Introduction:
Cellular-level simulation

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• The interior of the cell is crowded, and all the molecules jiggle about.
• Note that lots of molecules (e.g., water) aren’t even shown in this movie.
Molecules jiggle about because other molecules keep bumping into them

https://www.youtube.com/watch?v=1jYabtziQZo
Diffusion

• This “jiggling about” by lots of molecules leads to diffusion
• Individual molecules follow a random walk, due to collisions with surrounding molecules
• Diffusion = many random walks by many molecules
  – Substance goes from region of high concentration to region of lower concentration
Reaction-diffusion simulation

• A common way to model how molecules move within the cell involves *reaction-diffusion simulation*

• Basic rules:
  – Molecules move around by diffusion
  – When two molecules come close together, they have some probability of reacting to combine or modify one another

• Several implementation strategies:
  – Particle-based (Represent molecules by particles, and track the motion of each one)
  – Continuum models
  – In some (limited) cases, one can solve the partial differential equations analytically
Continuum approach

- Divide space into finite “voxels”
- Instead of tracking positions of molecules, track concentrations of each type of molecule in each voxel
- At each time step, update concentrations based on reactions of molecules within a voxel, and diffusion between neighboring voxels based on concentration differences
- One of the papers we’ll cover uses this approach (via the Virtual Cell platform), together with analytical solutions, to study the effect of cell shape on cell signaling
Increasing the realism of cellular-level simulations

• The second paper uses cryo-electron tomography (a variant of cryo-EM) to recover complicated cellular geometries for simulation

• The software employed (Lattice Microbes) uses a voxelized approach, but with “stochastic dynamics”
  – It can represent the exact number of particles (e.g., molecules) of a given type in each voxel, giving improved accuracy when the number of particles is very small
  – It captures the randomness in how particles move

Background information

• Review paper (Models at the single cell level, 2010)

• Slides from CS/CME/Biophys/BMI 279: