Mathematical Preliminaries / Notation

* Quantitative understanding of evolution requires math, so we'll assume comfort w/ manipulating eqs, calculus, etc.

* However, something you may not have seen in previous math/phys courses, but will be really useful here:

"Series expansions / approximations / self-consistency"

Can illustrate w/ simple example: $\epsilon x^2 + x - 1 = 0$ (which we already know how to solve)

$\Rightarrow$ positive root: $x = \dfrac{-1 + \sqrt{1+4\epsilon}}{2\epsilon} \equiv F(\epsilon)$

Often want to understand behavior in certain limits, e.g. $\epsilon \to 0$.

$\Rightarrow$ can use Talylor series: $x \approx F(0) + F'(0)\epsilon + \ldots$

$\approx (1) + (-\epsilon)$ [wolfram alpha is helpful!]

"leading order" "next order"

First term tells us how to approx x. Next term tells you how "good" approx is.

e.g. $x \approx F(0)$ if $F'(0)\epsilon \ll F(0)$, or $\epsilon \ll \epsilon^* \equiv \frac{F(0)}{F'(0)}$ [$=1$ here]

$\Rightarrow$ often write this as $x \approx 1 \quad (\epsilon \ll 1)$

can also do this directly from equation
("dominant balance")

step 1 guess ϵx^2 is much smaller than other terms $(x, -1)$

$$\cancel{\epsilon x^2} + x - 1 = 0 \Rightarrow \boxed{x = 1 \text{ (leading order approx)}}$$

step 2 can then check whether approx is self-consistent

$$\Rightarrow \epsilon x^2 \approx \epsilon (1)^2 \approx \epsilon, \; x \approx 1 \Rightarrow \epsilon x^2 \ll x, -1 \quad \boxed{\text{if } \epsilon \ll 1}$$

* tells you when approx breaks down! e.g. if $\epsilon A x^2 + x - 1 \approx 0$

(compare e.g. to math relation, $\lim_{\epsilon \to 0} x = 1$) $\Rightarrow \boxed{\epsilon \ll 1/A}$

This is really important when we want to start connecting w/ data & experiments.

Big theme of course will be figuring out leading order approximations $(x \approx 1)$ but also regions of validity $(\epsilon \ll 1)$ and using data to estimate when they might be good.

* self consistency check can also tell you if you guessed wrong

e.g. if we guessed $x \ll \epsilon x^2, -1 \Rightarrow x \approx \frac{1}{\sqrt{\epsilon}} \gg -1$ ~~X~~

inconsistent!

* can use same approach to calculate next order correction:

step 1 — write $x = 1 + \delta$ ← correction term.

step 2 — substitute into $\epsilon x^2 + x - 1 = 0$; expand to lowest order in δ.

$$\Rightarrow \quad \epsilon(1+2\delta) + (1+\delta) - 1 = 0 \Rightarrow \delta = \frac{-\epsilon}{1+2\epsilon} \approx -\epsilon$$

* can use same approach to understand opposite limit $(\epsilon \to \infty)$

$$\Rightarrow \quad x \approx \frac{1}{\sqrt{\epsilon}} - \frac{1}{2\epsilon} \qquad (\epsilon \ll 1)$$

This seems like a lot of work for answer we already know... $\left(x = \frac{-1+\sqrt{1+4\epsilon}}{2\epsilon}\right)$. But what if eq. was $\epsilon x^5 + x - 1 = 0$

No exact solution! But approximations all still work. This will be a <u>typical</u> case for us in evolutionary problems.

* Approx's also often useful in practical contexts. (data).

$\Rightarrow$ w/ all possible choices of ϵ, most are $\gg 1$ or $\ll 1$. Fine tuning needed for $\epsilon \simeq 1$

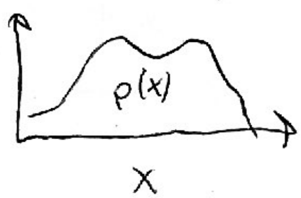
$\Rightarrow$ get a lot of mileage out of $\epsilon \ll 1$, $\epsilon \gg 1$ approximations.

This basic approach works for differential equations, stochastic differential equations, integrals, etc. and we will encounter it a lot in our course.

Probability

Since many aspects of evolution are stochastic, the other big tool we'll need is probability theory.

1. Random variables: I'll assume you're familiar with the concept of a random variable, $\hat{x}$, distributed according to some distribution, $p(x)$:



(we'll write $x \sim p(x)$)

with mean ("expected value") $\langle x \rangle \equiv E[x] \equiv \int x\,p(x)\,dx$

variance $\mathrm{Var}(x) = \langle x^2 \rangle - \langle x \rangle^2$

2. common distributions: $n \sim \mathrm{Binomial}(N,p)$ $\left[P(n) = \binom{N}{n} p^n (1-p)^{N-n}\right]$

$$n \sim \mathrm{Poisson}(\langle n \rangle) = \lim_{\substack{N\to\infty \\ p\to 0 \\ \text{fixed } \langle n \rangle}} \mathrm{Binomial}(N,p) \quad \left[P(n) = \frac{\langle n \rangle^n}{n!} e^{-\langle n \rangle}\right]$$

$x \sim$ Gaussian(μ, σ^2) $\left[p(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-x^2/2\sigma^2} \right]$

"Normal"

$\Rightarrow$ wikipedia is your friend for common dist'ns.

3 Joint dist'ns: $p(x,y)$ = prob of $\hat{x}=x$ & $\hat{y}=y$ @ same time.

conditional probability: $p(x|y) \equiv \frac{p(x,y)}{p(y)}$ (value of x given $\hat{y}=y$)

statistical independence: $p(x,y) = p(x)p(y)$ or $p(x|y) = p(x)$

$\mathrm{Var}(X+Y) = \mathrm{Var}(X) + \mathrm{Var}(Y)$

marginalization: $p(x) \equiv \int p(x,y)\,dy$

4 one thing that might be new: moment generating function

$$H_x(z) = \langle e^{-zx} \rangle = \int e^{-zx} p(x)\,dx$$ [i.e. laplace transform of $p(x)$]

(for positive random vars, $H(z) \approx$ probability that $x \lesssim 1/z$ (crudely)]

$H_x(z) \Leftrightarrow p(x)$ so either suffices.

$$H_x(z) = \int \left[1 - zx + \frac{1}{2} z^2 x^2 + \dots \right] p(x) = 1 - z\langle x \rangle + \frac{z^2}{2} \langle x^2 \rangle$$

(expansion gets you moments of x $\Rightarrow$ moment generating func)

Big payoff for $H(z)$ is that for <u>independent</u> r.v.'s:

$$H_{x+y}(z) = \langle e^{-z(x+y)} \rangle = \langle e^{-zx} e^{-zy} \rangle = \underbrace{\langle e^{-zx} \rangle \langle e^{-zy} \rangle}_{H_x(z)\, H_y(z)}$$

in many evolution problems, we'll find it easier to solve for $H(z)$ and then <u>invert</u> if we need to find $p(x)$.

$\Rightarrow$ in practice, easiest to do by remembering MGF for common distn's & then invert by inspection:

e.g. $\text{Poisson}(\langle n \rangle) \Longleftrightarrow H(z) = e^{-\langle n \rangle (1-e^{-z})}$

$\text{Gaussian}(\mu, \sigma^2) \Longleftrightarrow H(z) = e^{-\mu z + \frac{1}{2}\sigma^2 z^2}$

<u>Central limit theorem</u>

finally, we'll get a lot of mileage out of central limit theorem:

$X_1, X_2, \ldots, X_n$ independent, then

then $\sum_{i=1}^{n} X_i \rightarrow \text{Gaussian}(n\langle x \rangle, n \,\text{Var}(x))$

$$\Rightarrow \frac{1}{n}\sum_{i=1}^{n} X_i \approx \langle X \rangle \pm \frac{\text{Var}(X)}{n}$$

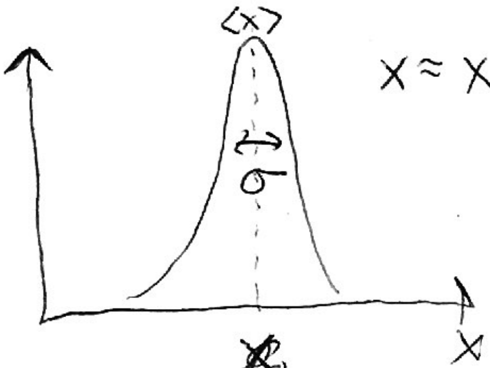
(for certain classes of X_i!)

Finally, one last note about intuition & probability
(or "average" vs "typical")

Probability is hard because it forces us to reason about a whole range of outcomes all @ once.
⇒ often need some way of summarizing typical behavior.

* there will be 2 main classes of behavior we will encounter:

case 1

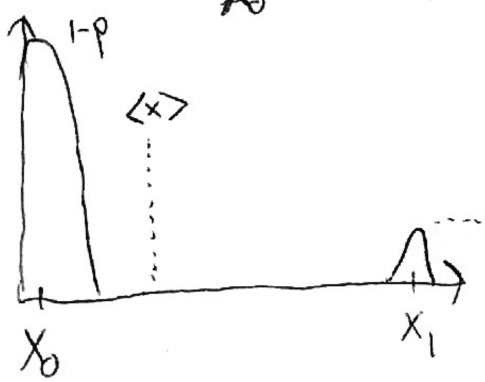


$x \approx x_0 \pm \sigma$

e.g. Binomial(N,p)
when $Np \gg 1$

in this case, average is good summary of typical

case 2



e.g. Binomial(N,p)
when $Np \ll 1$
[e.g. did a mutation occur?]

in this case, no actual realization of x will have $x = \langle x \rangle$!
⇒ mean is not good summary of typical.

* distinction becomes important if we then do something based on value of x (e.g. apply nonlinear function)

$Y = F(x)$ = later growth of x mutations.

in case 1: can get a lot of mileage by substituting $x = x_0 \pm \sigma$ and Talyor expanding:

$$Y \approx F(x_0 \pm \sigma) \approx F(x_0) + F'(x_0)\,\sigma$$ (error propagation in physics lab)

in case 2: need to consider bifurcating outcomes:

$$Y \approx \begin{cases} F(x_0) & \text{w/ prob } 1-p \\ F(x_1) & \text{w/ prob } p. \end{cases}$$

← this can be typical case most of time.

← treat rare cases where this happens separately

you'll notice that most of the randomness we're used to encountering is of the case 1 variety. in evolution, we'll encounter many phenomena of case 2, and this general strategy of breaking things up will be useful.

just like w/ $\epsilon x^2 + x - 1 = 0$ example, $Np \ll 1$ and $Np \gg 1$ covers most of param space for binomial. so these 2 pictures cover many practical scenarios.

* I encourage you to keep these 2 pictures in the back of your head as we deal w/ random phenomena in this course.