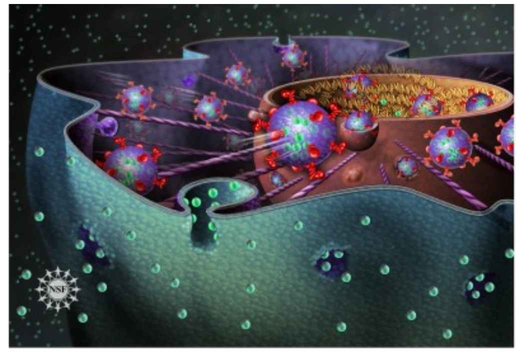
Diffusion and Transport in the Intracellular World



- All small particles jiggle around due to being kicked by moving molecules. This "random walk" motion is called **diffusion.**
- Diffusion makes particles mix and spread. But it is very slow over long distances.
- Living cells rely on **active transport**, using motors to carry particles in a persistent direction. At longer times, these particles start turning around and making random walks.
- The space where the particles are confined, and crowding in the fluid affect how quickly they can find each other.

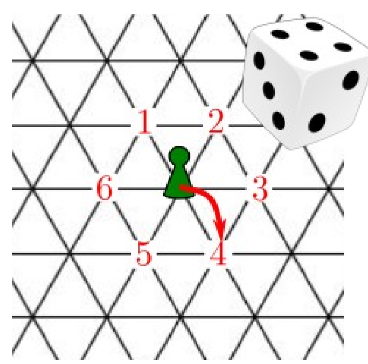
Part 1: Simulating Diffusion

We will use a simulation to understand the behavior of tiny diffusing particles.

1. Place your random walker on the central red star.

Suppose you could move make the walker step straight in the direction it needed to go.
How many steps would it take for it to move outside blue fence? ____________
How many steps would it take for it to move outside the red fence? __________

You will run a simulation where your walker represents a microscopic particle undergoing **diffusion** --- a random walk through space, where every step is chosen independent of previous steps.



2. Place your walker on the red star. Start rolling the dice, each time moving the walker in the direction shown.

Where is your walker after 5 steps?
(Draw the position on the big board in front)

All of our particles started at the same point. What happened to them after they had a chance to diffuse?
(a) They stayed where they started.
(b) They moved away but all stayed together
(c) They spread out, with some staying nearby and others moving further
(d) They all moved the same distance away from the center

3. Start back at the central star. Keep rolling the dice and moving your particle.

How many steps does it take for the particle to step outside the blue fence? ________
(write up your answer on the group board in front)

Make a prediction: on average, how many steps do you think it will take for the particle to step outside the red fence? ___________

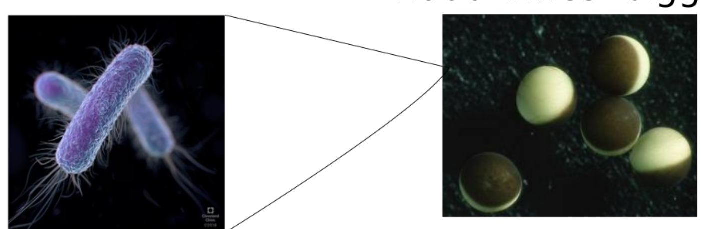
5. Start back at the center and keep rolling the dice.

How many steps does it actually take for the particle to step outside the red fence?
____
(write up your answer on the group board in front)

Be patient --- this can take a while! If you finish early, do another run so we can get more data.

Diffusion is very slow for moving molecules across large distances. Small cells (like bacteria) can wait for molecules to get where they need to go by diffusion. But large cells (like frog eggs or human nerve cells) can't rely on diffusion alone!

1000 times bigger!

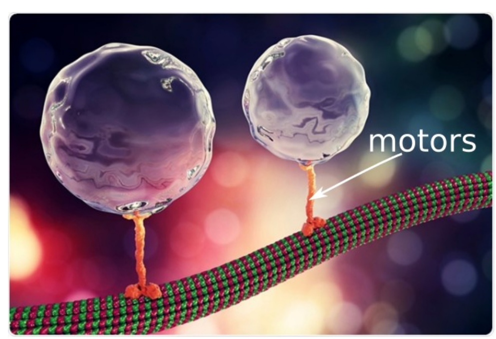


E. coli bacterium

frog oocyte

Part 2: Active Transport and Encounter Rates

The inside of a cell is a complex world full of filaments, obstacles, and crowders of all sorts. To move particles through this world, cells rely on <u>active transport</u> --- motors carrying cargo while walking along filaments that serve as highways. For many particles, this motor-driven motion is also a random walk, although it involves moving for short periods of time in a persistent direction.



We will use a hexbug to simulate an active particle moving randomly through a cell. Our goal will be to see what variables affect how quickly the particles find each other (a "reaction").

Work with a partner!

1) Place 2 hex-bugs into a plastic tray, starting in the center facing away from each other. Use the timer to determine how long until they first touch each other. Record the time in 3 separate trials and find an average:

Trial	Encounter time
1	
2	
3	

Average encounter time:

____

The inside of a cell is very crowded. Long filaments, sheets of membrane, and blobs of all sizes get in the way of particles that are moving through the cell.

3) To model a more crowded environment for your hexbug, pour rice into the tray. There should be enough rice to just barely cover the bottom with a thin, evenly spread layer. The rice represents small crowding particles in the cell.

4) Use the timer to measure how long it takes the hexbugs to find each other, starting from the same position (facing away from each other). Just do 1 trial

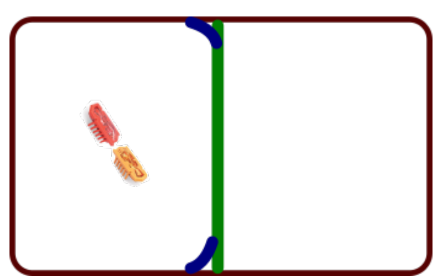
Encounter time in crowded environment: ______________________________

What does crowding do to the reaction time? __________________________

(Pour out the rice)

How does the encounter time depend on the space available for particles to explore? What happens if we confine the particles in a smaller box?

2) Roll a long thin snake of modeling clay and place it down the middle of the tray, separating it into two equal parts. Use a bit of clay placed diagonally to get rid of the sharp corners.



3) Place the two hexbugs in the middle of the same half, facing away from each other, and time how long it takes for them to first encounter each other.

Active particles in confinement:

Trial	Encounter time
1	
2	
3	

Average encounter time:

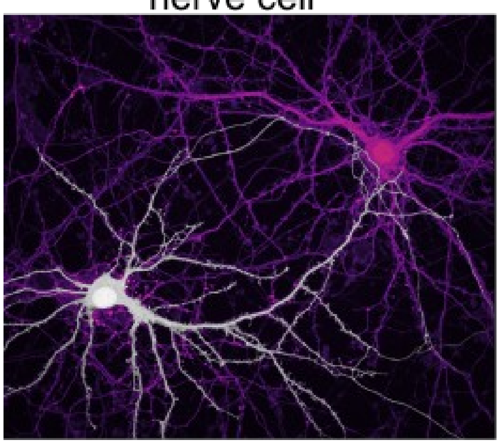
____

What happens to the reaction time when particles are confined together into a smaller space? ____

Cells use confinement into small compartments (called organelles) to speed up reaction rates. Molecules packaged into the same organelle can find each other faster.

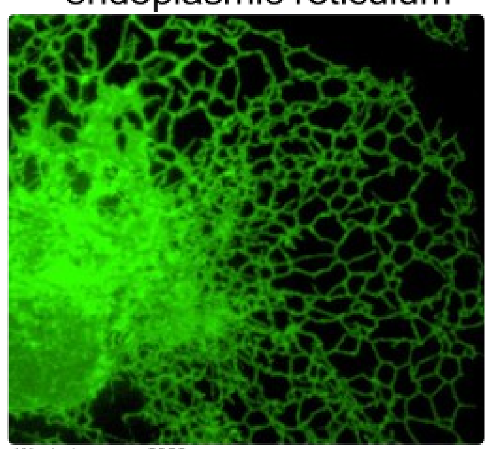
Some cells (like neurons) form shapes that provide long narrow pathways for particles that move actively along highways. Many such particles tend to go for a long time in one direction before turning around (very different from diffusing particles!). Other cells enclose a maze of tubules called an 'endoplasmic reticulum' that sets up a network of narrow tunnels through the inside of the cell.

nerve cell



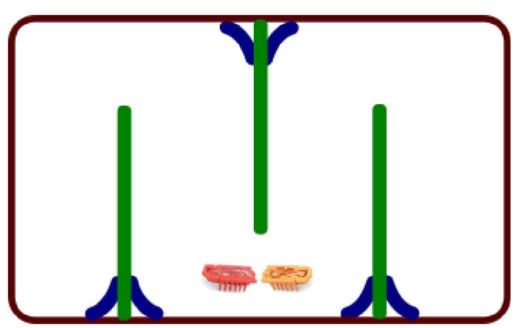
Kirk and Nguyen, Nikon Small World, 2020

endoplasmic reticulum



Westrate group, 2020

5) To see the effect of long narrow tunnels on two active particles trying to find each other, turn your tray into a maze such as the one shown here:



Start with the hexbugs in the middle, facing away from each other. Measure the time for them to find each other.

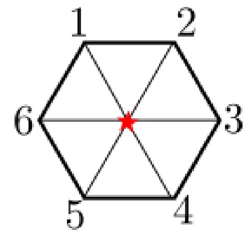
Trial	Encounter time
1	
2	
3	

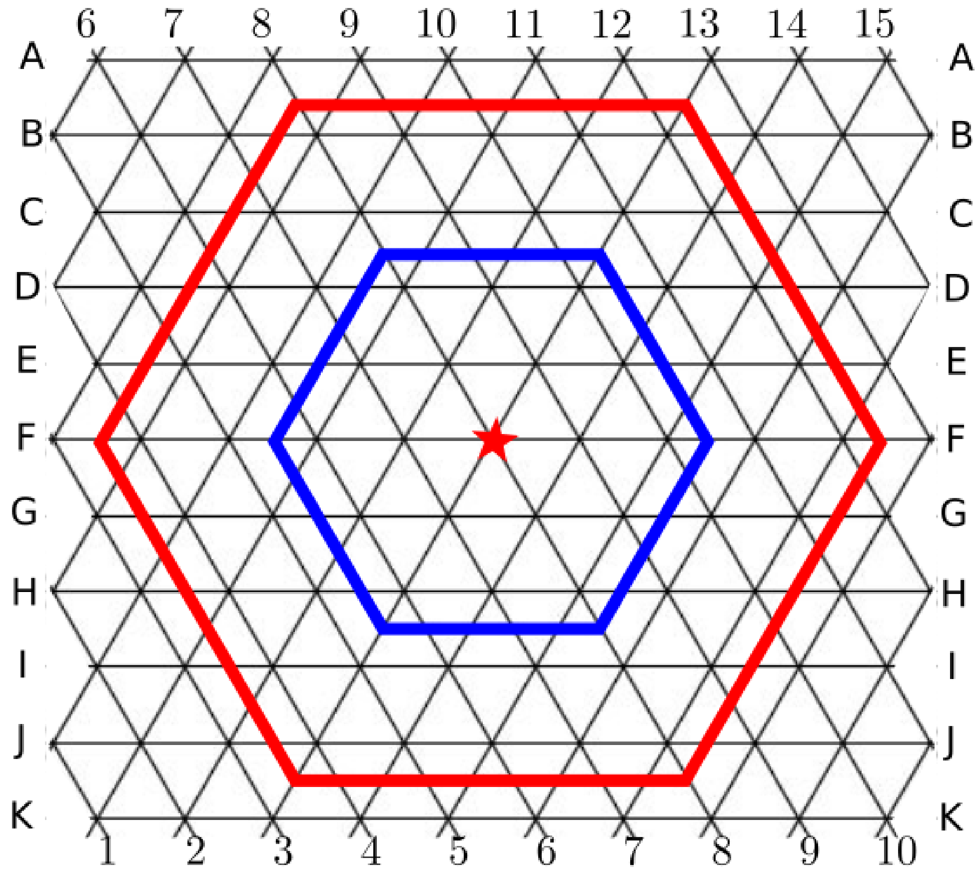
Average encounter time:

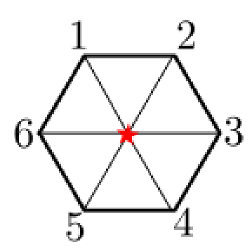
____

How did the encounter time in the maze compare to the encounter time in an empty region of the same size?

Do you think the results would change if the hexbugs were truly diffusing particles, that took random small steps in different directions instead of moving persistently?


1
2
6
3
5
4


6 7 8 9 10 11 12 13 14 15
A B C D E F G H I J K
1 2 3 4 5 6 7 8 9 10


1
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