Modeling with partial differential equations

Part 1

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Outline: Part 1

The Reaction-Diffusion equation

A second example: ionic concentration within a cell

Derivation of reaction-diffusion equation

Correspondence with the cable equation encountered previously

Where we left off last time

$$C_m \frac{\partial V}{\partial t} = \frac{a}{2\rho_i}\frac{\partial^2 V}{\partial x^2} - I_{ion}$$

1) This is a reaction-diffusion equation.

These equations appear in other contexts

For instance, sub-cellular diffusion of Ca^{2+}

We will discuss other examples of reaction-diffusion

2) This is a partial differential equation (PDE).

To obtain a numerical solution, must convert to discrete form in both space and time.

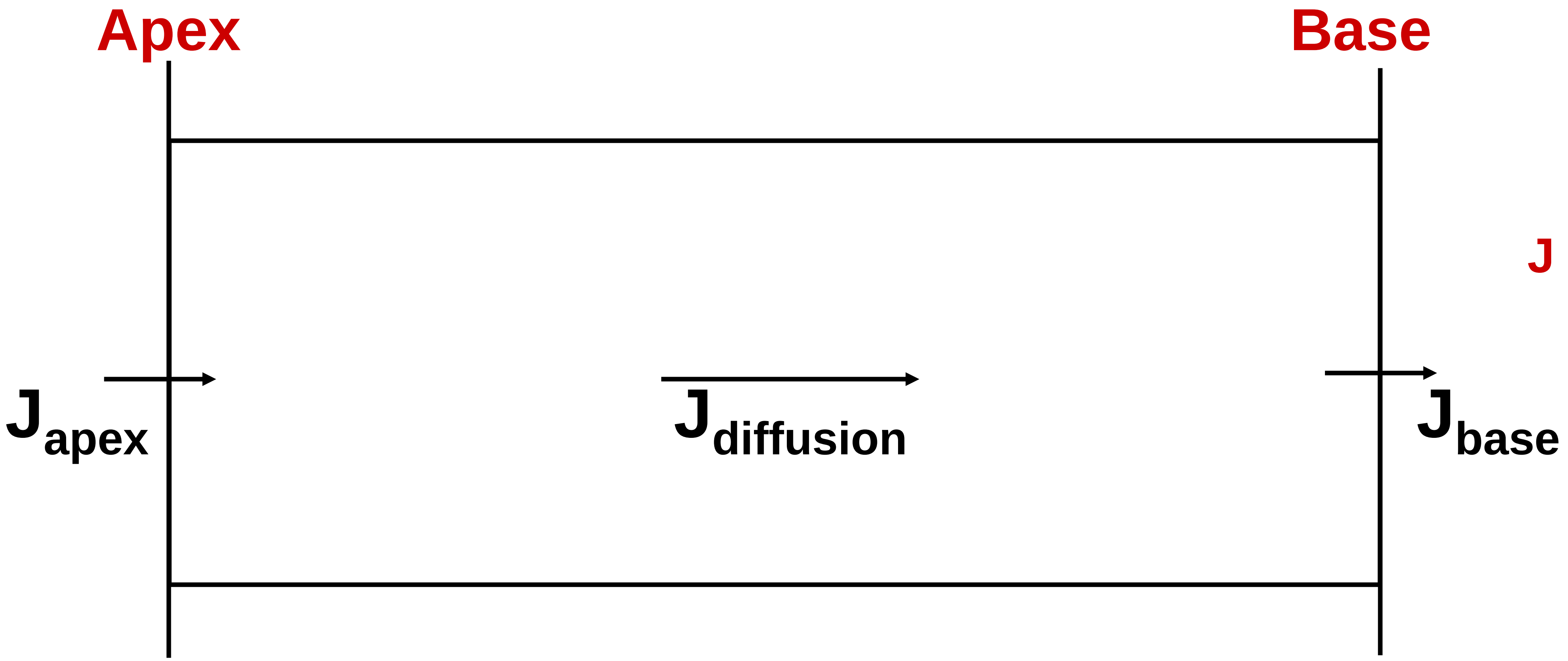
$$\left.\frac{\partial V}{\partial t}\right|_j^t \approx \frac{V_j^{t+\Delta t} - V_j^t}{\Delta t} \qquad \left.\frac{\partial^2 V}{\partial x^2}\right|_j^t \approx \frac{V_{j+1}^t - 2V_j^t + V_{j-1}^t}{\Delta x^2}$$

PDE solvers, like ODE solvers, are based on such discrete approximations.

Diffusion across an epithelial cell

Consider an example: HCO_3^- in renal proximal tubule

Kidneys regulate body pH by transporting bicarbonate across epithelia

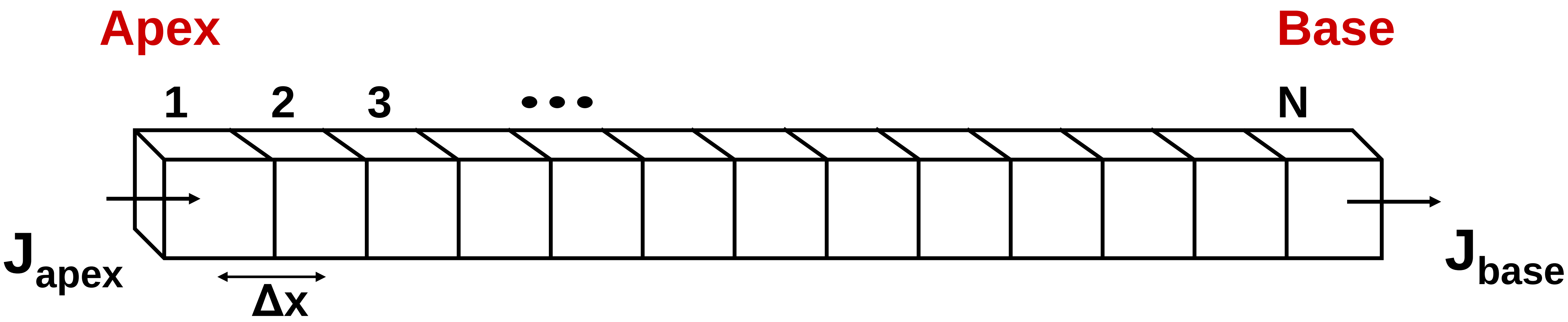


J = flux of ions

How do we describe movement of HCO_3^- from apex to base?

Diffusion across an epithelial cell

Represent cell as a series of discrete segments



$[HCO_3]_i$ = concentration in sub-cube i

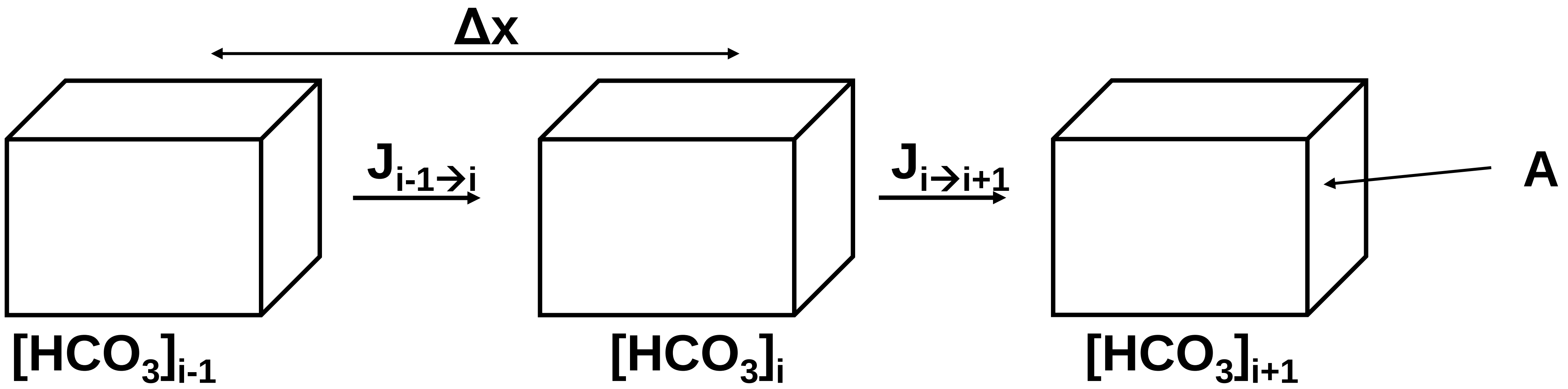
D_{HCO3} = intracellular diffusion constant

Δx = distance between adjacent sub-cubes

What are the equations that describe movement from apex to base?

Diffusion across an epithelial cell

First consider diffusion within three sub-cubes



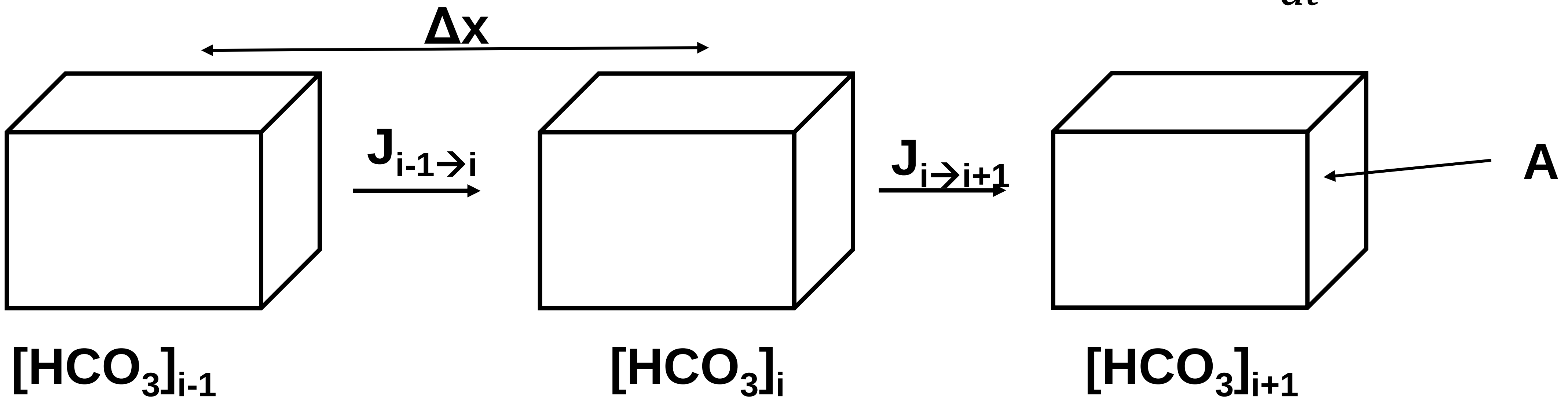
$$J_{i-1\rightarrow i} = D_{HCO_3} \frac{([HCO_3]_{i-1} - [HCO_3]_i)}{\Delta x}$$

$$J_{i\rightarrow i+1} = D_{HCO_3} \frac{([HCO_3]_i - [HCO_3]_{i+1})}{\Delta x}$$

Fick's first law of diffusion

Diffusion across an epithelial cell

How to relate to changes in $[HCO_3^-]_i$? $\frac{d[HCO_3]_i}{dt}$



Intuitively, $\frac{d[HCO_3]_i}{dt}$ depends on inflow vs. outflow, $J_{i-1\to i} - J_{i\to i+1}$

Need to consider units to express this precisely

Δx: cm
$[HCO_3]$: mM;
equivalent to μmol/cm³
D_{HCO3}: cm²/s

$$J_{i-1\to i} = D_{HCO_3} \frac{([HCO_3]_{i-1} - [HCO_3]_i)}{\Delta x}$$

$J_{i\to i+1}$: μmol/(cm² s)

Therefore we must convert from μmol/(cm² s) to μmol/(cm³ s)

Diffusion across an epithelial cell

Need to convert from μmol/(cm² s) to μmol/(cm³ s)

Multiply by inter-cube surface area A, then divide by volume (V_i)

$$\frac{d[HCO_3]_i}{dt} = \frac{A(J_{i-1\to i} - J_{i\to i+1})}{V_i}$$

But: $V_i = A\Delta x$

So: $$\frac{d[HCO_3]_i}{dt} = \frac{(J_{i-1\to i} - J_{i\to i+1})}{\Delta x}$$

Thus:

$$\frac{d[HCO_3]_i}{dt} = D_{HCO_3}\frac{\left[\frac{([HCO_3]_{i-1} - [HCO_3]_i)}{\Delta x} - \frac{([HCO_3]_i - [HCO_3]_{i+1})}{\Delta x}\right]}{\Delta x}$$

Diffusion across an epithelial cell

What is the limit as Δx→0?

$$\lim_{\Delta x \to 0} \frac{([HCO_3]_{i-1} - [HCO_3]_i)}{\Delta x} = \frac{d[HCO_3]}{dx}$$

$$\lim_{\Delta x \to 0} \frac{\left[\frac{([HCO_3]_{i-1} - [HCO_3]_i)}{\Delta x} - \frac{([HCO_3]_i - [HCO_3]_{i+1})}{\Delta x} \right]}{\Delta x} = \frac{d^2[HCO_3]}{dx^2}$$

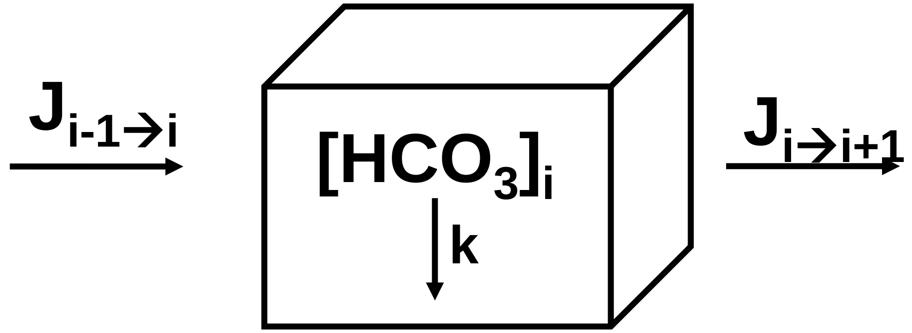
So, in the limit of small Δx, our equation becomes

$$\frac{\partial [HCO_3]_i}{\partial t} = D_{HCO_3} \frac{\partial^2 [HCO_3]}{\partial x^2}$$

This is a one-dimensional diffusion equation

Diffusion across an epithelial cell

What if some first order intracellular process is also consuming HCO_3?



Then,

$$\frac{d[HCO_3]_i}{dt} = \frac{J_{i-1 \to i}}{\Delta x} - \frac{J_{i \to i+1}}{\Delta x} - k[HCO_3]_i$$

In the continuum limit:

$$\frac{\partial [HCO_3]_i}{\partial t} = D_{HCO_3} \frac{\partial^2 [HCO_3]}{\partial x^2} - k[HCO_3]$$

This is a reaction-diffusion equation.
This should look familiar

1-D cable equation vs. epithelial reaction-diffusion equation

Cable equation:

diffusion

reaction that increases or decreases voltage

$$C_m \frac{\partial V}{\partial t} = \boxed{\frac{a}{2\rho_i} \frac{\partial^2 V}{\partial x^2}} - \boxed{I_{ion}}$$

Diffusion of $[HCO_3]$ across epithelium:

reaction that consumes [HCO3]

$$\frac{\partial [HCO_3]_i}{\partial t} = \boxed{D_{HCO_3} \frac{\partial^2 [HCO_3]}{\partial x}} - \boxed{k[HCO_3]}$$

diffusion

Summary

The PDE describing transport of an ion across a cell is analogous to the cable equation PDE we encountered in neurons.

Both PDEs are examples of <u>reaction-diffusion</u> equations.