System: any potential source of data
- boundary in vs. out
- inputs -> environ infl. system
- outputs -> system del. data

Experiment: Process of extracting data from a system
- observation of outputs
- perturbation of inputs & obser. of outputs

Model: A model of a system and a specific set of exp run anything to which the exp can be applied instead of the system.
- experimental frame of a model
- a model is a system
- need not be mathematical

Simulation: experiment performed on a model
- within exp frame
- need not be computational

Modeling: Process of building a model.

Continuous Assumption

\[ n = \text{concentration} \]

\[ n = \frac{\#}{V} \]
Knudsen number \( K_n = \frac{\lambda}{L} \)

\( K_n \ll 1 \rightarrow \) continuum if \( V > \lambda \)

\( K_n > 1 \rightarrow \) always discrete!
Time Scales

- Models only contain a limited spectrum of time scales.
  - Computational efficiency
  - Numerical stability

\[ \frac{dx}{dt} = f(x) \]

\[ x_{t+1} = x_t + h f(x_t) \]

\[ t = 0, \ldots, T \]

want that \( x_{t+1} \approx x((t+1)h) \)

\[ \frac{dx}{dt} = -ax \]

\[ \Rightarrow x(t) = x_0 e^{-at} \]

\[ x \]

\[ x_0 \]

\[ x(t) \]

\[ t \]

\[ * \Rightarrow x_{t+1} = x_t - ah x_t = x_t (1-ah) \]

used: \( |1-ah| < 1 \)

\[ \Rightarrow 1-ah > 0 \Rightarrow 1 + ah > X \]

\[ h > 0 \]

\[ 1-ah < 0 \Rightarrow -1 + ah < 1 \]

\[ ah < 2 \]

\[ h < \frac{2}{a_{\text{max}}} \]

\[ 0 < h \leq \frac{2}{a_{\text{max}}} \]
**Distinguish:**

- too slow \(\Rightarrow\) constant
- relevant \(\Rightarrow\) dynamic eqs. (ODE)
- too fast \(\Rightarrow\) algebraic eqs.

"Relevance" is defined by variables of interest & exp. frame of model.

**FRAP ex.** relevant: diffusion of protein, concentration field
slow: - room temp. changes
       - cell motion/deformation
fast: camera dynamics, laser switching dynamics.

**Reservoirs & Flows**

Dynamics \(\Leftrightarrow\) Reservoirs/Storage/Integrators

for extensive quantities: ex:
- mass
- energy
- money
- information

\(\Rightarrow\) Levels of reservoirs, called state vars.

\(\Rightarrow\) Flows between reservoirs.
Modeling Steps

1) Define system boundaries, inputs, outputs.

2) Identify reservoirs of relevant time scale and their levels. \[ \text{levels} \]  \Rightarrow \text{reservoirs are independent.} \]

3) Formulate algebraic eqs. for flows between reservoirs.

\[ \text{Flow} = f(\text{activ. level} - \text{inhibit. level}) \]

4) Formulate balance eqs. for the reservoirs.

\[ \sum \frac{d}{dt}(\text{level}) = \sum \text{inflows} - \sum \text{outflows} \]

5) Simplify eqs., re-cuve algebraic parts, non-dimensionalize, normalize, ...

6) Solve model eqs. (analytically, numerically)

\[ \text{Verify:} \rightarrow \text{level}(t) \mid _{t=0}^{T} \]

7) Identify unknown parameters by fitting solution to data

8) Validate model using parameter values from (7) or data not used in (7).
Example: PLIP - an experiment of ER lumina of living cells.

1) Boundary: ER membrane
   Inputs: bleaching
   Outputs: fluorescence, it is observation curve

2) Fluorescence washes in ER lumina
   Too fast: - fast & common
   - diffusion
   Too slow: - changes in time
   - gene expression

3) low infl. + high outflow = bleaching

4) $F(t) = \frac{t}{k_b} (H(t-t_b) - H(t-t_2-t_b))$

5) $\frac{dm}{dt} = -m_{out} = -\frac{V}{V_b} \beta (t-k\Delta t) m(t)$

6) $m(t) = m_0 e^{-kt}$; $k = \frac{V}{V_b}$

7) $k = \frac{V}{V}$

8) see slides

9) $H(t) = \begin{cases} 0, & t < 0 \\ 1, & t \geq 0 \end{cases}$
Vector Calculus

1) Fields

- scalar fields: $f : R^n \to R$ $(x) \to f(x)$
  e.g. temperature, pressure, density, ...
- vector fields: $\mathbf{v} : R^n \to R^m$ $(x) \to \mathbf{v}(x)$
  e.g. force, electric field, director, ...

**Field lines:** curves $\mathbf{x}(s) : s \to \mathbf{x}(s)$

that is tangent to $\mathbf{v}$ everywhere.

- stationary fields: value does not change over time
- unsteady fields: depend on time.

Derivatives of fields

\[
\frac{d}{dt}(a \cdot b) = \frac{da}{dt} \cdot b + \frac{db}{dt} \cdot a \\
\frac{d}{dt}(a \times b) = \frac{da}{dt} \times b + a \times \frac{db}{dt}
\]
2) Differential Operators

- **Gradient** $\text{grad } f(x)$

  in Cartesian $\mathbb{R}^3$:

  $$\text{grad } f(x) = \left( \frac{\partial f}{\partial x}, \frac{\partial f}{\partial y}, \frac{\partial f}{\partial z} \right)$$

  $f(x) = f(x, y, z)$

  in general:

  $$\text{grad } f := \lim_{\Delta u \to 0} \frac{\Delta f}{\Delta u}$$

  $f = f \Rightarrow \text{grad } f = 0$.

  $\text{grad } f$ points the direction of steepest increase of $f$.

  $\text{grad } f = 0 \Rightarrow$ extremum.

  Isosurfaces $\{ f = c \}$, $\text{grad } f = 0$.

  **Directional derivatives**

  $$\frac{df}{dc} \quad \text{with } |c| = 1.$$
- Divergence \( \text{div } \mathbf{v} \)

\[
\text{in Cartesian } \mathbb{R}^3:
\]
\[
\text{div } \mathbf{v}(x,y,z) = \frac{\partial v_1}{\partial x} + \frac{\partial v_2}{\partial y} + \frac{\partial v_3}{\partial z}
\]

\[
\text{in general:}
\]
\[
\text{div } \mathbf{v} := \lim_{\Delta V \to 0} \frac{\int_{\partial V} \mathbf{v} \cdot d\mathbf{s}}{\Delta V}
\]

\[
\mathbf{v} = \mathbf{0} \quad \Rightarrow \quad \text{div } \mathbf{v} = 0
\]

\[\text{div } \mathbf{v}(x) : \text{ source strength at } x.\]
\[-\text{Curl} \ v \ \\
\text{in Cartesian } \mathbb{R}^3: \ \\
\text{in general} \ \\
\text{curl } v = \lim_{\Delta u \to 0} \frac{\int_{\Sigma} d\mathbf{s} \times v}{\Delta u} \ \\
\text{curl } v := \lim_{\Delta u \to 0} \frac{\int_{\Sigma} d\mathbf{s} \times v}{\Delta u} \ \\
curl v(x) : \text{vortex strength at } x \ \\
(\text{vorticity})\]
\[ \nabla \cdot (\nabla f) = \Delta f \]

in Cartesian \( \mathbb{R}^3 \):

\[
\nabla f = \nabla \phi = \begin{pmatrix} \frac{\partial \phi}{\partial x} \\ \frac{\partial \phi}{\partial y} \\ \frac{\partial \phi}{\partial z} \end{pmatrix}
\]

\[
\nabla \cdot \nabla = \Delta = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}
\]

3) Flux \( \Phi \)

\[ \Phi : \text{ If } \mathbf{v} \text{ is a velocity field of a fluid, how much fluid is transported through a surface } \mathcal{S} \text{ per unit time?} \]

\[
\Phi = \int_{\mathcal{S}} \mathbf{v} \cdot d\mathbf{S}
\]

\[
\Phi = \int_{\mathcal{S}} \mathbf{v} \cdot d\mathbf{S}
\]
4) Work $W$

Q: If $\mathbf{F}$ is a force field, how much work is done by moving a point mass along path $L$ from $A$ to $B$.

$\mathbf{F} < \mathbf{dr} < L$

$dW = \mathbf{F} \cdot \mathbf{dr}$

$W = \int_{L} \mathbf{F} \cdot \mathbf{dr}$
5) Integral Theorems

**Gauss**

\[ \oint_{\partial B} \mathbf{v} \cdot d\mathbf{S} = \int_B \nabla \cdot \mathbf{v} \, dV \]

*net flow across \( \partial B \).*

Valid for any \( B \) of any size & shape.

**Stokes**

\[ \int_C \mathbf{v} \cdot d\mathbf{r} = \int_S \text{curl} \, \mathbf{v} \cdot d\mathbf{S} \]

**Green:** not elementary

\[ \text{Gauss: } \mathbf{v} = f(x, y, z) \]
6) Conservative Fields

**Def.:** A vector field $\mathbf{V}(x, y)$ is called conservative if the work along all paths from $A$ to $B$ is same, for all $(A, B)$.

$$W(L_1) = W(L_2) = W(L_3)$$

$\Rightarrow$ Work along any closed path is 0.

$\Rightarrow$ Work does not depend on path chosen, but only on start and end point.

$\Rightarrow$ $A$ & $B$ are state variables.

"friction/disruption-free." (x)

7) Differential Equations

- Laplace

\[ \Delta f = 0 \]

\[ \text{div}(\text{grad}(f)) = 0 \]

- Poisson

\[ \Delta f = g(x) \]

(*) fact: each gradient vector field is conservative and vice versa.

if $\mathbf{V}$ is conservative, then

$\exists f \text{ s.t. } \mathbf{V} = \text{grad}(f)$.

$f$ : potential

each conservative vector field is divergence free.

\[ \text{curl}(\text{grad}(f)) = 0 \]
Modeling Spatial Effects (Control Volume Reform)

Control Volumes

\[ \chi < |\text{control vol}| < \ell \]

Control Volume:
- volume of integration
- contained in a field
- arbitrary shape & location

Euler

\[ V(t) = V(t + \Delta t) \]
- fixed in space
- flux of \( V \) across boundary
- material goes in & out

Lagrange

\[ V(t) \rightarrow V(t + \Delta t) \]
- move with velocity \( V \)
- no flux of \( V \) across boundary
- always contains same material

is a reservoir
Change

field \( f(x,t) \) e.g. temperature

what is change in \( f \) that one measures in a control volume?

Euler

\[
\frac{df}{dt} \bigg|_{x=\text{const}}
\]

field derivative

Lagrange

\[
\frac{\partial}{\partial t} \left( f(x(t), t) \right) ; \quad \frac{dx}{dt} = v
\]

\[
= \frac{2f_{2x} + 2f}{2x + 2t} \quad \text{velocity } v
\]

Lagrangian derivative

\[
\frac{df}{dt} + \frac{\partial f}{\partial x} \cdot v + \frac{Df}{Dt}
\]

\[
\frac{df}{dt} \quad v
\]

\[
f(x,t)
\]

\[
\frac{\partial f}{\partial x} \cdot v \quad \frac{\partial f}{\partial t} = 0
\]
Reynolds Transport Theorem (1875)

Extensive
Lagrangian
Reservoir levels
\[ \text{simulate} \]

Intensive
Eulerian

How does an extensive quantity \( q = \int f \, dV \) change over time in a Lagrangian control volume?

For intensive quantities:
\[ \frac{Df}{Dt} = \frac{df}{dt} + \gamma f \nu \]

Convection: An extensive quantity that is constant in a Lagrangian control volume is conserved.
\[ \frac{Dq}{Dt} = 0 \]

\[ \frac{Dq}{Dt} = \frac{D}{Dt} \left( \int f \, dV(t) \right) \]

\[ = \int \frac{Df}{Dt} \, dV(t) + \int f \frac{D}{Dt} (dV(t)) \]

\[ = \int \left[ \frac{Df}{Dt} \right] + f \nu \cdot \frac{Dv}{Dt} \, dV(t) \]

\[ = \int \left[ \frac{Df}{Dt} + \nu \cdot \frac{df}{dt} \right] dV(t) \]

\[ = \int \left[ \frac{Df}{Dt} + \nu \cdot (f \nu) \right] dV(t) \]

\[ = \int \left[ \frac{Df}{Dt} + \nu \cdot (f \nu) \right] dV(t) \]

\[ \frac{Dq}{Dt} = \int \frac{Df}{Dt} (dV(t)) + \int f \nu \cdot \frac{Dv}{Dt} (dS(t)) \]

Balance equation

Inertial term model

Fluxes
Example: Diffusion

concentration \( c(x, t) \)

1) Which quantity to model?
   mass \( m = \int_V \rho c dV \)

2) Conservation law: assume conservation of mass
   \[ \frac{Dm}{Dt} = 0 \]

3) Apply Reynolds Transport Theorem
   \[ \frac{Dm}{Dt} = \int_V \frac{\partial}{\partial t} \rho c dV + \int_{\partial V} \rho c \mathbf{v} \cdot dS = 0 \]

4) Algebraic equations for flows
   flux \( \mathbf{u} \cdot \frac{\partial}{\partial t} \rho c \mathbf{v} = -D \mathbf{u} \cdot \mathbf{v} \) (Fick’s law)
   diffusion constant \( [D] = \frac{c^2}{t} \)

5) Balance equations
   \[ \int_V \frac{\partial}{\partial t} \rho c dV = \int_{\partial V} \rho c \mathbf{u} \cdot dS = \int_{\partial V} \sigma \cdot (D \mathbf{u}) dV \]

6) Simplify:
   \[ \int_V \left[ \frac{\partial}{\partial t} - \sigma \cdot (D \mathbf{u}) \right] dV = 0 \]

7) Go to arbitrary control volumes:
   \[ \frac{\partial}{\partial t} - \sigma \cdot (D \mathbf{u}) = 0 \]

   Diffusion equation

   Assume: \( D(x, t) = D = \text{const} \)
   \[ \frac{\partial c}{\partial t} = D \Delta c \]
Particle Methods for Spatio-temporal Simulation

- Function approximations
- Operator approximations

Modeling → Graph of intersecting reservoirs → PDE

\[ u(x, t) \rightarrow \mathbf{u}(x_p, t_j) \]

\[ p = 1, \ldots, N \]
\[ j = 1, \ldots, T \]

\[ \bigcirc \]

finite diff. \hspace{1cm} FEM \hspace{1cm} FV \hspace{1cm} Particle Methods

1) Particle = Lagrangian Control Volume
   Particle carry extensive quantities.

   \implies close to the model.

2) In complex geometries.
   In moving geometries.

3) Universal.

4) Numerical stability. No CFL condition.

- Boundaries are harder
- More costly
- Need extra "tricks" (e.g. cell lists, remeshing, etc.)
Particle: \((x, \omega, V)_p; p = 1, \ldots, N\)

property: \(x_p = V_p \in \mathcal{L}(x_p, t)\)

because \(V_p \in \mathcal{L}^3; \mathcal{L}^3 v_p = 12\)

\[
\begin{align*}
\frac{dx_p}{dt} &= \sum_{q=1}^{N} K(x_p, x_q, c_p, c_q) = v_p \\
\frac{dx_q}{dt} &= \sum_{q=1}^{N} F(x_p, x_q, c_p, c_q)
\end{align*}
\]

\(K: ?\) evolution kernel

\(F: ?\) interaction kernel

Ex:

\[
\begin{align*}
\frac{du}{dt} &= f \\
\text{model} &
\end{align*}
\]

\[
\begin{align*}
\text{exact} &
\end{align*}
\]

\[
\begin{align*}
\text{solution} &
\end{align*}
\]

\[
\begin{align*}
\text{accuracy} &
\end{align*}
\]

\[
\begin{align*}
\text{error consistency} (1) &
\end{align*}
\]

\[
\begin{align*}
\text{discrete eqs.} &
\end{align*}
\]

\[
\begin{align*}
\text{accuracy} &
\end{align*}
\]

\[
\begin{align*}
\text{stability} (2) &
\end{align*}
\]

\[
\begin{align*}
\text{intensive methods} &\rightarrow f \\
\text{extensive methods} &\rightarrow \int f dt
\end{align*}
\]
Function approximation \( u(x) : \mathbb{R}^d \to \mathbb{R} \)

**Diffusion**

**Governing equation**

\[
\frac{\partial u}{\partial t} = \nabla \cdot (D(x,t) \nabla u)
\]

\( D(x,t) \): Diffusion tensor

in Cartesian \( \mathbb{R}^3 \):

\[
D = \begin{pmatrix}
D_{xx} & D_{xy} & D_{xz} \\
D_{yx} & D_{yy} & D_{yz} \\
D_{zx} & D_{zy} & D_{zz}
\end{pmatrix}
\]

\( D_{ij} \): diffusion coefficient for gradients in direction \( i \) causing flux in direction \( j \).

- If \( D(x,t) = D(x,t) I \)
  \( \Rightarrow \) isotropic vs. anisotropic
- \( D \) is not a function of \( x \)
  \( \Rightarrow \) homogeneous vs. inhomogeneous
- \( D \) is not a function of \( t \)
  \( \Rightarrow \) normal vs. anomalous.

If isotropic & homogeneous & normal

\[
\frac{\partial u}{\partial t} = D \Delta u
\]

\( \Delta \): Laplacian operator

**Anisotropic materials**
Anomalous Diffusion

below \( \lambda \): \[
\langle x^2(t) \rangle \propto DT^{\alpha}
\]

\(\lambda \): \[
\frac{2D}{\alpha t} = D\alpha t
\]

above \( \lambda \): \[
\langle x^2(t) \rangle > DT^\alpha, \alpha \neq 1
\]

\(\alpha < 1\): subdiffusion
\(\alpha = 1\): diffusion / Brownian motion
\(\alpha > 1\): superdiffusion

\[\tilde{D}(t) = \tilde{D}(t)t^{\alpha-1}\]

\[\tilde{D}(t) = \tilde{D}(t)t\]

\[\langle x^2(t) \rangle \propto DT^{\alpha} = DT^{\alpha-1}\]

\[\alpha < 1\]: subdiffusion
\[\alpha = 1\]: diffusion / Brownian motion
\[\alpha > 1\]: superdiffusion

Lévy flights
Random Walk (RW)

\[ \frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2} \quad ; \quad u(x, 0) = u_0(x) \]

Solution

"Green's function"

\[ u(x, t) = \int \frac{\delta(x - y, t)}{2} u_0(y) \, dy \]

\[ G(x, y, t) = \frac{1}{\sqrt{4\pi D t}} e^{-\frac{|x-y|^2}{4Dt}} \]

\[ \delta(0) \]

\[ 2\sqrt{Dt} \]

Simulate Brownian motion of control volumes (\( \rightarrow \)), then this is a numerical approx. of integral (\( \rightarrow \))

\[ \rightarrow \text{Monte Carlo Integration.} \]
Particles: \( x_p(t) \), \( w_p = V \exp(x_p) = \phi \)

\[
\begin{align*}
\frac{dx_p}{dt} &= \mathcal{N}(0, 2D) + v \\
\frac{dw_p}{dt} &= 0
\end{align*}
\]

Algorithm:

Initialize: \( x_p(0) \Rightarrow w_p(0) = V \exp(x_p(0)) \)

Loop:

\( d \sim \mathcal{N}(0, 2D \Delta t) \)

\( x_p = x_p + d \)

\( t = t + \Delta t \)

End:

\( \frac{1}{2} \int \sum_{p \in S} [x_p(t) - \phi]_+ \) choosing direction

\( \varphi \sim (0, \pi) \)

step length \( \mathcal{N}(0, 2D \Delta t) \)

\( + \) easy to implement

\( + \) extends to more complex diffusion

\( + \) easy to include flows

\( - \) inaccurate error \( O(N^{-1/2}) \)

\( - \) only works for "intermediate" \( D \)

\( \text{small } D < \frac{\Delta x^2}{\Delta t} \)

\( \text{error } = KD/\sqrt{N} \)

\( - \) complicated in bounded domains.

\( \sum \) \( N \) triangles

\( \sum \) \( N \) particles

\( O(MN) \)
Particle Strength Exchange (PSE)

\[ \frac{dm}{dt} = \sum F(\ldots) \]

\[ \frac{du}{dt} = D \frac{\partial^2 u}{\partial x^2} \] (ND)

\[ \lambda(y) = u(x) + (y-x) \frac{\partial u}{\partial x} + \frac{1}{2} (y-x)^2 \frac{\partial^2 u}{\partial x^2} + \ldots \]

\[ \phi \int \left[ (u(y) - u(x)) \lambda e(y-x) \right] dy = \int \left[ (y-x) \frac{\partial u}{\partial x} \lambda e(y-x) \right] dy + \frac{1}{2} (y-x)^2 \frac{\partial^2 u}{\partial x^2} \lambda e(y-x) dy + \frac{1}{2} (y-x) \frac{\partial^2 u}{\partial x^2} \lambda e(y-x) dy + \ldots \]

Choose \( \lambda \) to be: 1) even \( \rightarrow \) all odd moments vanish
2) \( M_2[\lambda] = 2 \)
3) \( M_i[\lambda] = 0 \quad \forall 2 < i \leq r + 1 \)

\[ \phi \int \left[ (u(y) - u(x)) \lambda e(y-x) \right] dy = \frac{\partial^2 u}{\partial x^2} \phi e(x^2) + O(\phi^{1+}) \]
\[
\frac{\partial^2 u}{\partial x^2} = \frac{1}{\varepsilon^2} \left[ \nu(y) - u(x) \right] \frac{1}{\varepsilon} y(x-x) dy + o(\varepsilon^4)
\]

\[
\Rightarrow \frac{\partial^2 u}{\partial x^2} \approx \frac{1}{\varepsilon^2} \sum_{q=1}^{N} \frac{v_q(u(x_q) - u(x_p))}{\nu(x_q - x_p)}
\]

Algorithm:
\[
\begin{align*}
\frac{dx_q}{dt} &= \sqrt{\frac{v_q}{\varepsilon^2}} \\
\frac{dp_q}{dt} &= \sum_{p=1}^{N} \frac{v_{q-p} (x_q - x_p)}{\nu(x_q - x_p)}
\end{align*}
\]

\[= \varepsilon F(\ldots)\]

\[F(x_q, x_p, c_q, c_p) = \frac{v_{q-p}}{\varepsilon^2} \sum (x_q - x_p) \frac{1}{\nu(x_q - x_p)}\]

+ arbitrarily accurate
+ fast \(O(N)\)
+ include flows
+ easy in complex geometries
+ easy to implement

\(\frac{\partial u}{\partial n} = 0\)

\(\text{boundary conditions are hard.}\)
### Reaction-Diffusion Equation

\[ \frac{\partial u_i}{\partial t} = D \frac{\partial^2 u_i}{\partial x^2} + f_i(u_1, u_2, \ldots, u_N); \forall i = 1, \ldots, N \]

where:
- \( u_i \) is the concentration of the \( i \)th species,
- \( D \) is the diffusion coefficient,
- \( f_i \) is the reaction term for the \( i \)th species.

\( \mathbf{u} = (u_1, u_2, \ldots, u_N) \) is the concentration vector.

**Chemical Reactions**

"reaction-diffusion equation"

"Fisher - KPP equation" (1937)

**Simulation**

Particles:
- locations: \( \mathbf{x}_p(t) \)
- strengths: \( \mathbf{u}_p(t) \)

\[ \mathbf{u}_{p,i} = \mathbf{u}_p \mathbf{u}_i(\mathbf{x}_p) \]

\[ \mathbf{w} = (\mathbf{u}_1, \mathbf{u}_2, \ldots, \mathbf{u}_N) \]

- more particles \( \mathcal{O}(NM) \)
- interpolation required for reactions evaluation
- adapt to different scales in distributions

\( \mathbf{u} \) is good for multi-scale problems.
observed:
- diffusion of all $u_i$ is independent
- coupling is purely local (no differential operators)

$\Rightarrow$ simulate diffusion part
$\nabla \cdot (D_i \xi u_i)$
using PSE for independently for each $i = 1, \ldots, N$.

$\Rightarrow$ simulate reaction part
$f_i(u)$ independently for each particle.
Add the results to form
$\nabla \cdot (D_i \xi u_i) + f_i(u)$
in each particle. Do time step.

Evaluate reaction terms

- continuous (mass-action kinetics)
  $A + 2B \rightarrow C$
  $f_C = k_c u_A u_B^2$

  \[
  \begin{align*}
  \frac{du_A}{dt} &= k_c u_A u_B^2 \\
  \frac{du_B}{dt} &= -k_c u_A u_B^2 \\
  \frac{du_C}{dt} &= 2k_c u_A u_B^2 \\
  \end{align*}
  \]

  \[
  \begin{align*}
  \frac{du_i}{dt} &= f_i(u) \\
  f_i &= -k_c u_A u_B^2
  \end{align*}
  \]

$\Rightarrow$ ODEs on concentration fields
- particles carry strength = # molecules
  each particle is well mixed because its size < L.

Gillespie:

\[ a : \text{probability that a collision leads to a reaction} \]

"specific probability rate": \[ k = \frac{hv}{c} \]

\[ h = \# \text{possible collision pairs} \]

\[ v_n = \left( \begin{array}{c} n-1 \\ 0 \\ 1 \\ 0 \end{array} \right) \Gamma_{v_0} \frac{a_1}{a_2} \frac{a_2}{a_3} \frac{a_3}{a_4} \cdots \frac{a_{n-1}}{a_n} \]

\[ h_1 = X_0 X_1; h_2 = X_0; h_3 = X_1 \]

\[ a = h c : \text{"reaction propensity"} \]

probability of reaction in the next DT:

\[ \SS k : \]

1) First-reaction method:

\[ a_1, a_2, a_3, \ldots, a_m \]

\[ \mu : \text{total } \# \text{ of reactions} \]

\[ a_\mu ; \mu = 1, \ldots, \mu \]

\[ a_\mu = \sum_{\mu=1}^{\mu} a_\mu \]

Bernoulli process.

\[ \Rightarrow \text{ waiting time } T \sim \text{Exp}(a) \]

\[ T = \frac{\ln(v)}{a}; r \sim \text{Exp}(1) \]

\[ a_1 \rightarrow \tau_1 = \frac{a_1}{a_2} \ln(v_1) \]

\[ a_2 \rightarrow \tau_2 = \frac{a_2}{a_3} \ln(v_2) \]

\[ \vdots \]

\[ a_m \rightarrow \tau_m = \frac{a_m}{a_1} \ln(v_m) \]

\[ T = \min \{ \tau_1, \tau_2, \ldots, \tau_m \} \]

\[ t = t + \tau \]

\[ X = X + \mu \mu ; a_\mu = \text{deg}_\mu \mu \]

\[ 0(1) \]
2) Direct Method

\[ \begin{pmatrix} a_1 & a_2 & a_3 & \cdots & a_M \end{pmatrix} \]

\[ P(\text{reaction } \mu) = \frac{a_\mu}{a}; \quad a = \sum a_\mu \]

- Find smallest \( \mu \) s.t. \( \Gamma_\mu \leq \sum \frac{a_\mu}{\mu} \)
- \( \tau = \frac{1}{a} \ln(\tau_2) \)
- \( \mu = a_\mu \mu_0 \mu \)
- \( t = t + \tau \)

In each particle separately!

**Overall Algorithm**

for time step \( n = 1 \ldots, T \) do
- \( \textsc{ode} \) due to reactions \( \textsc{ode} \text{ or ssa} \)
- \( \textsc{pse} \) due to diffusion (\text{for pse})
- total change of strength \( \textsc{ode} = \textsc{pse} + \text{kin} \)
- evolve \( \textsc{ode} \)
- move \( x_p = x_p + \Delta x_p \) (\text{for pse})
- advance time
  \[ t = t + \frac{\xi \Delta t}{a} \] (\text{for ode})
  \[ t = t + \Delta t \] (\text{for ssa})
end

**Examples:**

\[ \rightarrow \textsc{ode} \text{ & pse} \rightarrow \Delta t \]
\[ \rightarrow \textsc{ssa} \text{ & pse} \rightarrow \text{convert } m = MH \]
\[ \text{time step } \tau \]
\[ \rightarrow \textsc{ssa} \text{ & pse} \rightarrow \text{time step } \tau \]
\[ \text{particle's move} \]
\[ \rightarrow \textsc{ode} \text{ & pse} \rightarrow \Delta t \]
1) Traveling fronts

\[ A + B \rightarrow 2A \]

look like waves, but is not a wave.

\[
\frac{\partial u}{\partial t} + v \cdot (b \cdot \nabla u) + f \leq 0
\]

\[
\frac{\partial^2 u}{\partial x^2} = c^2 \Delta u
\]

CAMP waves

Ca\(^{2+}\) waves

ATP waves

2) Turing patterns

for \( t \to \infty \)

non-equilibrium steady state

"treadmilling"