The Structure, Function, and Evolution of Biological Systems

Instructor: Van Savage
Spring 2017 Quarter
5/10/2017
Outline

1. Finite size populations and genetic drift
2. Coalescence
3. Understanding directional and nondirectional forces
4. General Diffusion Equation
5. Biology
   a. Bacterium’s use of diffusion (physical constraint)
   b. Population genetics--combining selection and drift in evolution (Conceptual analogy)
      Derive equations in this context
What is stochasticity?

- Randomness
- Noise (in sense of signal to noise)
- No pattern, not predictable, not repeating
- Increasing entropy with no counterbalance
At what levels of biology does it show up?

- Mutation—drug resistance, disease
- Genetic drift, neutral evolution—used in bioinformatics and genomics
- Gene expression
- Cell movement/migration
- Cancer initiation
- Species extinction
- Biodiversity
- All levels in different ways
65% of cancers due to random mutations

Cancer’s Random Assault

By DENISE GRADY JAN. 5, 2015

It may sound flippant to say that many cases of cancer are caused by bad luck, but that is what two scientists suggested in an article published last week in the journal Science. The bad luck comes in the form of random genetic mistakes, or mutations, that happen when healthy cells divide.

Random mutations may account for two-thirds of the risk of getting many types of cancer, leaving the usual suspects — heredity and environmental factors — to account for only one-third, say the authors, Cristian Tomasetti and Dr. Bert Vogelstein, of Johns Hopkins University School of Medicine. “We do think this is a fundamental mechanism, and this is the first time there’s been a measure of it,” said Dr. Tomasetti, an applied mathematician.
Mathematical theory of noise and information

Claude Shannon and Norbert Wiener—tied to foundations of cybernetics
Mathematical theory of noise and information

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Genetic Drift in biology--
Nondirectional force

Drift*--by random, transient, non-genetic events, individuals that would be highly reproductive in a “repeated” experiment are lost to death.

Imagine a population of identical individuals that are being chosen for mating. Random chance that a given individual will be chosen.

*Drift in physics is actually convection or directional term. Very confusing so keep straight!
Genetic Drift

Model this by randomly sampling from entire population (Wright-Fisher model). Population size, $N$, is constant, and individuals are randomly selected for mating.

Each individual has $1/N$ chance of reproducing.

We get a binomial tree that depends on allele frequency, $p$, and total population size, $N$. Mean number with certain allele $= 2Np$
Genetic Drift

So, rate of spread of the width of distribution is $\sim p(1-p)/2N$.

Must go to fixation or extinction. What about intermediate times?
Coalescence: Look backwards in time
Quick results

1. \( P(\text{fixation}) = p \)

2. \( P(\text{fixation new individual mutant}) = 1/2N \)

3. Total number of mutations per generation = \( 2N\mu \)

4. Chance of some mutant reaching fixation = \( \mu \)

5. Probability of coalescing \( t+1 \) generations back is \( (1/2N)e^{-t/2N} \)
Using last result

1. $\langle T \rangle = 2N$

2. $\text{StDev}(T) = 2N$
General diffusion equation
and
combining selection and drift
Directional Forces: Go with the flow
Directional Forces

1. Crowd running towards a celebrity or away from a fire.
2. Pushing or rolling any ball or object
3. A river flowing towards the sea or ocean
Nondirectional forces: No flow
Nondirectional forces: No flow
Nondirectional forces

1. Lost in a crowded intersection
2. Drop of dye in water
3. Smoke
4. Choosing each step after flipping a coin
Net Flow--Directional Forces

Net Flow=Flow In-Flow Out
=Flow from left(i-1->i) - Flow to right(i->i+1)
->\( f(i,t+1)-f(i,t)=v(i-1)f(i-1,t)-v(i)f(i,t) \)
Continuum limit:
->\( \frac{df}{dt}=-\frac{d(vf)}{dx} \) (i.e., distance=velocity*time)

\( f(i,t) \) is abundance or probability of being in bin \( i \) at time, \( t \).

\( v(i) \) is speed of flow out of bin \( i \).
Net Flow--Nondirectional Forces

Net Flow = Flow In - Flow Out
= Flow from left (i-1->i) + Flow from right (i+1->i)
- Flow to right (i->i-1) - Flow to left (i->i+1)
-> f(i,t+1) - f(i,t) = D(i-1)f(i-1,t) + D(i+1)f(i+1,t) - 2*D(i)f(i,t)
D(i) is the diffusion rate

Continuum limit:
-> df/dt = d^2(Df)/dx^2 (Second derivative)

Local process and affects width of distribution, not mean
Global signature of diffusion

Random walk
\( x(t+1) = x(t) \pm 1 \)
\( \Rightarrow x^2(t+1) = x^2(t) + 2x(t) + 1 \) (1/2 of time)
\( = x^2(t) - 2x(t) + 1 \) (1/2 of time)

\( \langle x^2(t+1) \rangle = (1/2) \langle (x^2(t) + 2x(t) + 1) \rangle 
+ (1/2) \langle (x^2(t) - 2x(t) + 1) \rangle 
= \langle x^2(t) \rangle + 1 = \langle x^2(t-1) \rangle + 2 \)

Iterating this gives: \( \langle x^2(t+1) \rangle \approx \text{Number of time steps} \sim t \)

\[ \Rightarrow |x| = \sqrt{x^2} \propto \sqrt{t} \]
Diffusion properties and simulation

https://www.youtube.com/watch?v=bYb9iIwTaEU

Internal dynamics of diffusion are not immediately obvious from global behaviors, whereas it is for directional forces.

Nondirectional force (diffusion) affects width of distribution, and directional forces affect the mean.

Diffusion process is NOT time reversible. Initial conditions are forgotten.
2. Combined Effects

Person trying to walk north (directional) through a busy intersection (nondirectional)

Net Flow = Directional Flow + Nondirectional Flow

Diffusion Equation
(Also known as Kolmogorov forward equation or like Fokker-Planck equation)

\[ \frac{\partial f}{\partial t} = - \frac{\partial (vf)}{\partial x} + \frac{\partial^2 (Df)}{\partial x^2} \]
Often, $v$ and $D$ are constant, so:

\[
\frac{\partial f}{\partial t} = -v \frac{\partial f}{\partial x} + D \frac{\partial^2 f}{\partial x^2}
\]
3. Physics--Brownian Motion

Molecule in glass of water is analogous to our person walking through a crowd. Since molecule is so small (mass is so little), gravity’s effect (directional force) is negligible. Hence,

\[
\frac{\partial f}{\partial t} = D \frac{\partial^2 f}{\partial x^2}
\]

(Heat Equation)
Some Bacteria

Better conditions at bottom (oxygen pressure) Weigh so little that gravity is negligible, and they do not know which way is down.

Magnetotactic bacteria
They have internalized enough magnetite particles so that earth’s magnetic field can just overcome nondirectional forces of Brownian Motion. Since magnetic fields go into earth, they can now sense down. So, they “solve” problem from previous slide! Bacteria in north and south are polarized differently.
Apply magnetic field to diffusing particles

This gives a directional force, and since magnetic force is much stronger than gravity, this is not negligible. Must return to full equation.

\[
\frac{\partial f}{\partial t} = - \frac{\partial (vf)}{\partial x} + \frac{\partial^2 (Df)}{\partial x^2}
\]

\(v\) depends on strength of magnetic field
4. Biology—Magnetotactic Bacteria

**Fig. 1**
Magnetotactic bacteria with chain of magnetite crystals.

**Fig. 2**
Close up of the chain of magnetite crystals.
Types of multidisciplinary influences

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<td>-&gt; Combine natural selection and genetic drift</td>
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