Phase Separation Memory

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Intracellular Spatial Patterns

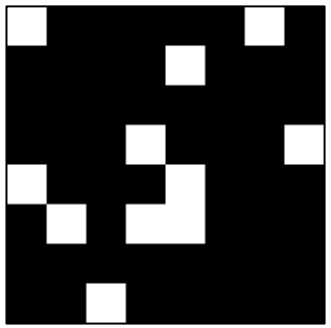
- Cells often possess internal gradients (asymmetric distribution)
  - Common in development and motility
  - Can be generated from signals, or in absence of external input
- Usually assumed to be caused by genetic or signaling networks
- Many proteins involved in spatial patterns have hallmarks of phase separation
  - Turing Processes
  - Auto regulatory feedback of proteins

Protein Phase Separation and Intrinsically Disordered Domains

- Many spatially regulated proteins form aggregates or liquid like droplets
  - Liquid droplets can merge into larger droplets
- Often mediated by ”intrinsically disordered domains”
  - Enriched in transcription factors, polymerases, RNA binding proteins
  - Often mediated by charge
  - Dysregulation linked to several disease states

Modeling Spatial Memory using Phase Separation

- proteins move randomly to unoccupied positions with reaction rate based on number of neighbors
- reaction rate

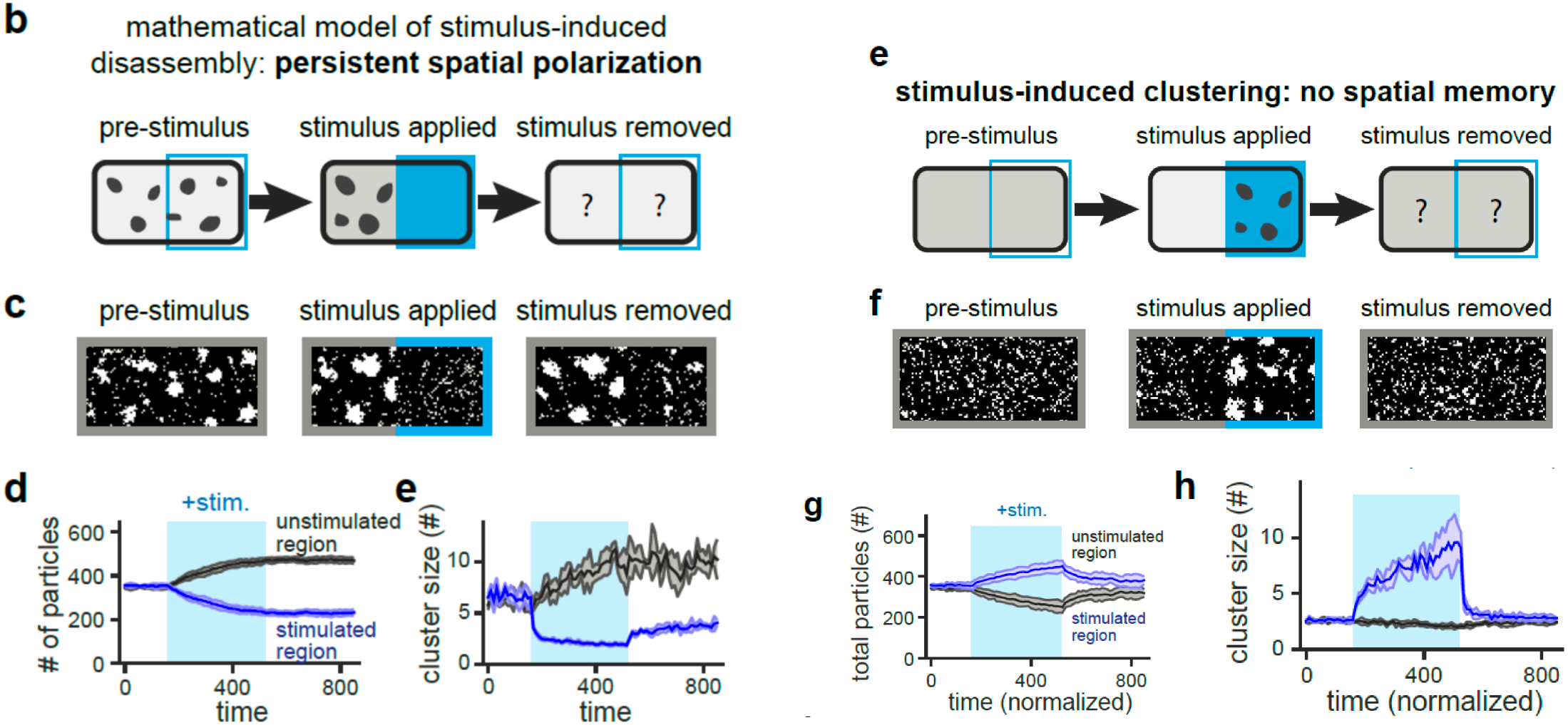


$$k = k_0 * e^{\frac{\Delta E * n_{lost}}{\theta(x,y,t)}}$$

$\Delta E = \text{interaction energy} = 1$
$n_{lost} = \text{number of bonds broken}$
$\theta(x, y, t) = \text{temperature-like stimulus}$
$k_0 = \text{constant} = 1$

- r = random number in (0,1]
- move if k>r

Persistent asymmetry of cluster dissociation



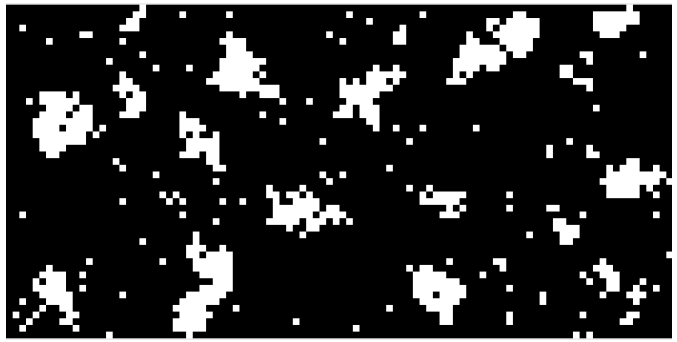
Implementation

- Recreated model using python/Scipy
  - Numpy arrays for performance
- Created interactive GUI to visualize and allow interaction with model
- Parameters can be tuned and results recorded
  - Destabilize $\theta(x, y, t) = 1 \rightarrow \theta(x, y, t) = 2$
  - Stabilize $\theta(x, y, t) = 2 \rightarrow \theta(x, y, t) = 1$

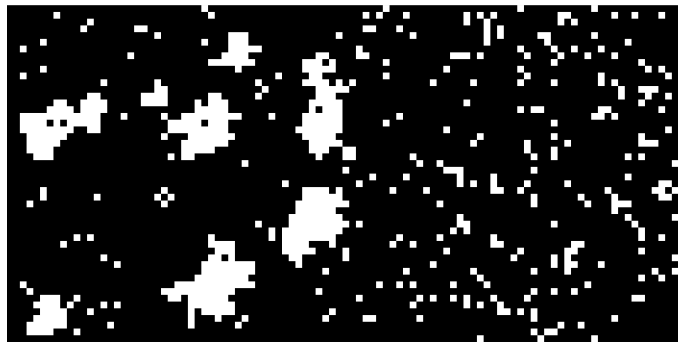
Classic Phase Separation Behavior

- Long-term model simulation (>5x10^6) show Ostwald ripening
  - small droplets dissolve and reassemble to become stable large droplets

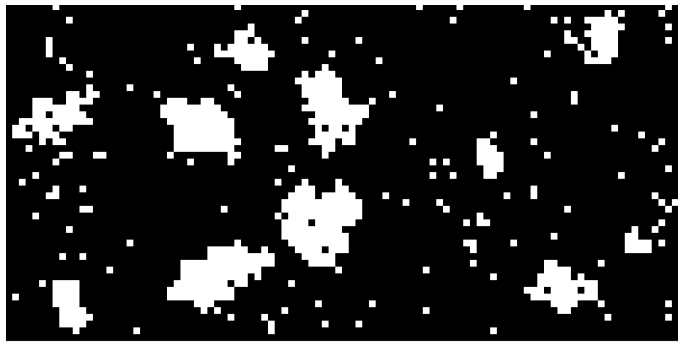
Persistent asymmetry after stimulus-induced disassembly



pre-stimulus



stimulus applied



stimulus removed