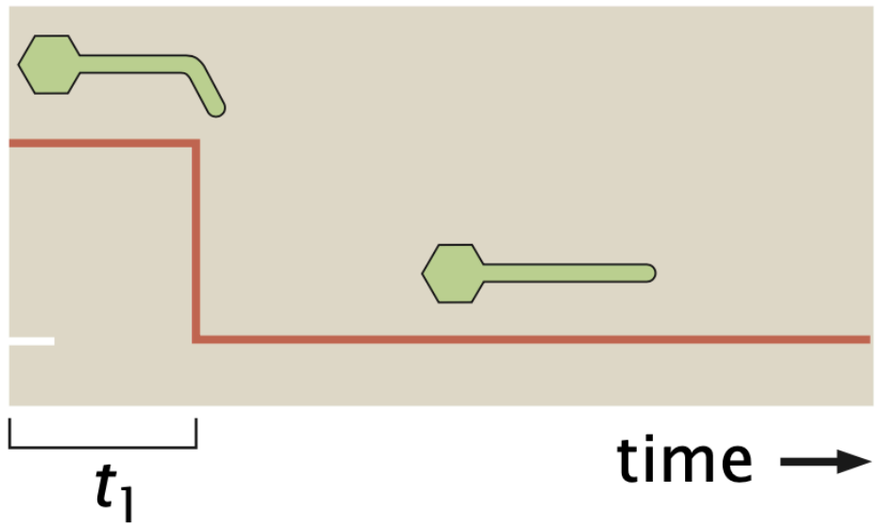
ILAS Seminal-E2:

Computer Simulations in Biology

Giovanni Brandani (brandani@biophys.kyoto-u.ac.jp)

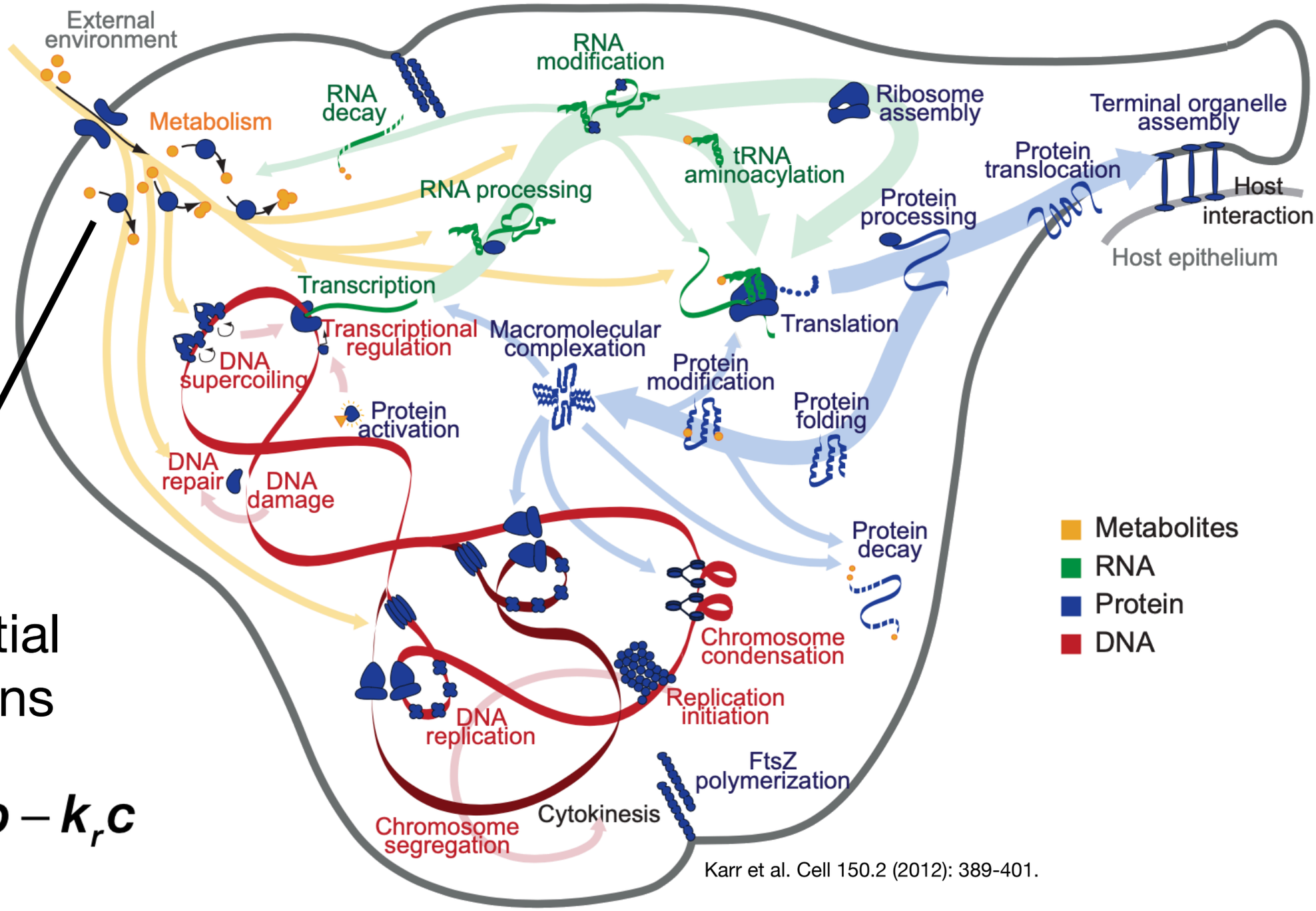
村田 隆 (murata@theory.biophys.kyoto-u.ac.jp)

Reaction dynamics and the Euler algorithm



Models of the living world often use **differential equations**. What are they? And how do we solve them?

Example: a full cell model



Karr et al. Cell 150.2 (2012): 389-401.

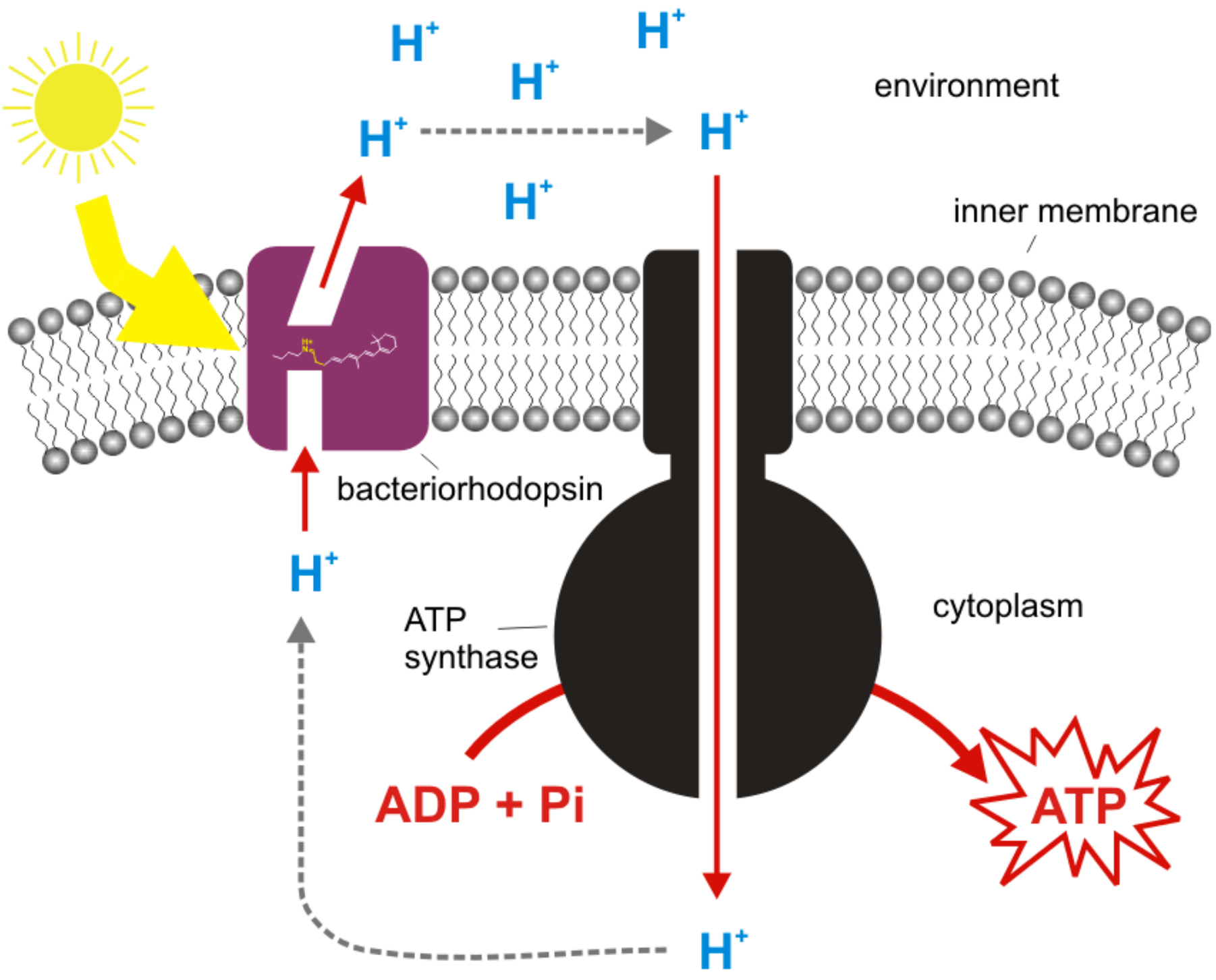
differential equations

$$\frac{dc}{dt} = k_f ab - k_r c$$

?

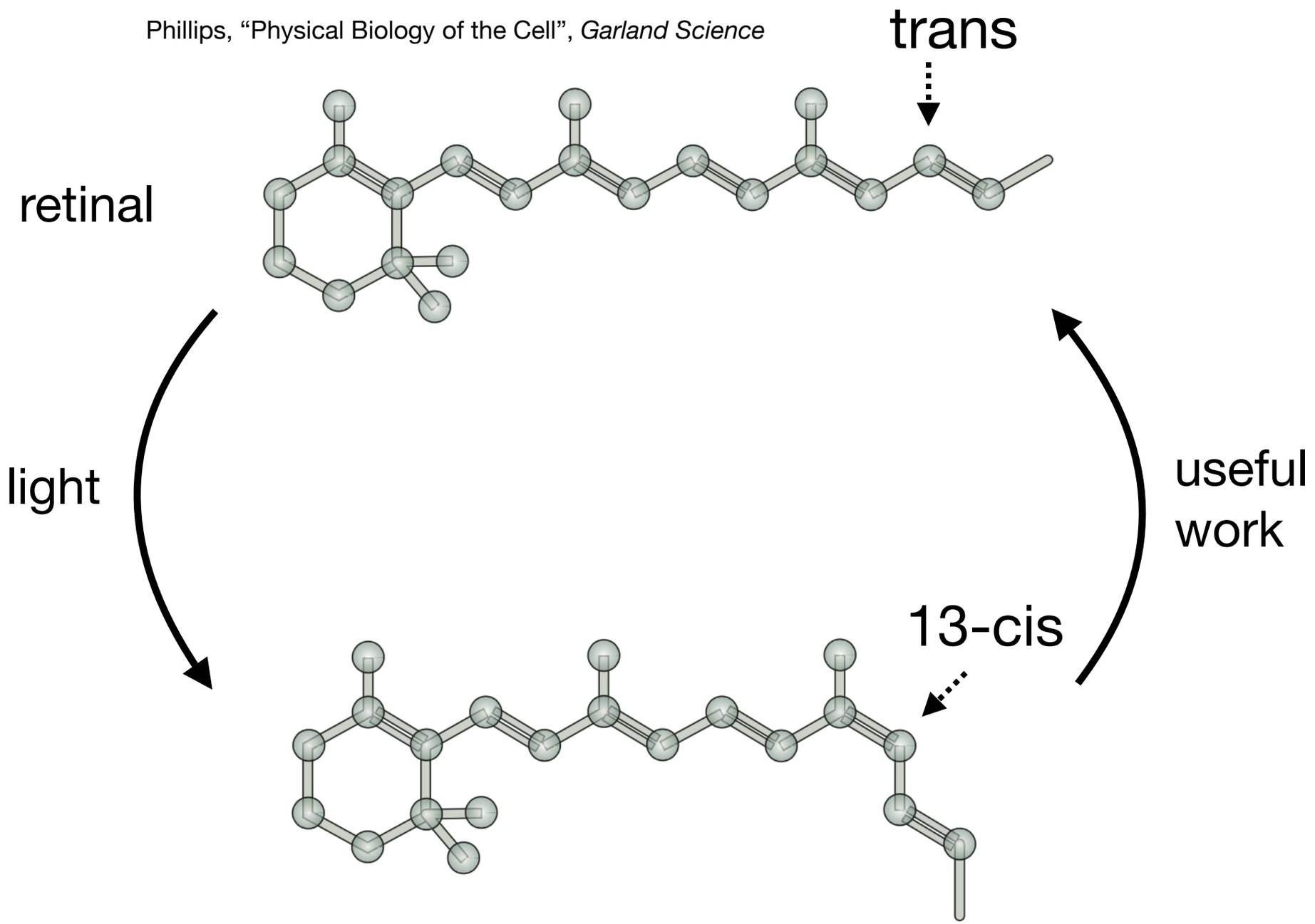
Case study: energy production in archaea

Retinal-bacteriorhodopsin complex used to pump H^+ ions using light



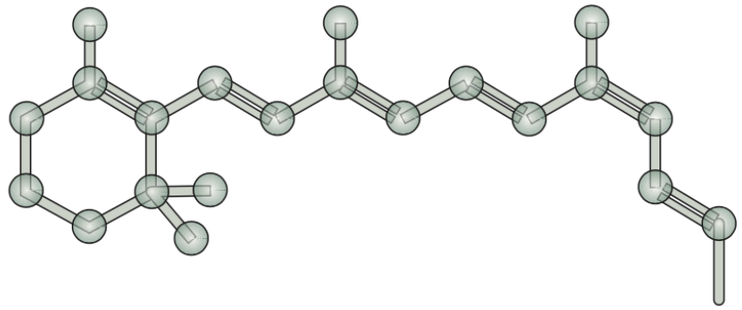
wikipedia

Work by bacteriorhodopsin exploits **reaction kinetics** of retinal

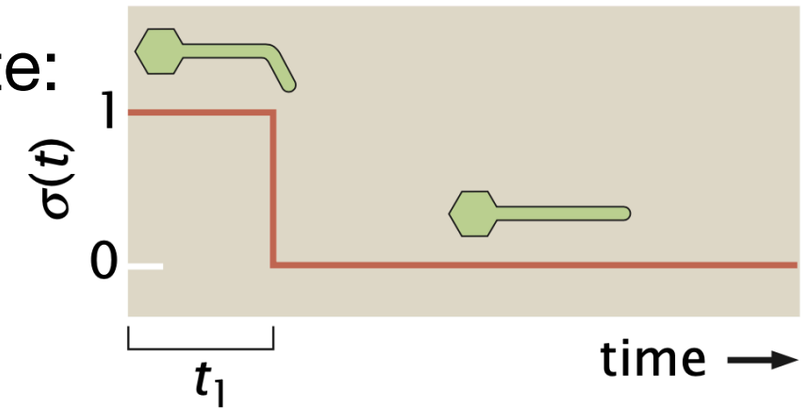


Dynamics of retinal can be studied at various levels

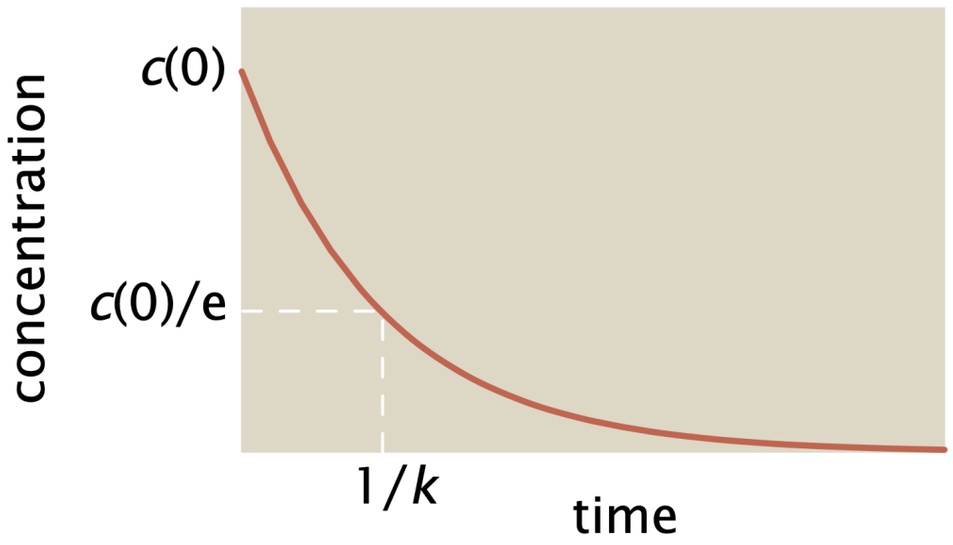
All-atom



Single molecule state:
- 1 (cis)
- 0 (trans)



Cis (or trans) concentration



resolution

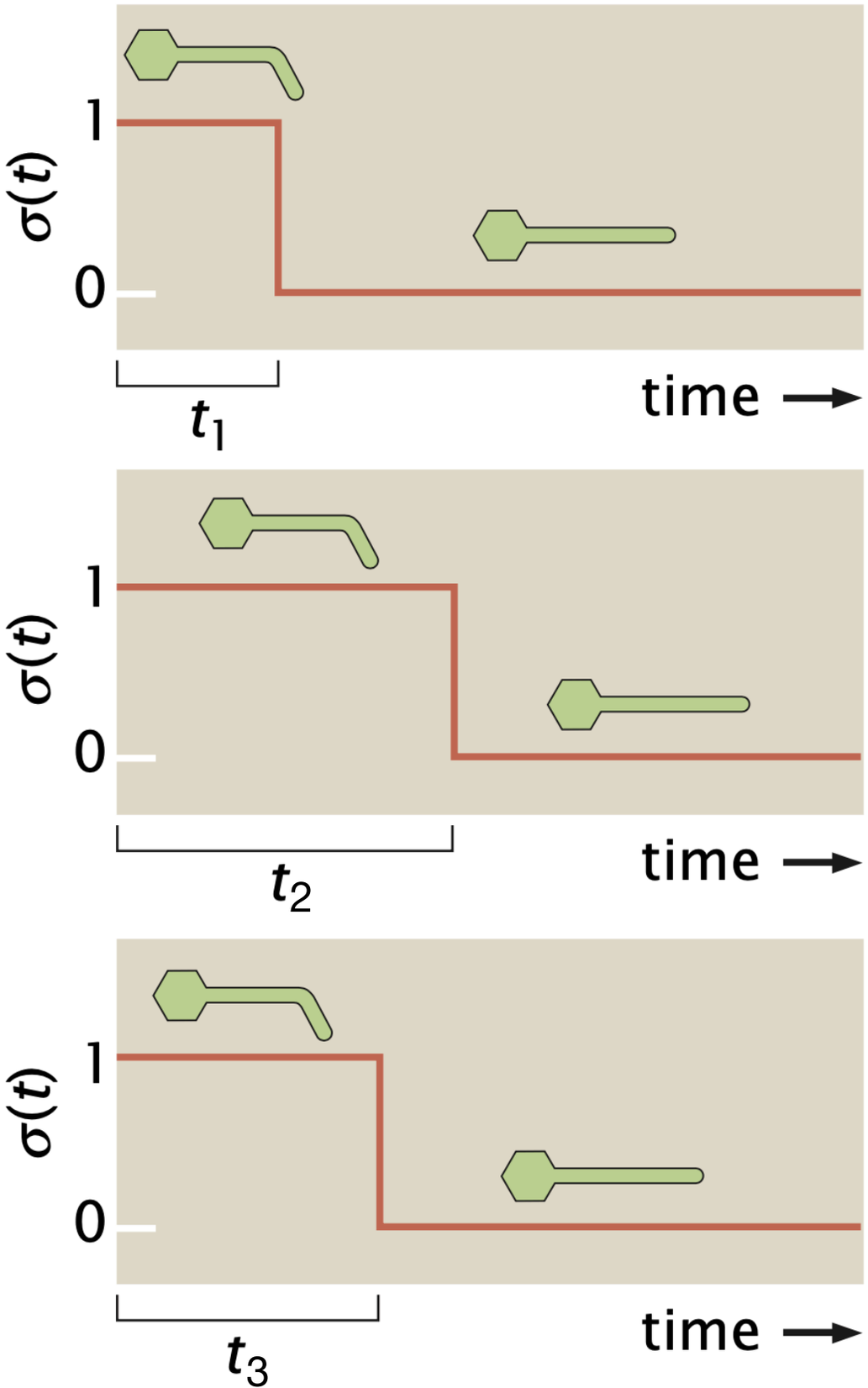
simplicity of modeling

Understanding dynamics at molecular level can informs us about how to build a simple, yet predictive model

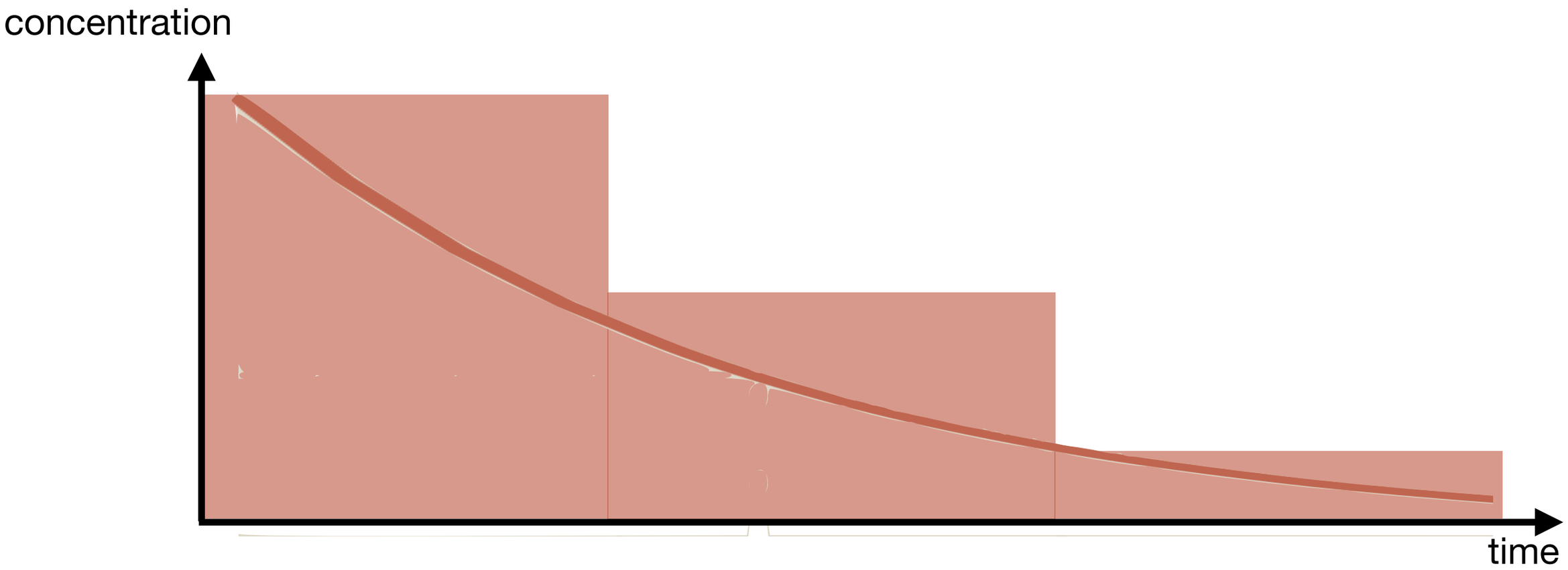
From the cis state, a retinal molecule should have at any give time interval a constant probability to transition into the trans state

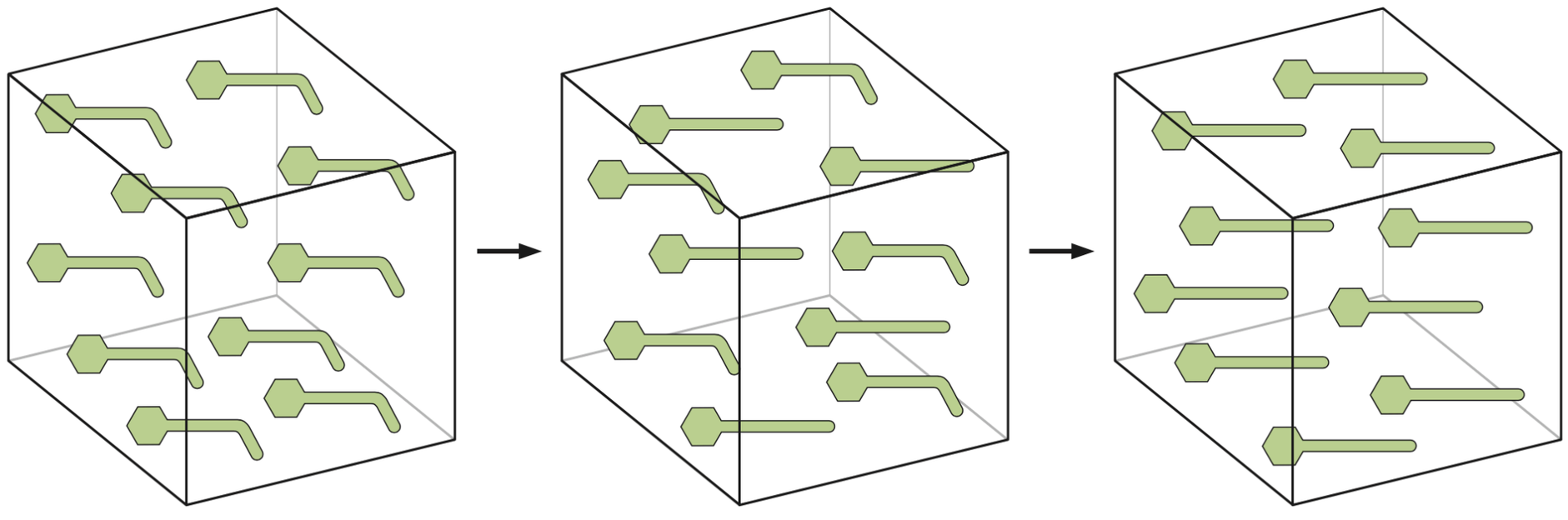
Different molecules will in general transition at different times

The trans state is the equilibrium state, so a spontaneous transition back to the cis state is not possible

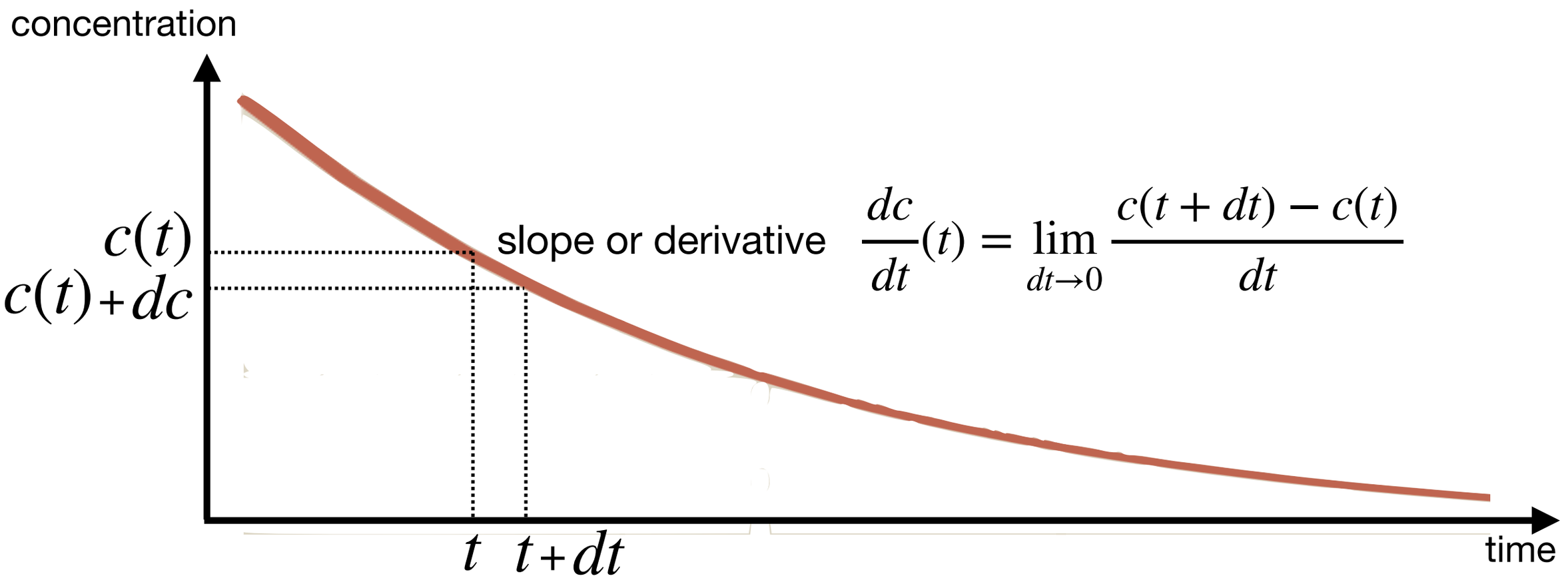


If we observe many molecules, how should concentration change as a function of time?





A simple differential equation describes retinal kinetics



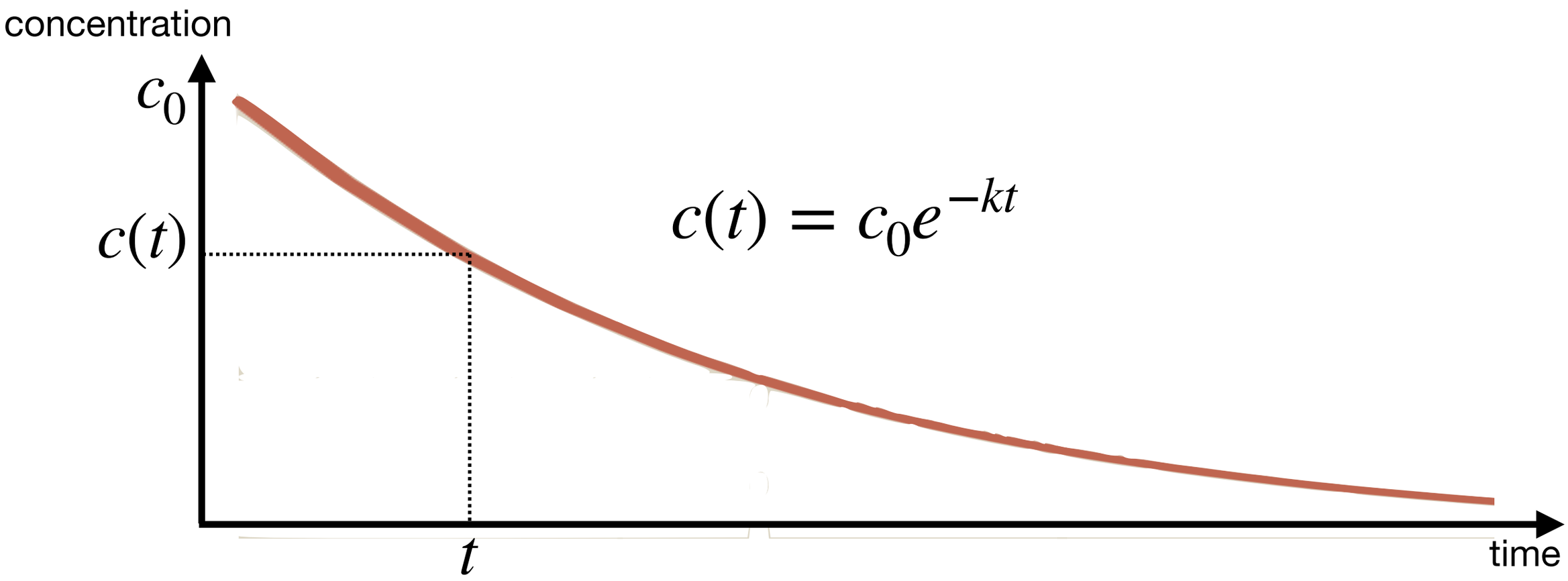
slope or derivative $\frac{dc}{dt}(t) = \lim_{dt \to 0} \frac{c(t+dt) - c(t)}{dt}$

Since retinal molecules decay at a constant rate, the change in concentration per unit time (the derivative) should be proportional to the concentration itself

$$\frac{dc}{dt} = -kc(t)$$

Where k is a rate constant with units of inverse time

In this case, the solution to the equation is an exponential



$$c(t) = c_0 e^{-kt}$$

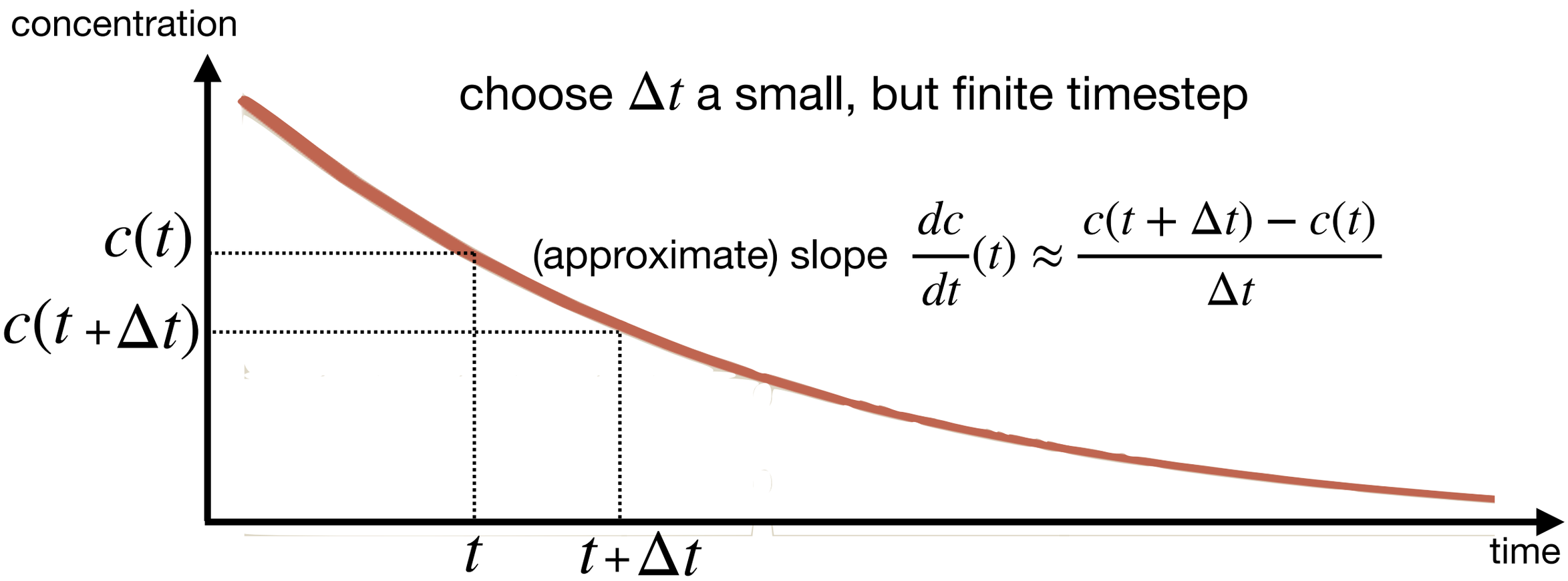
Since retinal molecules decay at a constant rate, the change in concentration per unit time (the derivative) should be proportional to the concentration itself

$$\frac{dc}{dt} = -kc(t)$$

Where k is a rate constant with units of inverse time

In general, how do we solve differential equations numerically?

The **Euler algorithm**



If my timestep Δt is small, and I know the concentration *c(t)* at time *t* and the derivative *dc/dt*, then I can easily estimate the concentration at time $t+\Delta t$ as:

$$c(t + \Delta t) = c(t) + \frac{dc}{dt}\Delta t$$

I can integrate my differential equation(s) by applying this until the desired time

How to run a simulation using the Euler algorithm

Model defined by one or more ordinary differential equations (ODEs):

$$\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x})$$

Initial conditions: $\mathbf{x}(t = 0) = \mathbf{x_0}$

Simulation:

1. Choose a small **timestep Δt**
2. Break time interval into $N = t_{max}/\Delta t$ timesteps
3. Starting from $\mathbf{x}(t = 0) = \mathbf{x_0}$,

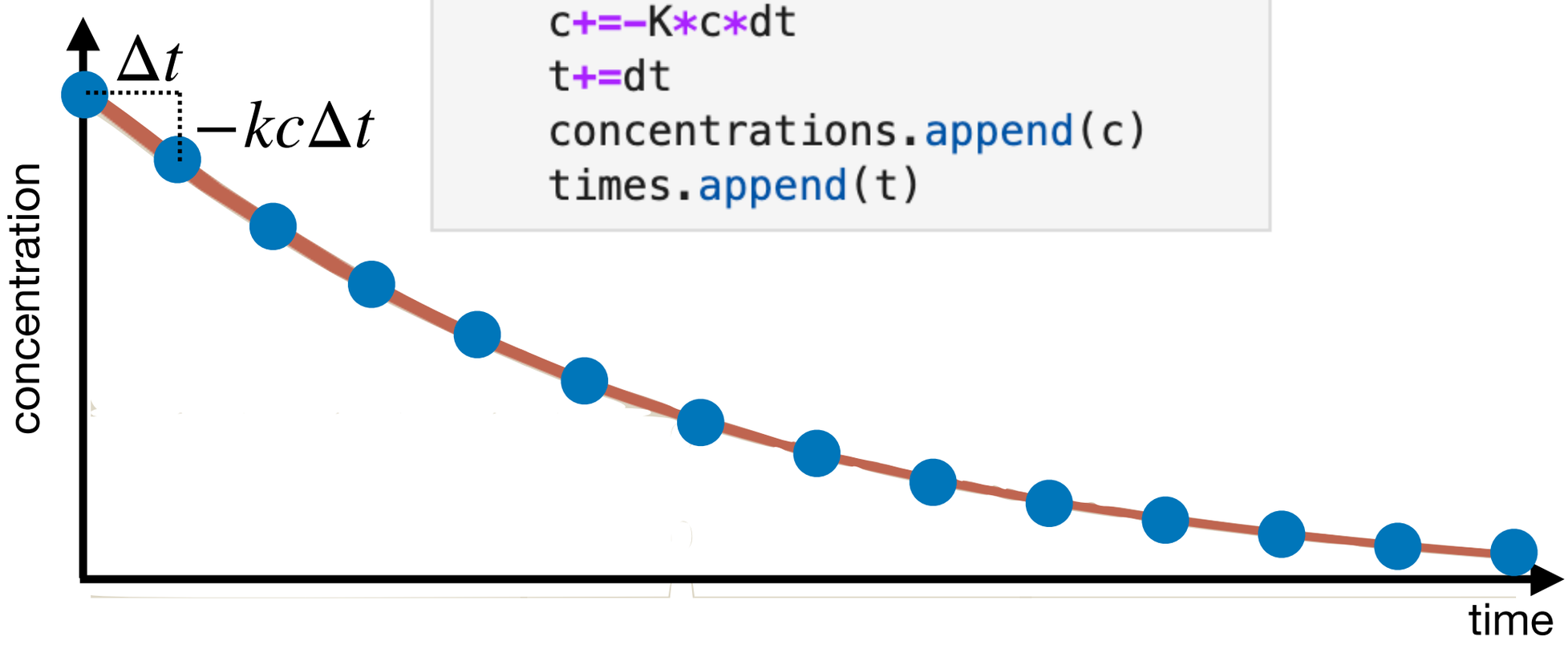
   estimate the change in $\mathbf{x}$ after a time Δt:

   $$\mathbf{x}(t + \Delta t) = \mathbf{x}(t) + \frac{d\mathbf{x}}{dt}\Delta t = \mathbf{x}(t) + \mathbf{f}(\mathbf{x}(t))\Delta t$$

4. Repeat *N* times until you reach time t_{max}

Example: a simulation of exponential decay

[1]:
```
K=2.3
c0=1.0
dt=0.001
Tmax=5.0
N=int(Tmax/dt)
c=c0
t=0.0
concentrations=[c0]
times=[0.0]
for i in range(N):
    c+=-K*c*dt
    t+=dt
    concentrations.append(c)
    times.append(t)
```



How do I choose the size of my timestep Δt?

- A **large** timestep makes my simulation **fast**
- but it also increases the **error** of my calculation

  because the Euler algorithm is only an approximation

Choice is based on the size of the error that can be **tolerated**

and the amount of available **computational resources**