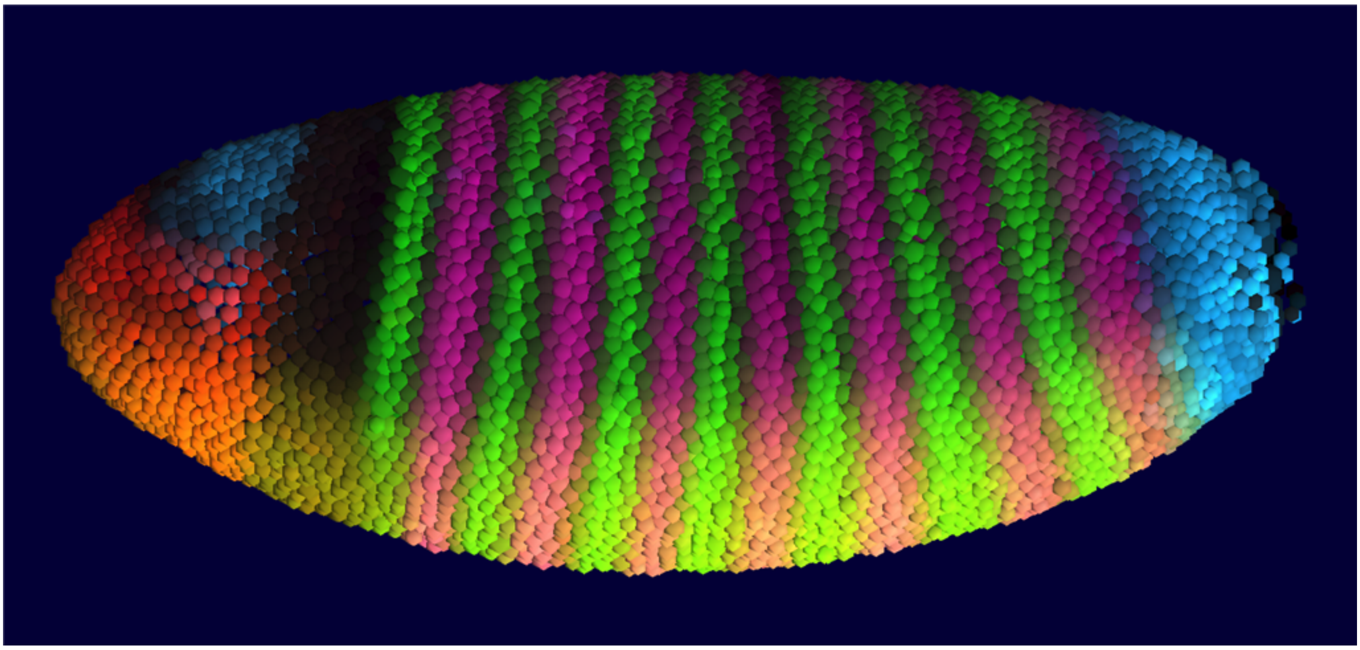
Morphogen gradients

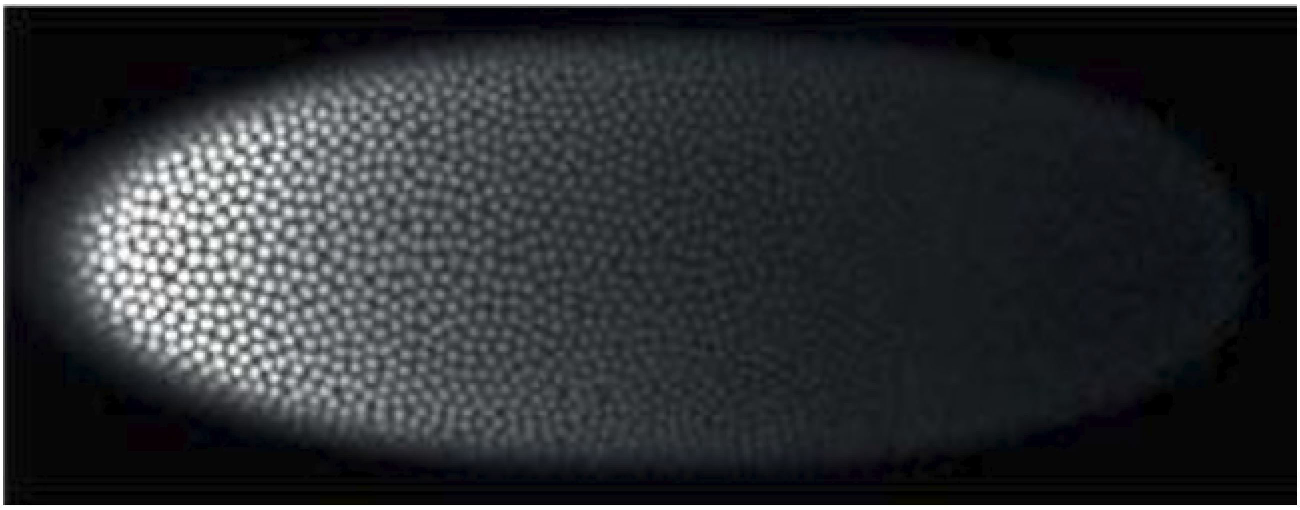
Expression of genes not only needs to be regulated in time within a cell, but needs to be coordinated across cells.

- different cell types
- high order structures
- essentially all of developmental biology
- but also in bacterial biofilms and other unexpected places.



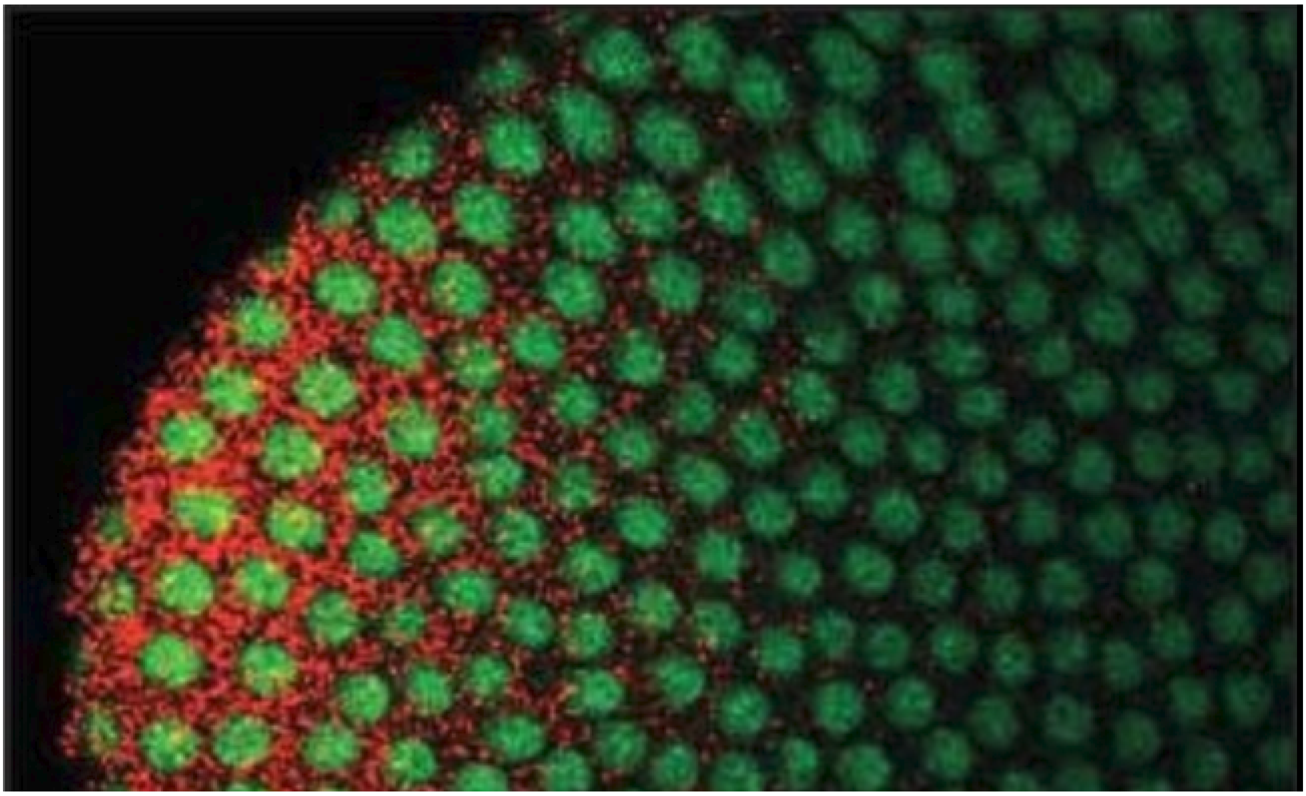
Computational synthesis of gene expression patters in the fly embryo (from https://dav.lbl.gov/archive/Events/SC05/Drosophilia/index.html (https://dav.lbl.gov/archive/Events/SC05/Drosophilia/index.html)).

The bicoid gradient



Bicoid gradient, image by Thomas Gregor et al

The result of localized mRNA at the pole:



The bicoid protein gradient is then read out and is responsible for patterned expression of downstream genes.

Gradient formation by diffusion and decay

Gradients through diffusion from a localized source if the protein has a finite lifetime τ. Such diffusion is described by

$$\frac{dP(x,t)}{dt} = D\frac{d^2P(x,t)}{dx^2} - \frac{1}{\tau}P(x,t)$$

The second term here describes the decay with lifetime τ (without the diffusion term, this equation reduces to exponential decay).

At steady state, that is when $\frac{dP(x,t)}{dt} = 0$, we have:

$$P(x) = \tau D\frac{d^2P(x)}{dx^2}$$

which is solved by $P(x) = Ce^{-x/\sqrt{D\tau}}$

- Exponential decay with length scale $\sqrt{D\tau}$
- Overall level is undetermined -> need to incorporate the source term
- Protein is produced at the left ($x = 0$) end of the embryo at rate α
- Production is balanced by a flux to the right.

$$\alpha = D\frac{dP(x)}{dx}|_{x=0} = D\frac{C}{\sqrt{D\tau}} = \frac{C\sqrt{D}}{\sqrt{\tau}}$$

and hence

$$C = \alpha\sqrt{\frac{\tau}{D}}$$

- $D \approx 5\mu m^2/s$
- $\tau = 30$min or 1800s

Hence we have $l = \sqrt{9000}\mu m \approx 100\mu m$

(this is somewhat more complicated in reality -- bicoid is move around by cycles of replications).

In [1]:

```
# import standard libraries
import numpy as np
import matplotlib.pyplot as plt

def bicoid_change(b, dx, alpha, D, beta):
    jump_rate = D/dx**2
    dbdt = np.zeros_like(b)
    # source alpha in zero bin -- contributes alpha/dx since bin has width dx
    dbdt[0] = alpha/dx - b[0]*beta - b[0]*jump_rate + b[1]*jump_rate
    # the remainder is just diffusion and the degradation term
    dbdt[1:-1] = -2*jump_rate*b[1:-1]+jump_rate*(b[0:-2] + b[2:]) - beta*b[1:-1]
    dbdt[-1] = -jump_rate*b[-1] + jump_rate*b[-2] - beta*b[-1]
    return dbdt
```

In [2]:

```
L = 500       #micrometers
D = 5         #micrometer^2/s
tau = 60*30   #30min, in seconds
alpha = 1     #the production rate doesn't matter, just rescales the result
```

In [3]:

```
N = 100    # the number of discrete time steps we will use
dx = L/N    # the width of the bins
```

In [4]:

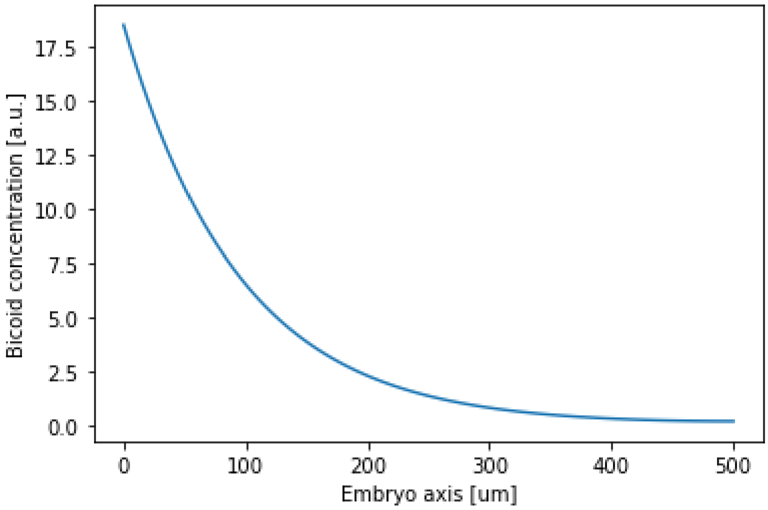
```
b = np.zeros(N)
dt = .1 # number of seconds per time step
tmax = 60*200
t=0

while t<tmax:
    b += dt*bicoid_change(b, dx, alpha, D, 1/tau)
    t += dt
```

In [5]:

```
plt.plot(L*np.linspace(0,1,N), b)
plt.xlabel('Embryo axis [um]')
plt.ylabel('Bicoid concentration [a.u.]')
```

Out[5]:

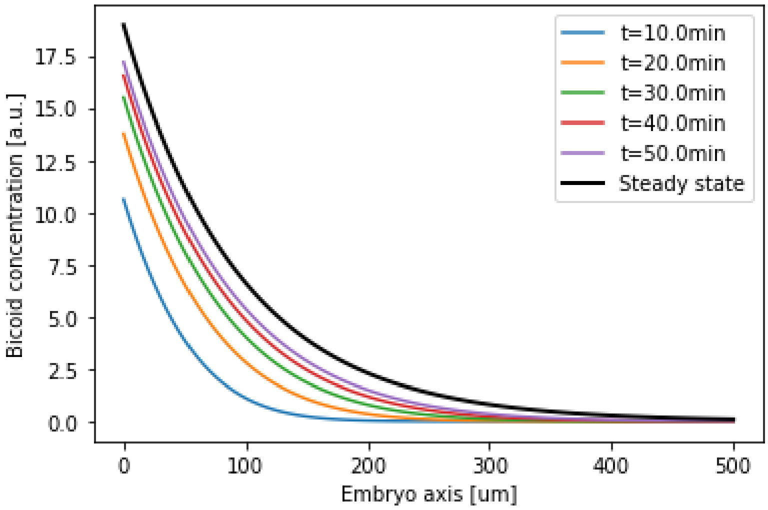
```
Text(0, 0.5, 'Bicoid concentration [a.u.]')
```



In [6]:

```
b = np.zeros(N)

plot_dt = 60*10
for i in range(5):
    t=0
    while t<plot_dt:
        b += dt*bicoid_change(b, dx, alpha, D, 1/tau)
        t += dt
    plt.plot(L*np.linspace(0,1,N), b, label=f't={(i+1)*plot_dt/60}min')
plt.xlabel('Embryo axis [um]')
plt.ylabel('Bicoid concentration [a.u.]')

x = L*np.linspace(0,1,N)
plt.plot(x, alpha*np.sqrt(tau/D)*np.exp(-x/np.sqrt(D*tau)), lw=2, c='k', label=
"Steady state")
plt.legend()
print("length scale:",np.sqrt(D*tau))
```

```
length scale: 94.86832980505137
```



In [ ]: