et al. 2025



Mulla et al. 2022

- **For filaments**
  - At biologically accessible strains (5%), **random pruning of filaments destroy rigidity** at $\bar{z} > 4$.
  - **Tension-inhibited pruning** of filaments preserves rigidity at $\bar{z} \leq 4$.
- **For crosslinkers**
  - Weak **catch bonds** can make stronger networks
  - Common crosslinkers (α-actinin, vinculin) exhibit crosslinking property

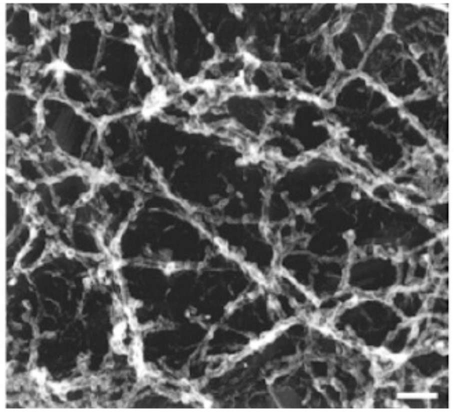
Marco A. Galvani Cunha et al.
Phys. Rev. Research 2025

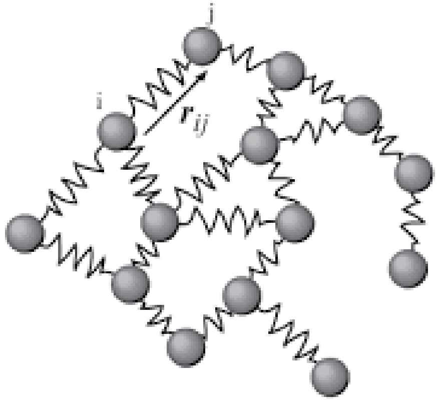
Goals

- To understand how **tensional rigidity** of the actin cortex can persist amid **complete structural turnover**.
- To understand the role of **mechano-sensitive local rules** in rigidity homeostasis:
  - Can cortex-like behavior emerge from a **minimal set** of rules governing filament and crosslinker dynamics?
- To study **topological and geometrical properties** of the cortex models.

Models

Model cortex as spring network

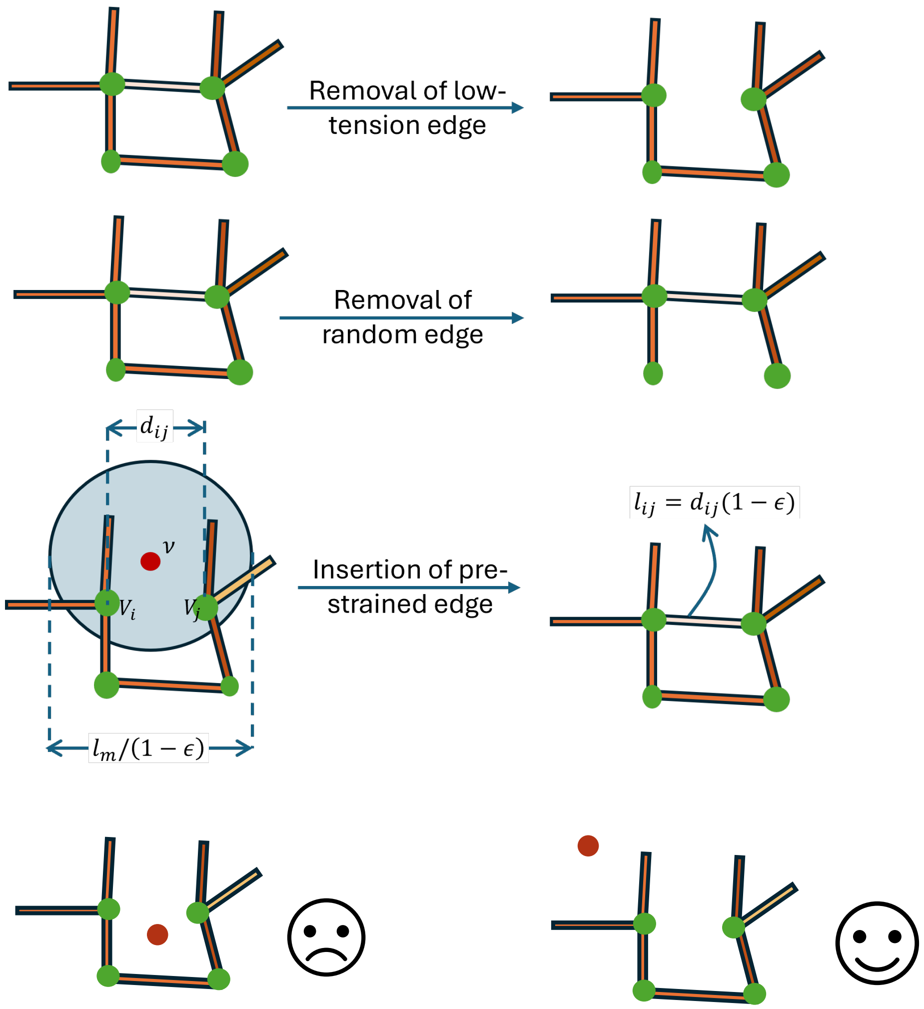




$z \leq 4$ for every node

- Actin filaments → edges; Crosslinkers → nodes
- Incorporation and pruning of filaments → Addition/deletion of edges
- Binding/unbinding of crosslinkers → Splits and merges of nodes: $z_i \longleftrightarrow\ z_i - 1$ and 1
- Assume tension-dominated regime: no bending rigidity

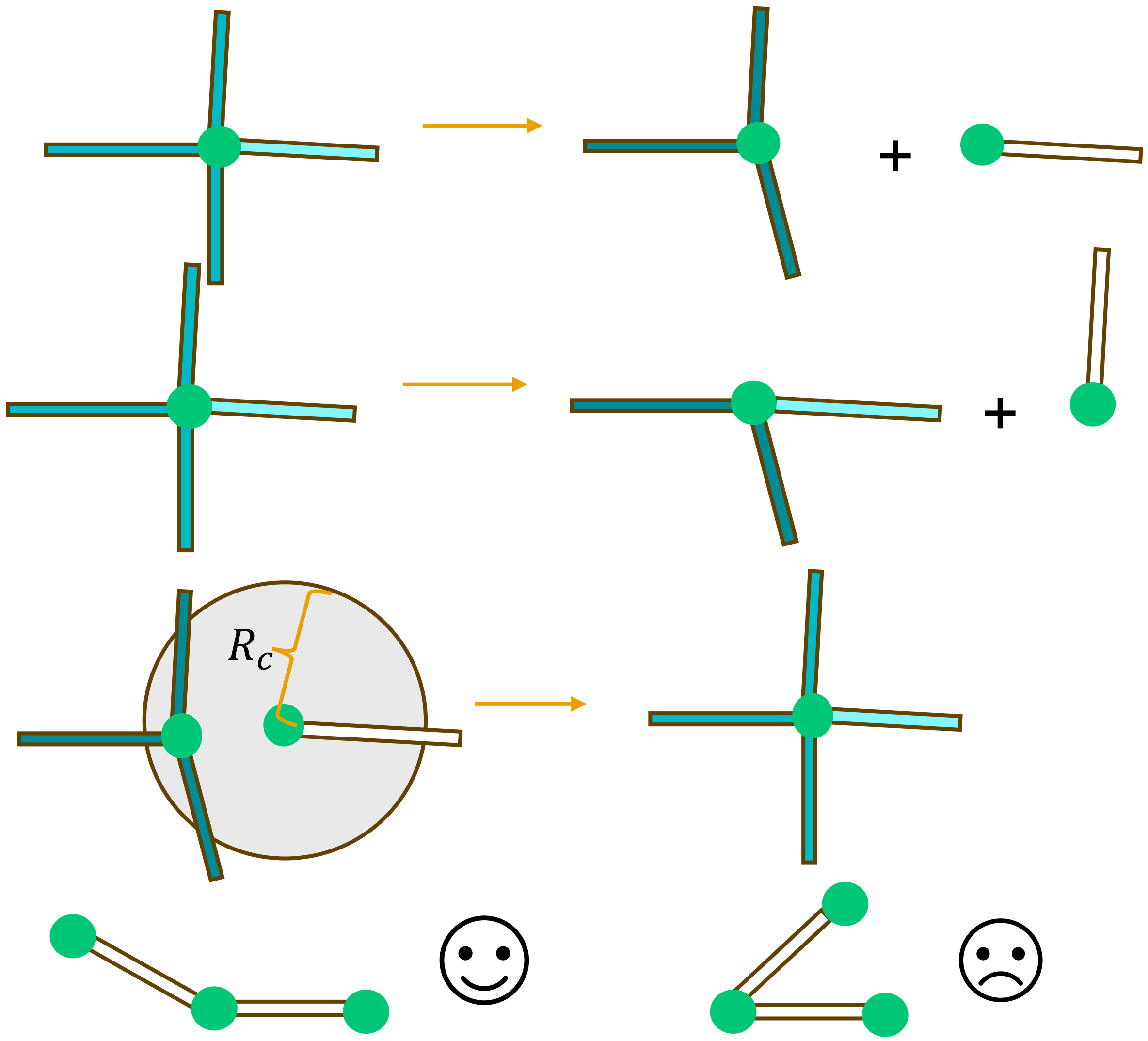
Dynamic edge model



- **Tension-inhibited pruning.** An edge under low tension below threshold Θ_E is always removed
- **Small fraction of random pruning.** An edge can be randomly removed with a small probability regardless of its tension
- **Insertion of prestrained edges.** Energy is injected
- **Steric repulsion.** New nuclei are preferentially formed where the local filament density is smaller

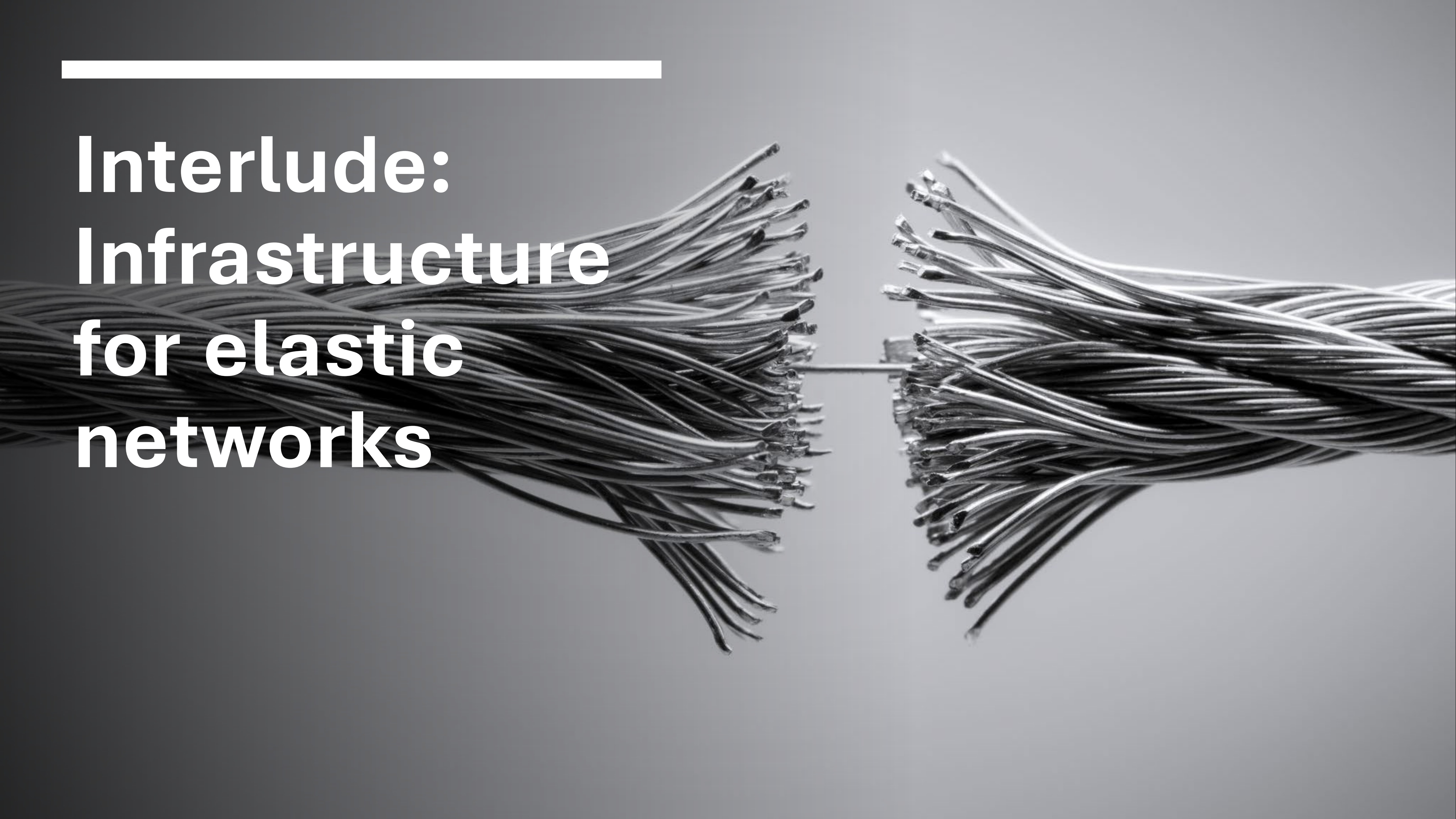
Marco A. Galvani Cunha

Dynamic node model

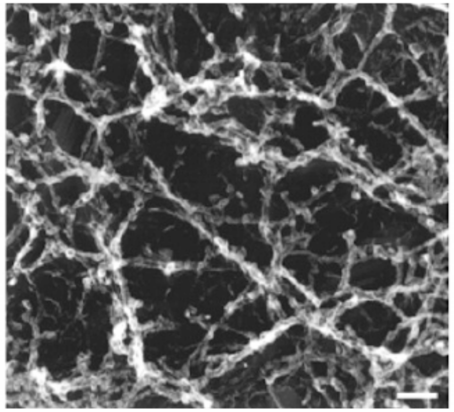


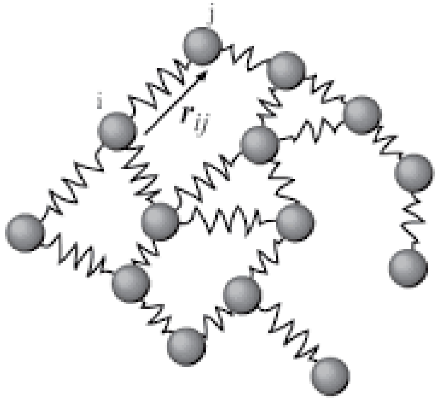
- **Force-sensitive disassembly.** A node splits into nodes with degrees $z-1$ and 1 if the tension on one of its edges < threshold Θ_V
- **Small fraction of random disassembly.** A nodes can be randomly split with a small probability regardless of tensions on the associated edges
- **Assembly + Energy injection.** A $z=1$ node merges with its nearest $z \leq 3$ node in a capture sphere of radius R_c
- **Steric repulsion.** To orient edges at large angles

Interlude: Infrastructure for elastic networks



Elastic networks: Excellent models for metamaterials





- Elastic network have been “rediscovered” many times in biology and civilizations alike!
  - Lightweight yet stiff, saves materials
  - Highly programmable structures down to individual edges and nodes
  - “Many more is more different”
- I developed a package, ElasticNetwork.jl, to treat them generally.

The `Network` data structure

`ElasticNetworks.Network` — Type

```
mutable struct Network
```

Models a Hookean spring network.

Fields

- `g::SimpleGraph` : Graph specifying the connectivity of the network.
- `basis::Matrix{Float64}` : Basis for the nodes.
- `points::Matrix{Float64}` : Coordinates of the nodes in space.
- `rest_lengths::Dict{Graphs.SimpleGraphs.SimpleEdge{Int64}, Float64}` : Rest lengths of the spring edges in the network.
- `image_info::Dict{Graphs.SimpleGraphs.SimpleEdge{Int64}, Vector{Int}}` : Specifies which image of node `j` node `i` is connected to in periodic boundary conditions.
- `youngs::Dict{Graphs.SimpleGraphs.SimpleEdge{Int64}, Float64}` : Young's modulus of the spring edges, defining their stiffness.

source

Demo:
Create & modify networks & Compute elasticity tensor

```julia
using ElasticNetworks
```
✓ 1m 36.4s

```julia
l = 10 #box side length
ϵ = 0.05 #edge prestrain
diamond_net = diamond1000(l, ϵ)
visualize_net(diamond_net)
```
✓ 0.3s

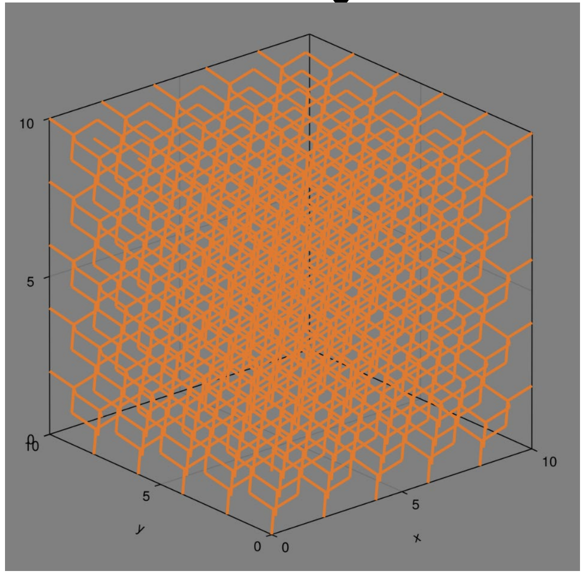
```julia
collect(edges(diamond_net.g))
```
✓ 1.0s

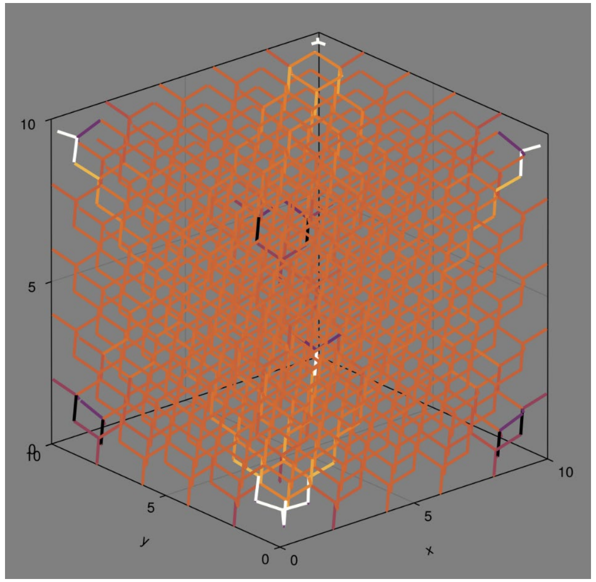
```
2000-element Vector{Graphs.SimpleGraphs.SimpleEdge{Int64}}:
 Edge 1 => 501
 Edge 1 => 746
 Edge 1 => 775
 Edge 1 => 980
```

```julia
ElasticNetworks.rem_edge!(diamond_net, 1, 501)
```
✓ 0.2s

```
1.0
```

```julia
relax!(diamond_net)
visualize_net(diamond_net)
```

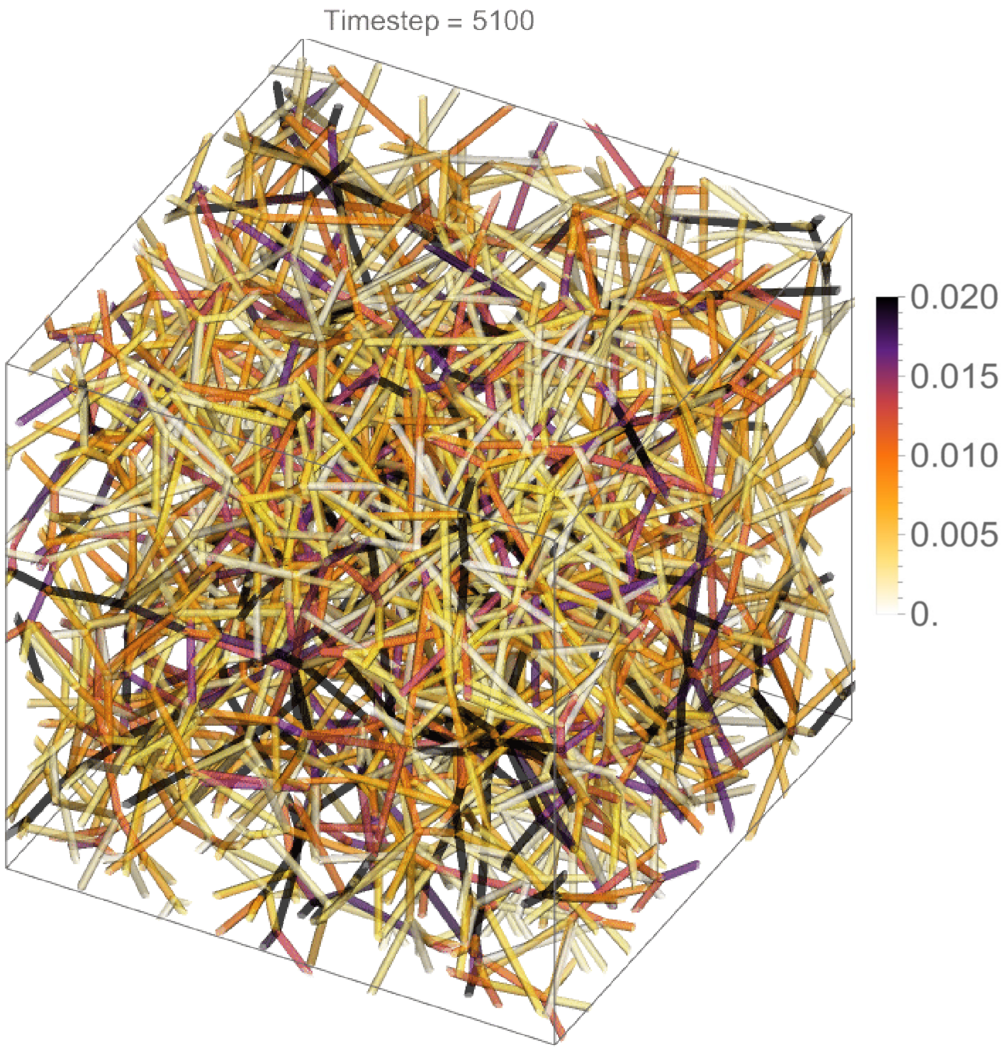


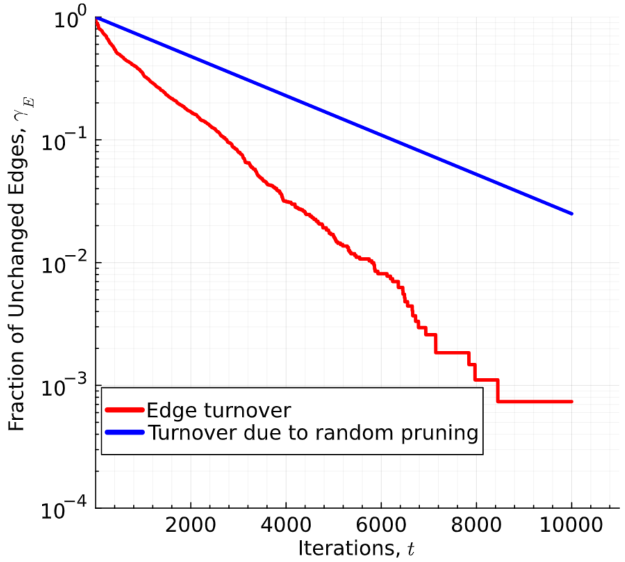



```
julia> moduli(d)[3]
6×6 Matrix{Float64}:
 0.253246     0.232323     0.232323      2.30984e-17   1.65179e-17   1.72611e-17
 0.232323     0.253246     0.232323      1.62234e-17   1.38788e-17   1.88164e-17
 0.232323     0.232323     0.253246      1.77788e-17   1.7949e-17    9.92385e-17
 2.30984e-17  1.62234e-17  1.77788e-17   0.0401173     1.06088e-16  -2.43431e-18
 1.65179e-17  1.38788e-17  1.7949e-17    1.06088e-16   0.0401173    -4.73978e-19
 1.72611e-17  1.88164e-17  9.92385e-17  -2.43431e-18  -4.73978e-19   0.0401173
```

Results for rigidity homeostasis of the actin cortex

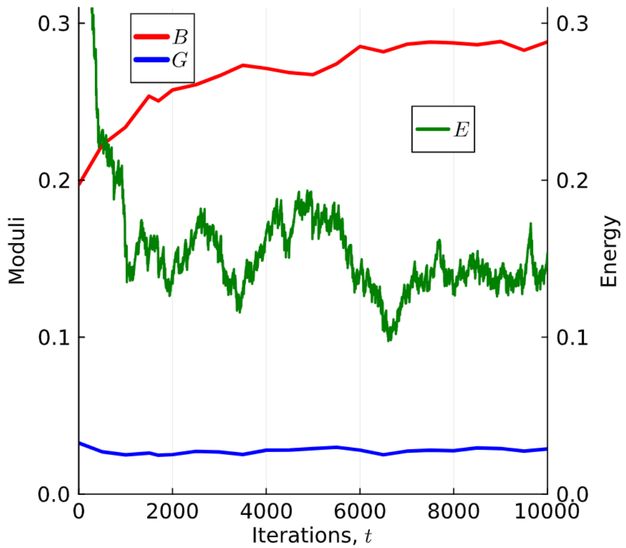
Rigidity homeostasis with complete edge turnover





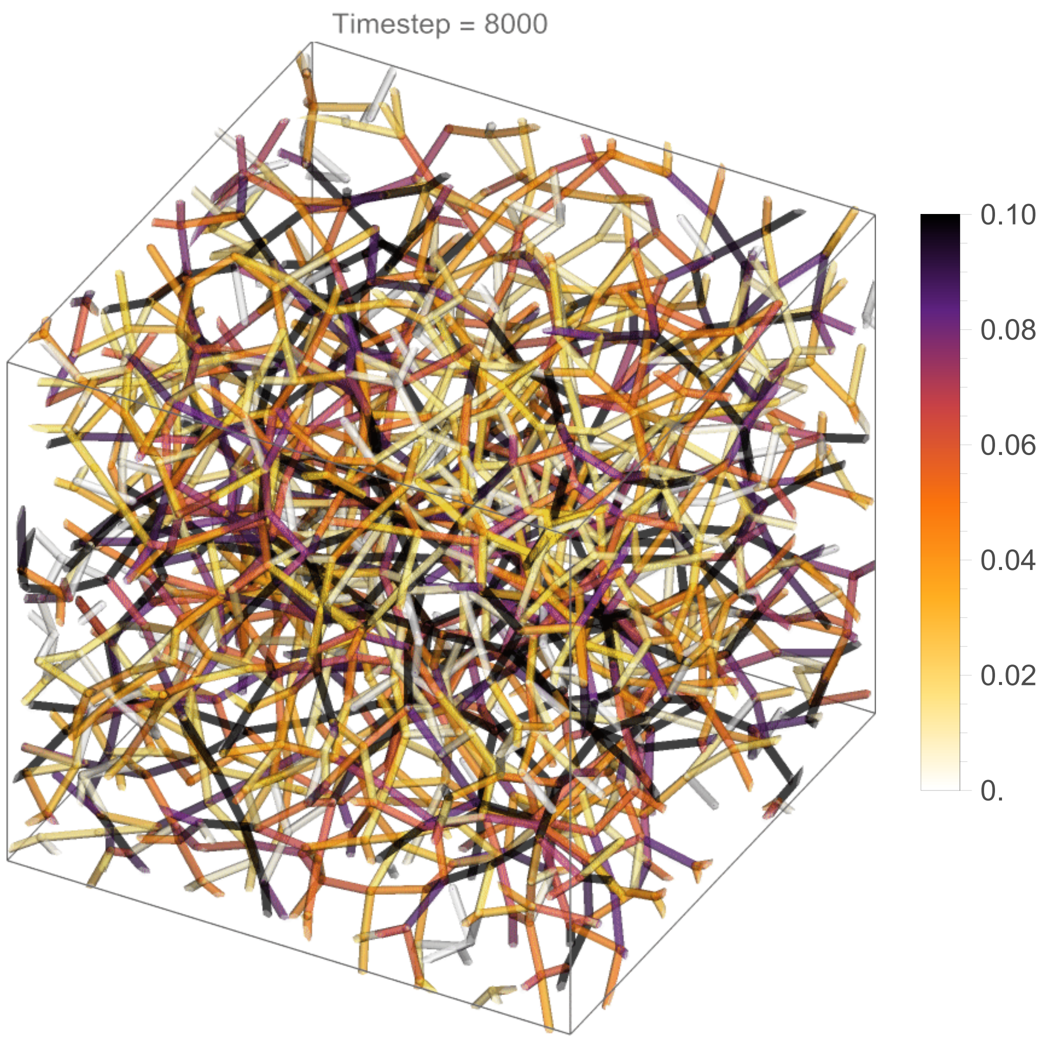
Exponential decay of edge labels

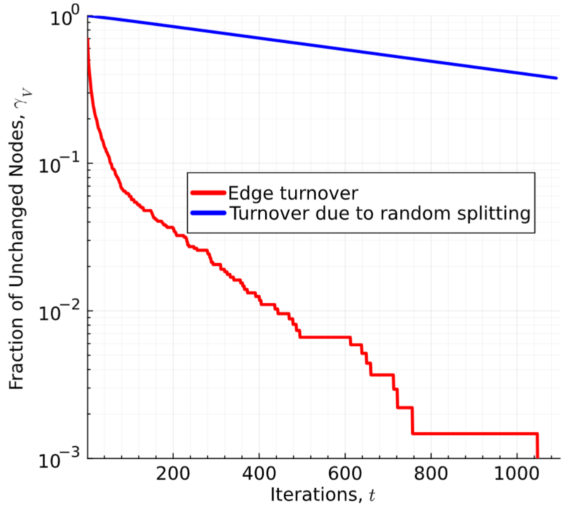
Turnover time scale τ = 1335 timesteps



Mechanical properties reach steady states

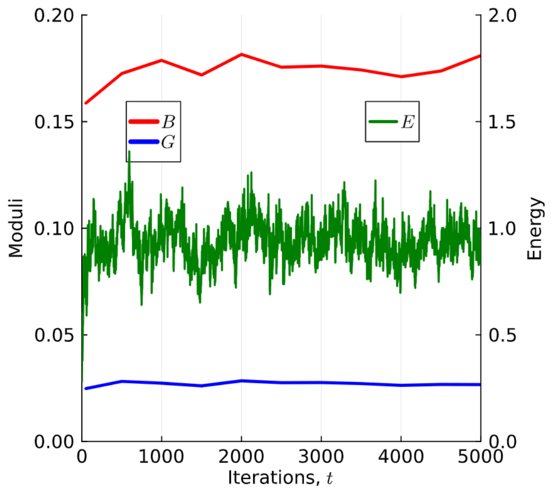
Rigidity homeostasis with complete node turnover





Exponential decay of node labels

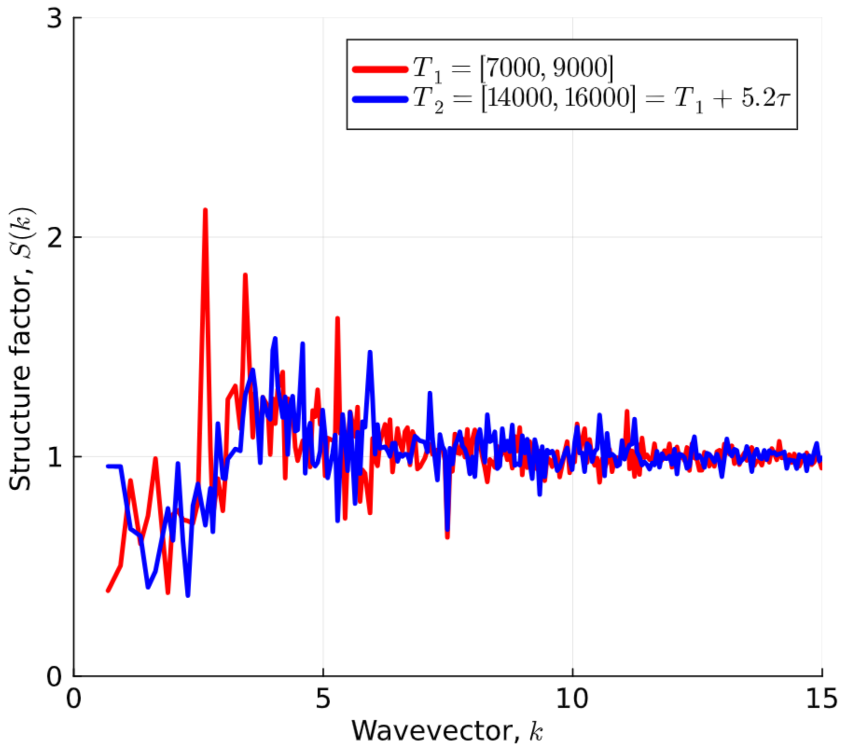
Turnover time scale τ_V = 173 timesteps

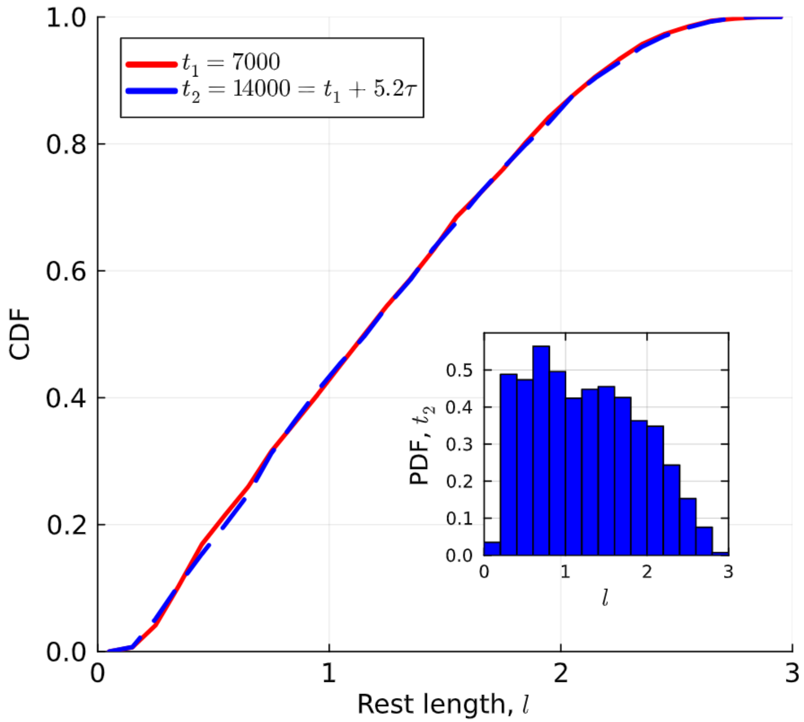


Mechanical properties reach steady states

Structural properties also reach steady states

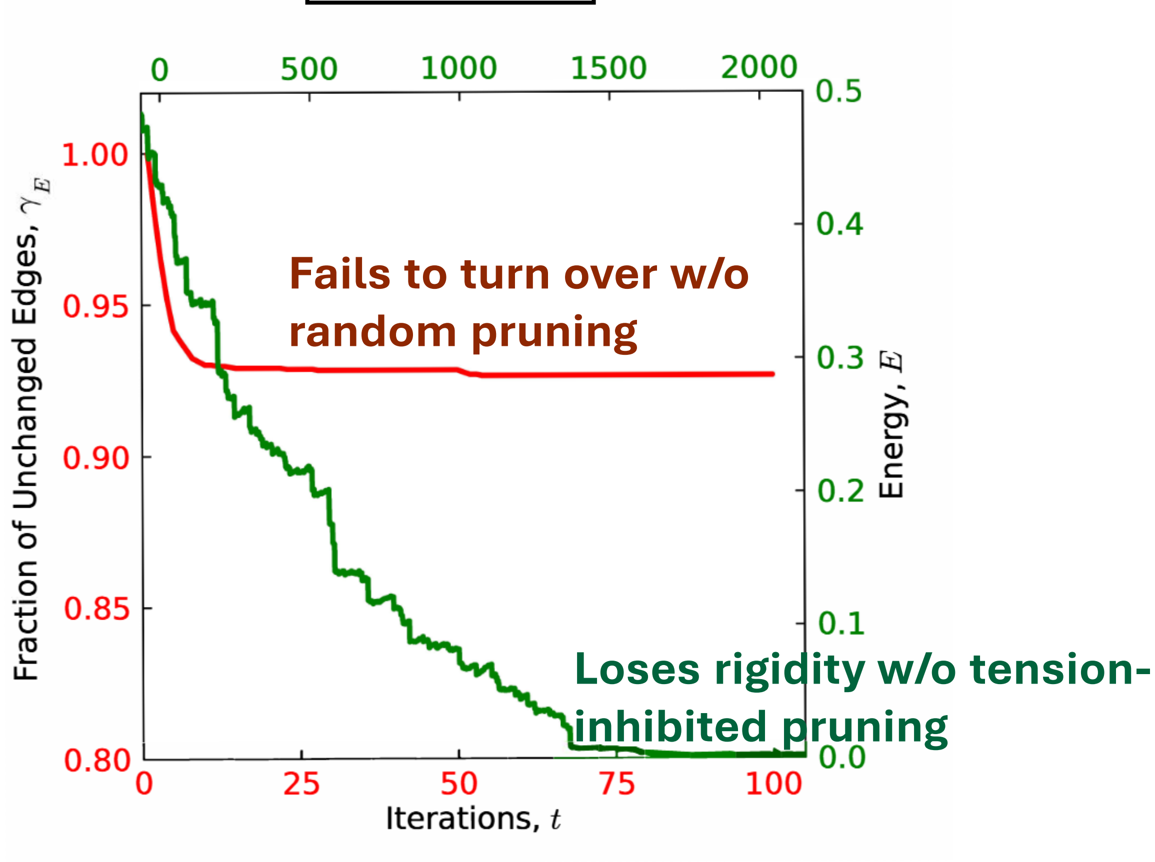
Edge model



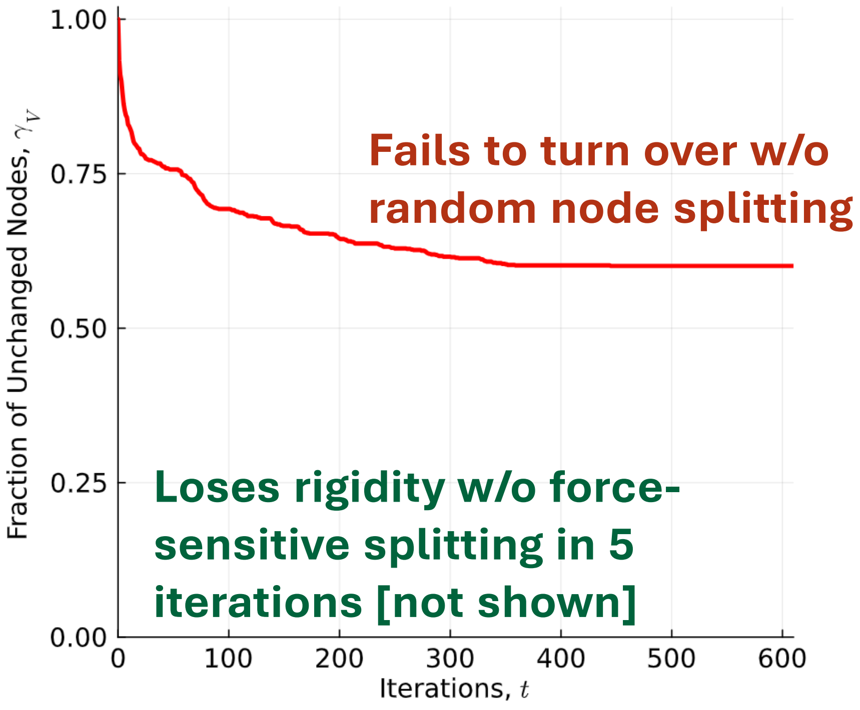


Ingredients in our models are indeed minimal

Edge model

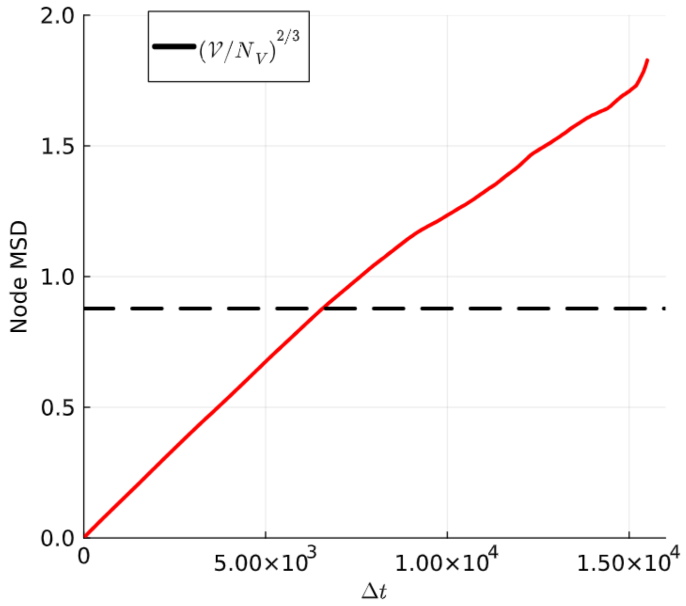


Node model

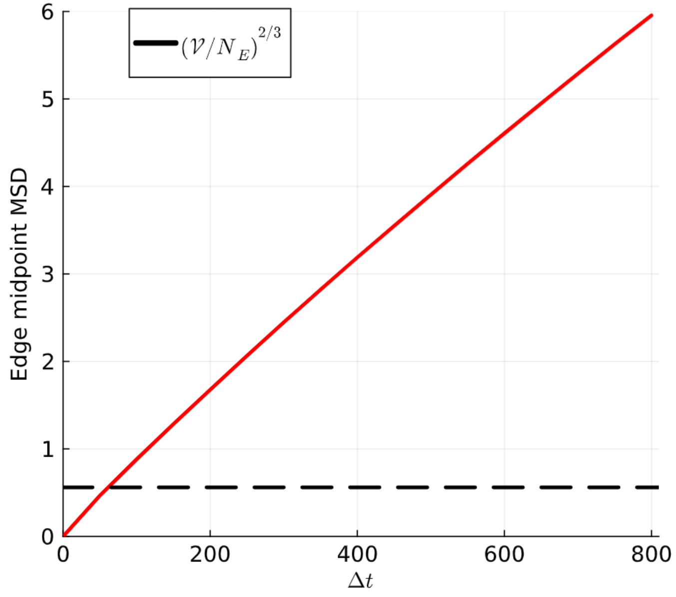


Network constituents undergo diffusion

Edge model

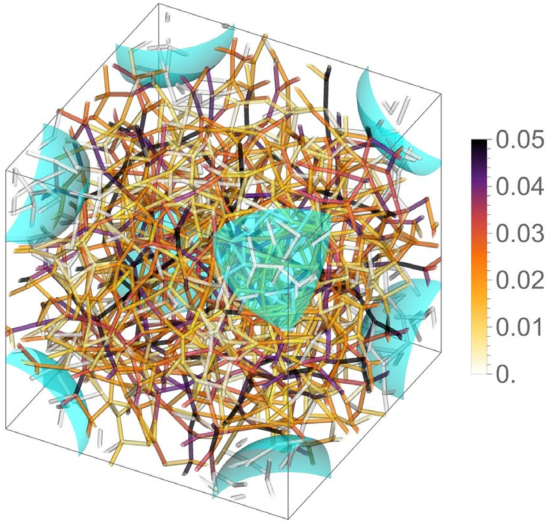


Node model

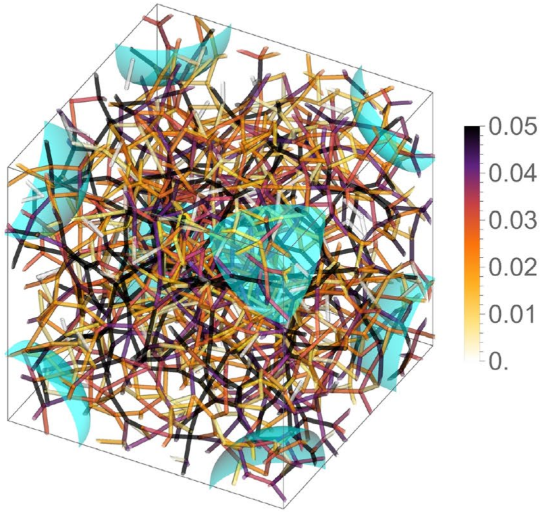


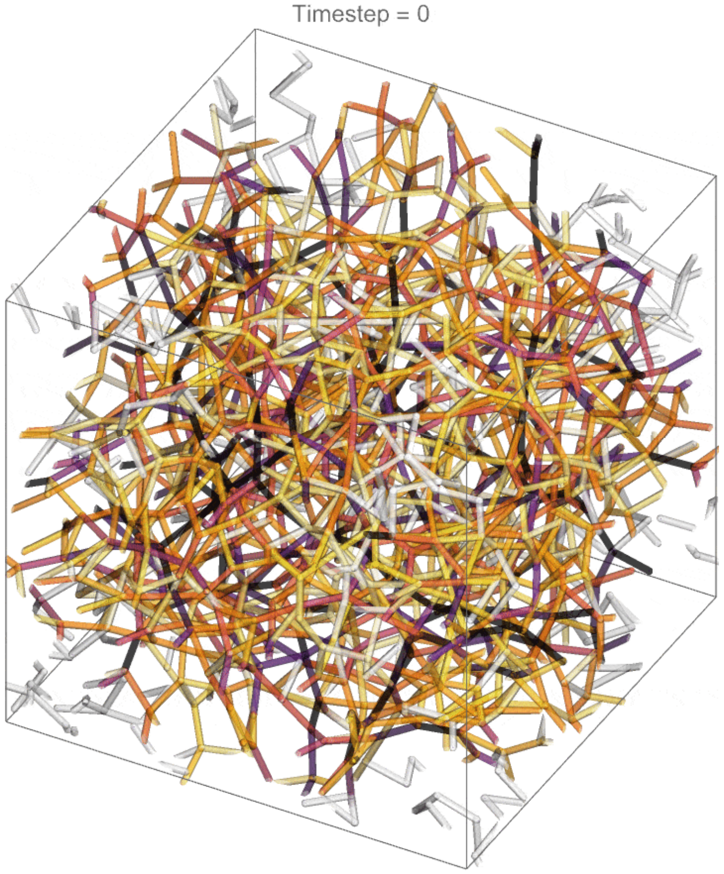
No permanently protected local structures or correlations.
Models capture **viscoelasticity:** Elasticity is partially stored and partially dissipated.
Representational drift: Shifting microscopic encoding for a steady global function.

Networks can heal from severe damages

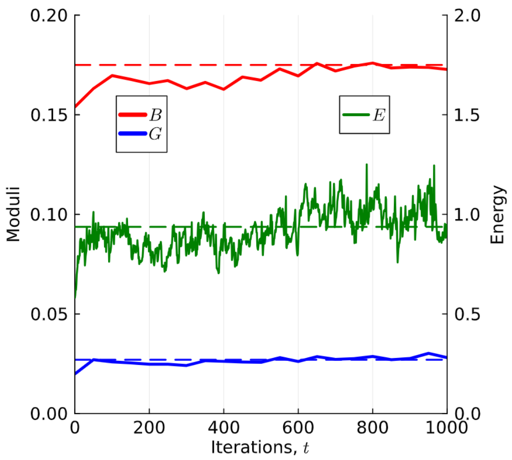


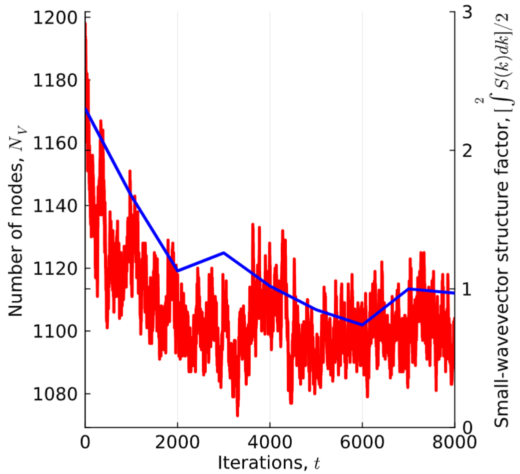
8000 iterations





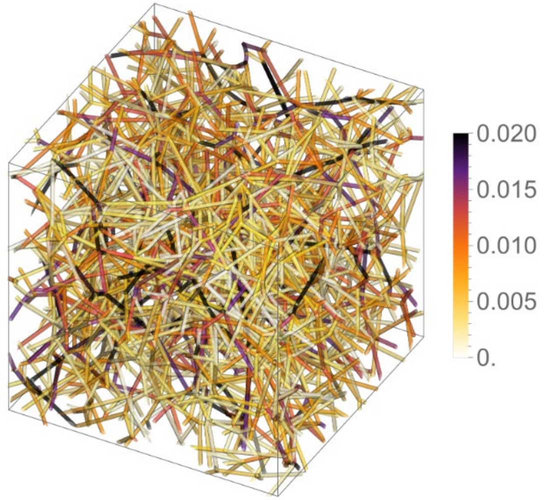
The **mechanical properties** recover much faster than **structural properties**

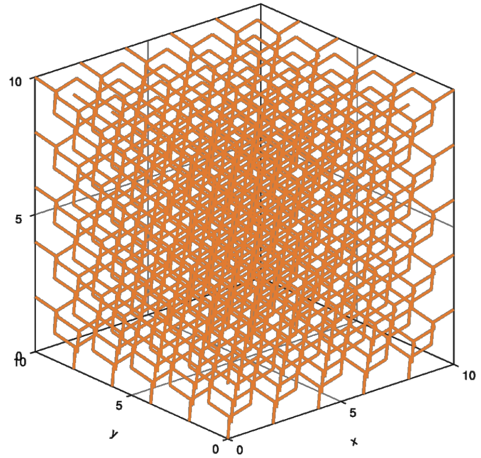




The actin cortex as a graph theorist?

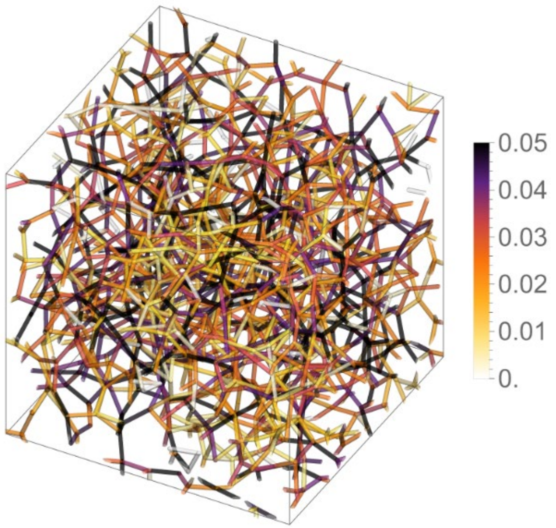
- Consider the steady state of the dynamic edge model
  - $\bar{z} = 3.992$, very close to the diamond network for which $z = 4$ for every node
  - Mean edge tension = 0.85%
  - $B = 0.283, G = 0.0298$
- For a **diamond** network with the same **mean edge tension** and **edge rest length (“stuff”) per volume**:
  - $B = 0.453, G = 0.0159$
  - Note the “tradeoff” between bulk and shear moduli.

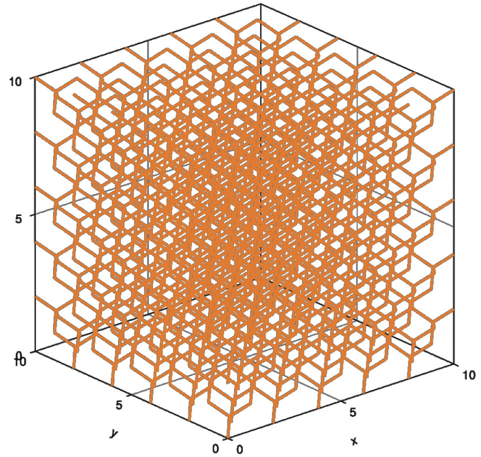




The actin cortex as a graph theorist?

- Now consider the steady state of the dynamic node model
  - $\bar{z} = 3.82, B = 0.181, G = 0.0352$
  - Mean edge tension = 3.00%
- For a **diamond** network with the same **mean edge tension** and **edge rest length per volume**:
  - $\bar{z} = 4, B = 0.239, G = 0.0282$
  - The cortex model resists shear better despite a lower $\bar{z}$.
- How does the topology of the actin network allow it to achieve higher shear modulus than the diamond network?





Graph theoretical metrics

- Triangles resist shear, so we count triangular loops:
  - Mean **number of triangles per node** = **0.177** for edge model, **0.218** for node model, **0** for diamond.
- **Closeness centrality**: The reciprocal of the sum of shortest path lengths between the node and all other nodes in the graph.

$$C(x) = \frac{N-1}{\sum_y d(y,x)}.$$

  - Mean closeness centrality = **0.156** for edge model, **0.133** for node model, **0.124** for diamond.
- **Betweenness centrality**: The degree to which nodes stand between each other

$$g(v) = \sum_{s \neq v \neq t} \frac{\sigma_{st}(v)}{\sigma_{st}}$$

  - Mean betweenness centrality = **0.00398** for edge model, **0.00617** for node model, **0.00708** for diamond.

Thus:
- There are many more triangular loops in the cortex models than in diamond network
- The cortex models are "denser" topologically than the diamond network
- Paths between nodes pass through fewer bottleneck nodes → Robust to damage

Experiments welcome!!

Summary

- Elements needed for rigidity homeostasis:
  - **Force-sensitive disassembly**
  - Small fraction of **random disassembly**
  - **Energy injection** (upon assembly)
- Graph-theoretical metrics allows us to elucidate how cells exploit topology to build stronger biopolymer networks.
- Future: Can our networks remain rigid (desired output) under fluctuating stresses (inputs)?

Acknowledgements

Preprint on arXiv soon!

Rigidity homeostasis of the actin cortex emerging from mechano-sensitive filament and crosslinker dynamics

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