Phylogenetics 101

Part 3a: Bayesian statistics and MCMC

- Bayesian inference
- Markov chain Monte Carlo
- MCMC in phylogenetics

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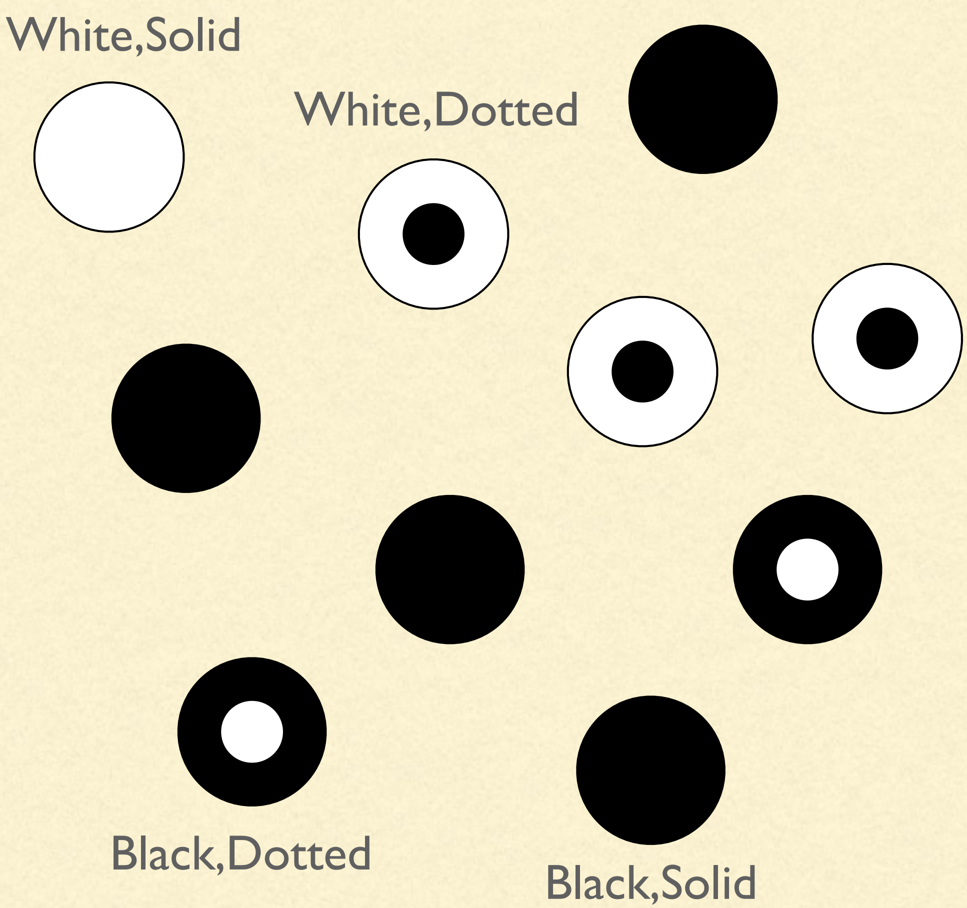
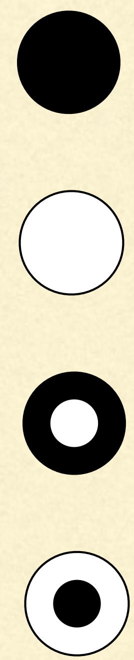
DEB-1354146 Broader Impacts

Bayesian inference

Joint probabilities



10 marbles in a bag
Sampling with replacement



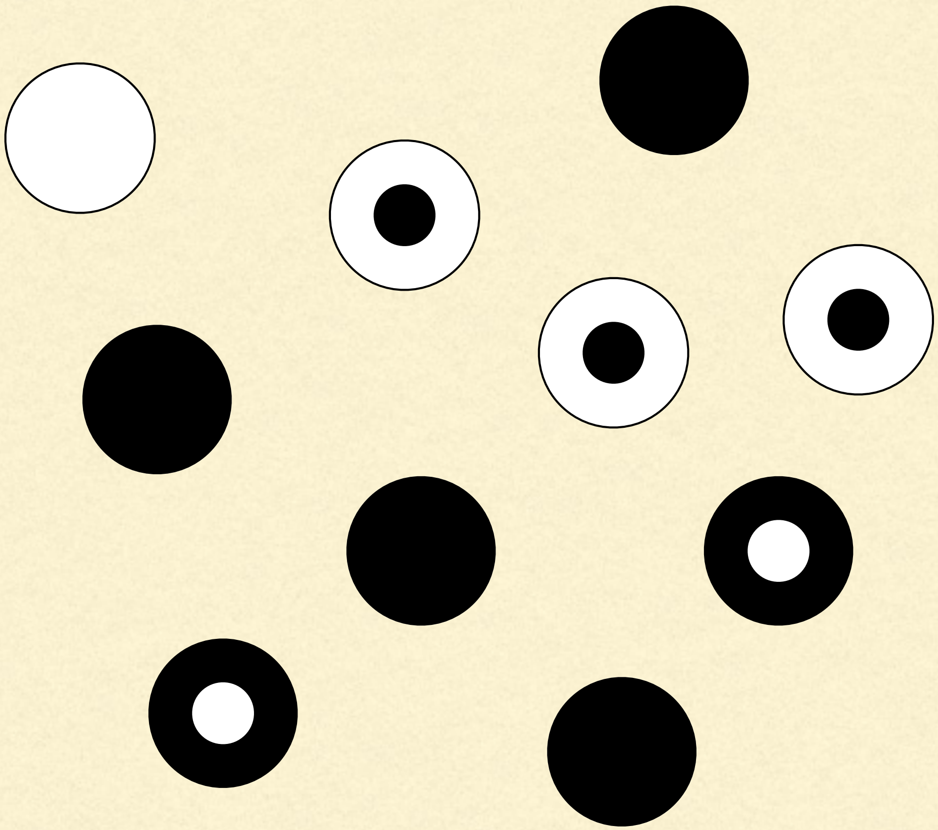
$\Pr(B,S) = 0.4$

$\Pr(W,S) = 0.1$

$\Pr(B,D) = 0.2$

$\Pr(W,D) = 0.3$

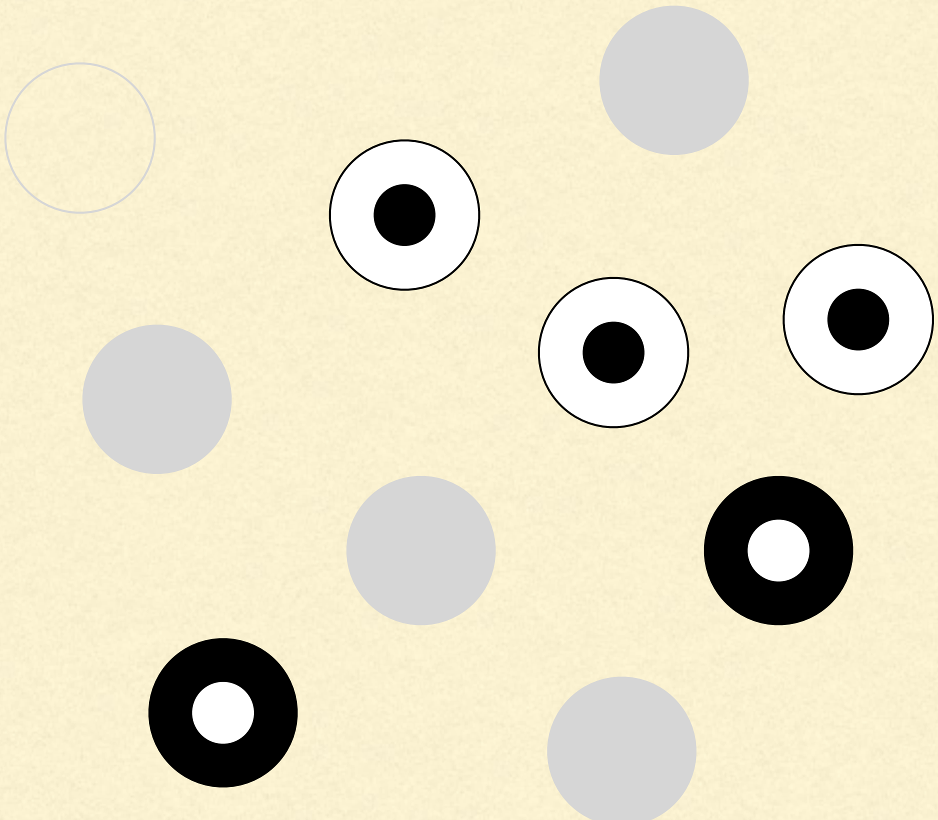
Conditional probabilities



What's the probability that a marble is black given that it is dotted?

$$\Pr(B|D) = \frac{2}{5}$$

Conditional probabilities

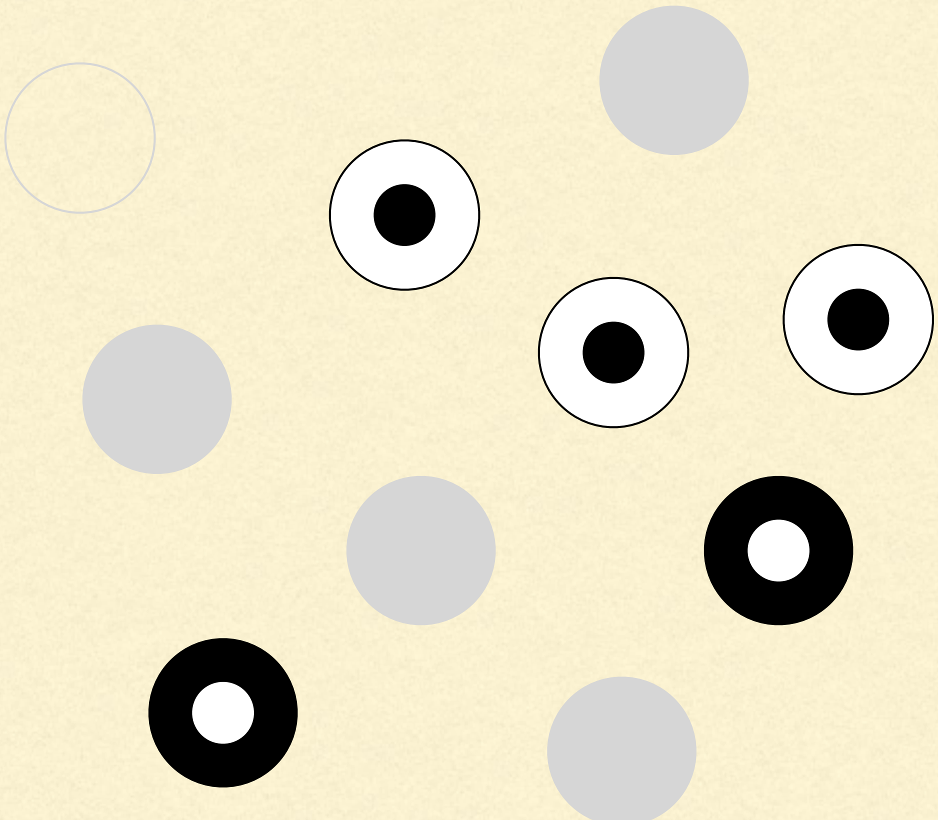


What's the probability that a marble is black given that it is dotted?

5 marbles satisfy the condition (D)

$$\Pr(B|D) = \frac{2}{5}$$

Conditional probabilities



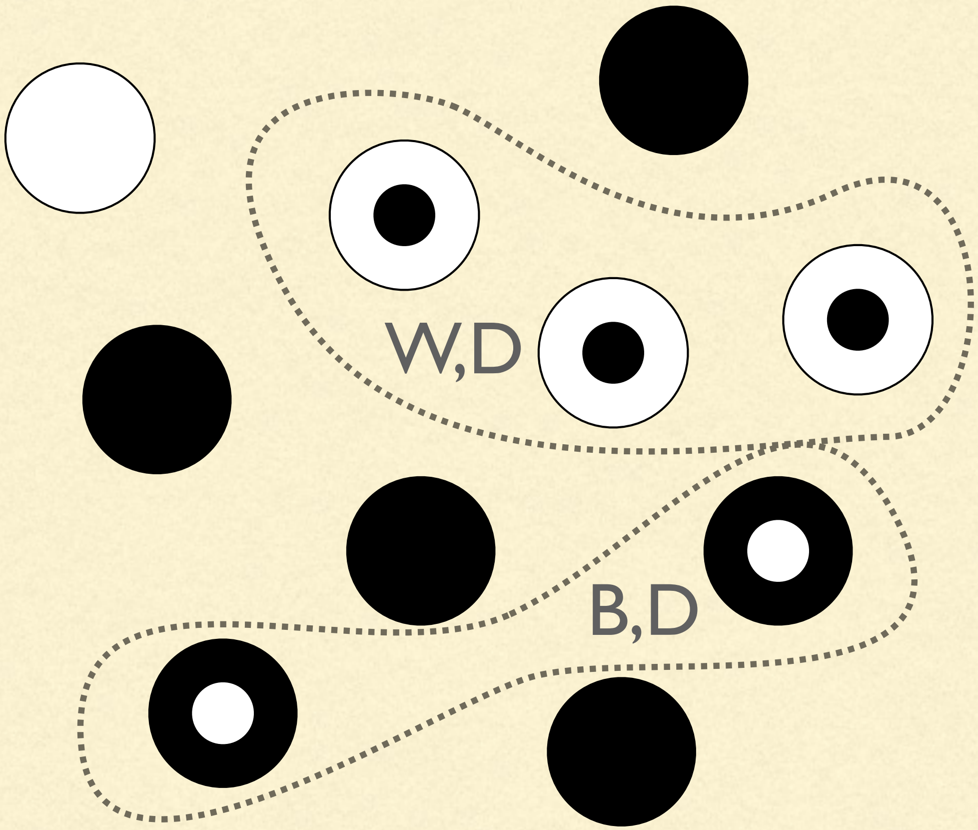
What's the probability that a marble is black given that it is dotted?

5 marbles satisfy the condition (D)

$$\Pr(B|D) = \frac{2}{5}$$

2 remaining marbles are black (B)

Marginal probabilities



Marginalizing over color yields the total probability that a marble is dotted (D)

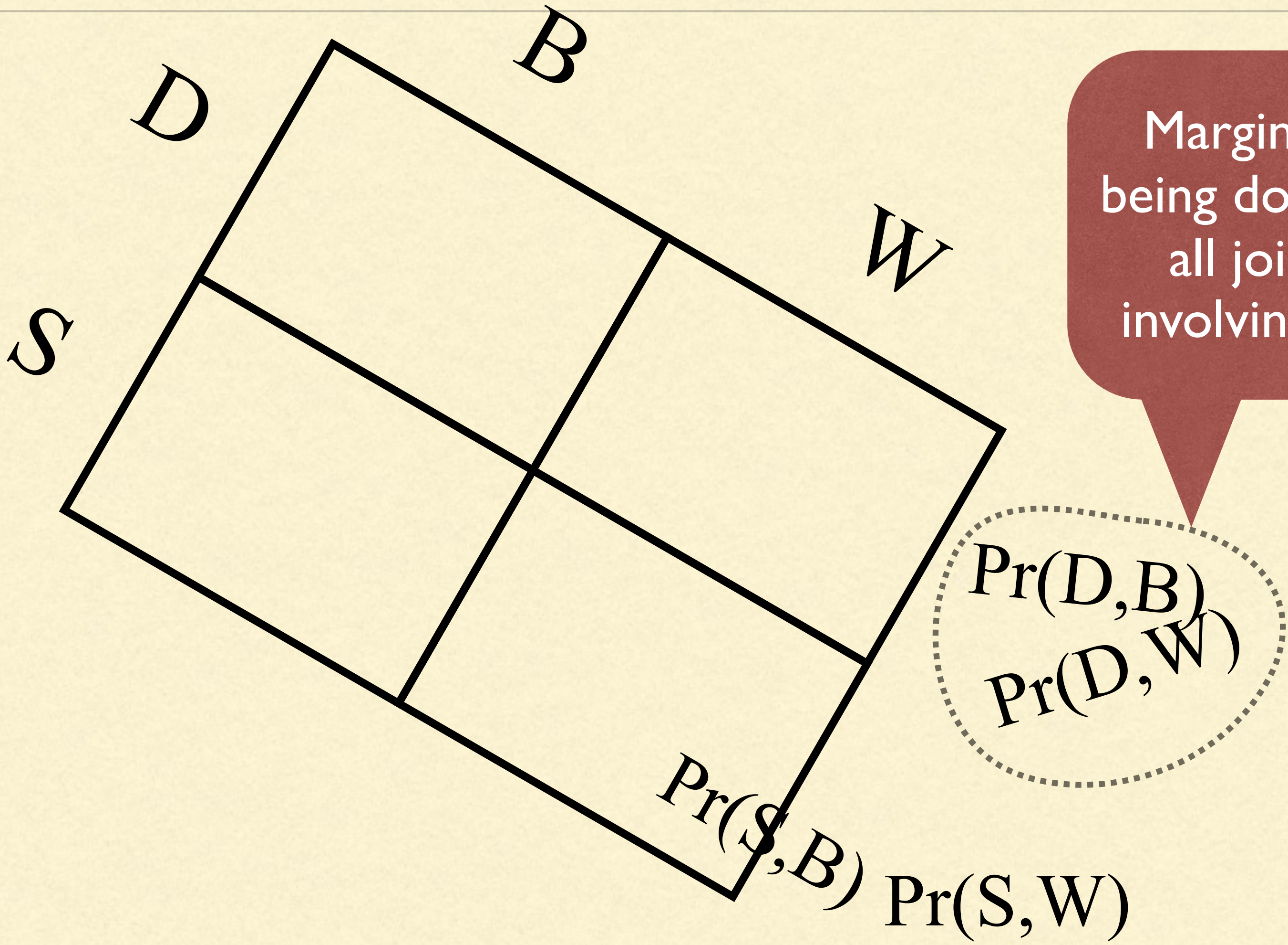
$$\Pr(\mathbf{D}) = \Pr(B,\mathbf{D}) + \Pr(W,\mathbf{D})$$
$$= 0.2 + 0.3$$
$$= 0.5$$

Marginalization involves summing all joint probabilities containing D

Marginalization

	B	W
D	Pr(D,B)	Pr(D,W)
S	Pr(S,B)	Pr(S,W)

Marginalizing over colors



Marginal probability of being dotted is the sum of all joint probabilities involving dotted marbles

Marginal probabilities

	B	W
D		
S		

Pr(D) = marginal probability of being dotted

Pr(D,B) + Pr(D,W)

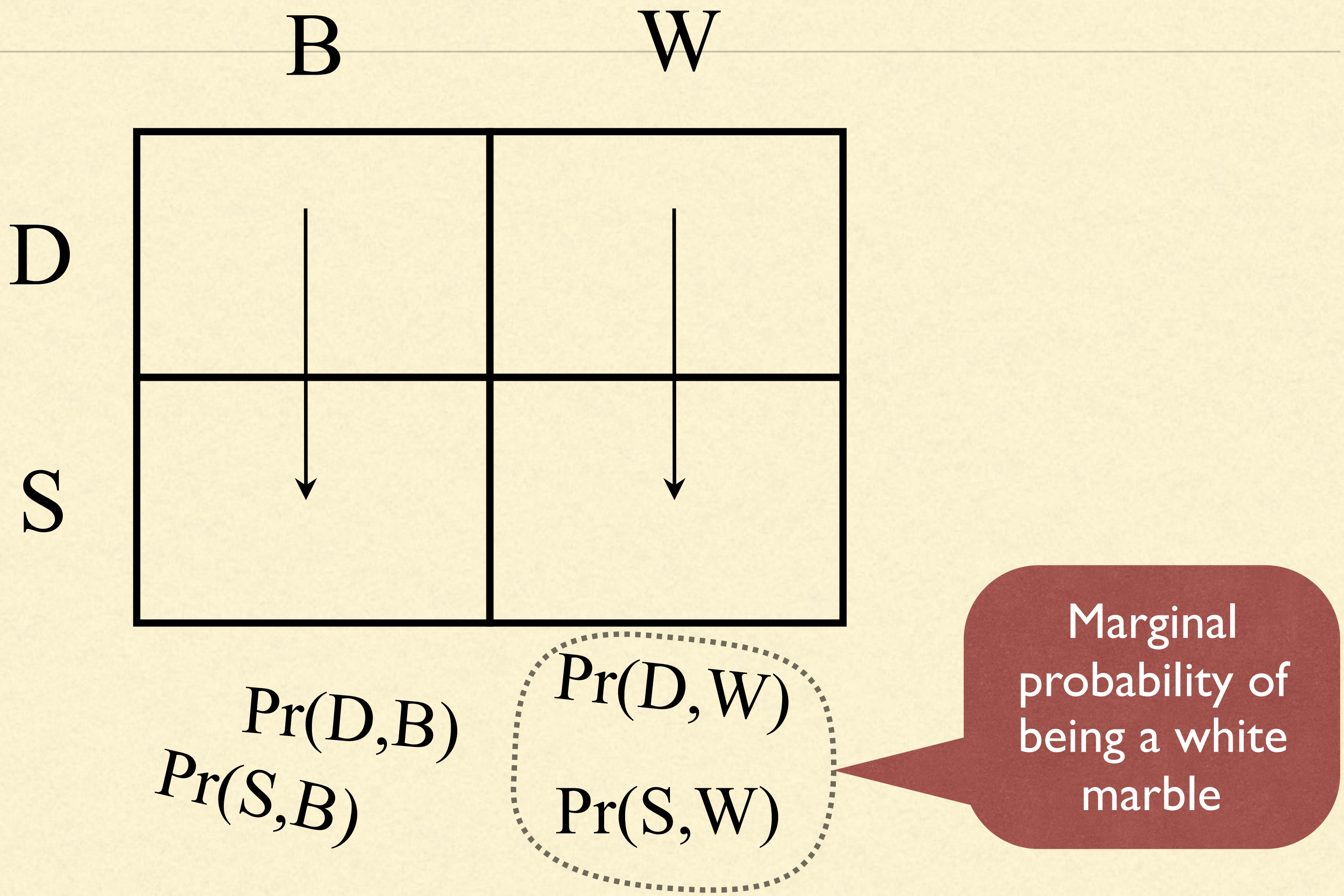
Pr(S,B) + Pr(S,W)

Pr(S) = marginal probability of being solid

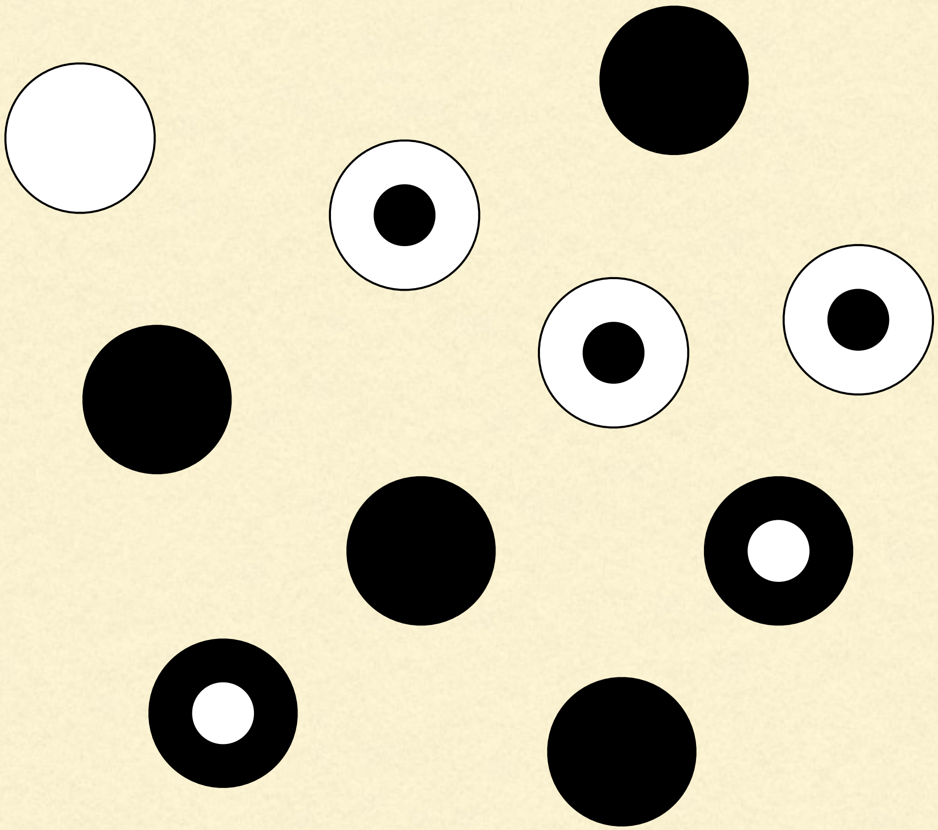
Joint probabilities

	B	W
D	Pr(D,B)	Pr(D,W)
S	Pr(S,B)	Pr(S,W)

Marginalizing over "dottedness"



Bayes' rule



The joint probability Pr(B,D) can be written as the product of a *conditional probability* and the *probability of that condition*

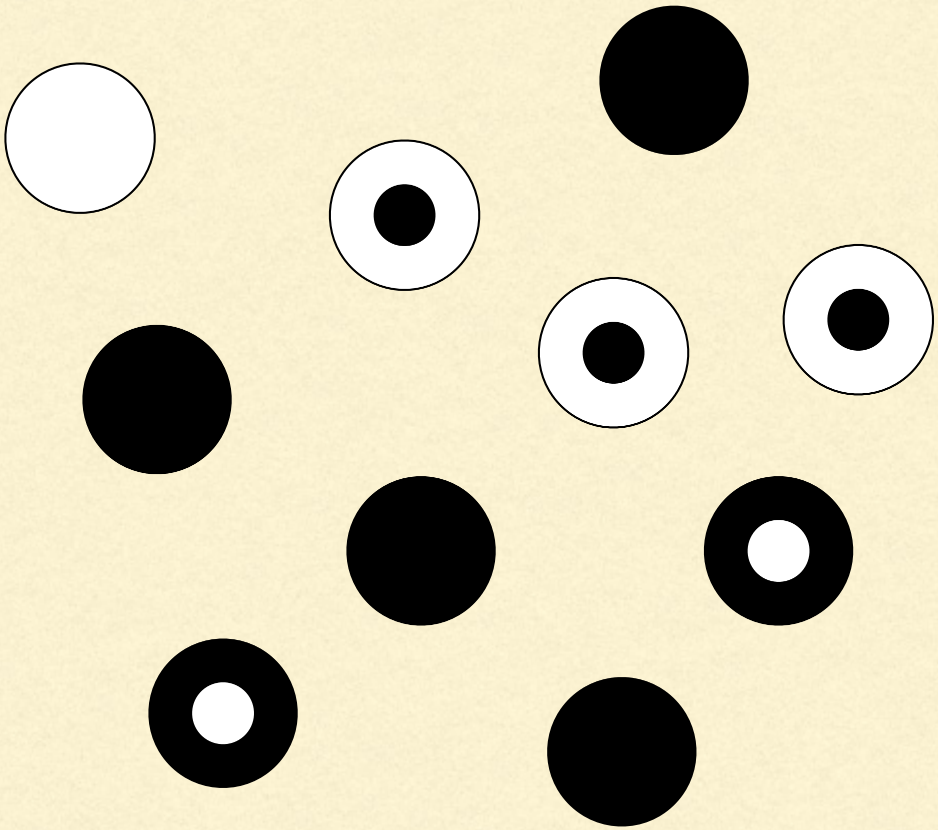
Pr(B|D) Pr(D)

Pr(B,D)

Either B or D can be the condition

Pr(D|B) Pr(B)

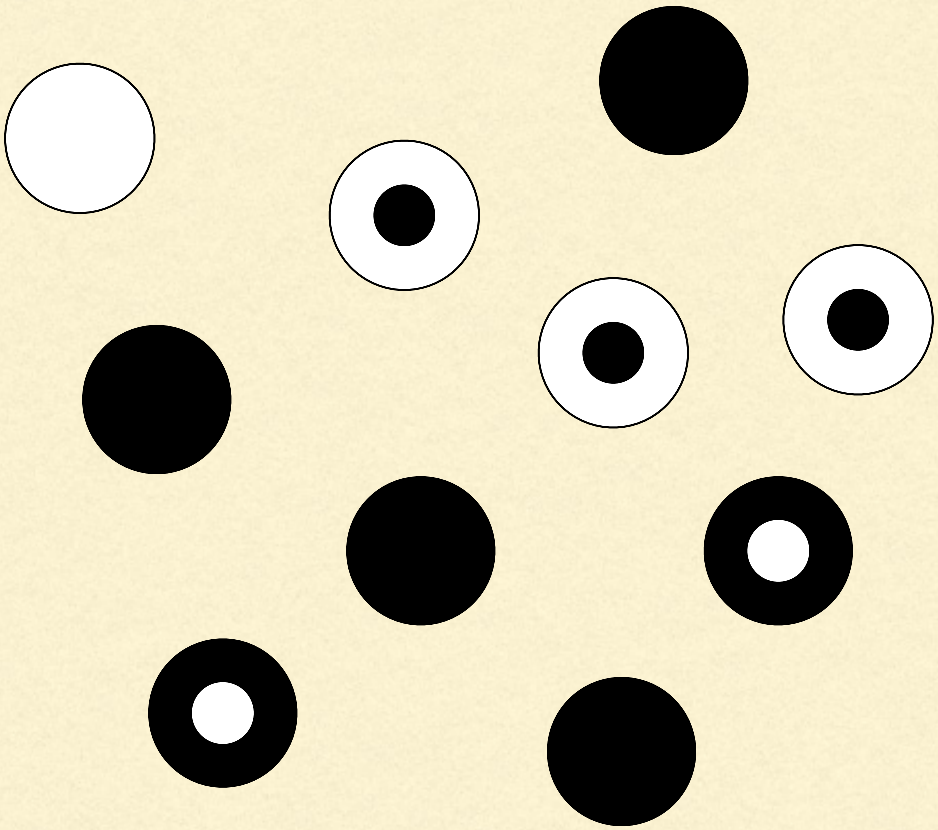
Bayes' rule



Equate the two ways of writing Pr(B,D)

$$Pr(B|D)\ Pr(D) = Pr(D|B)\ Pr(B)$$

Bayes' rule



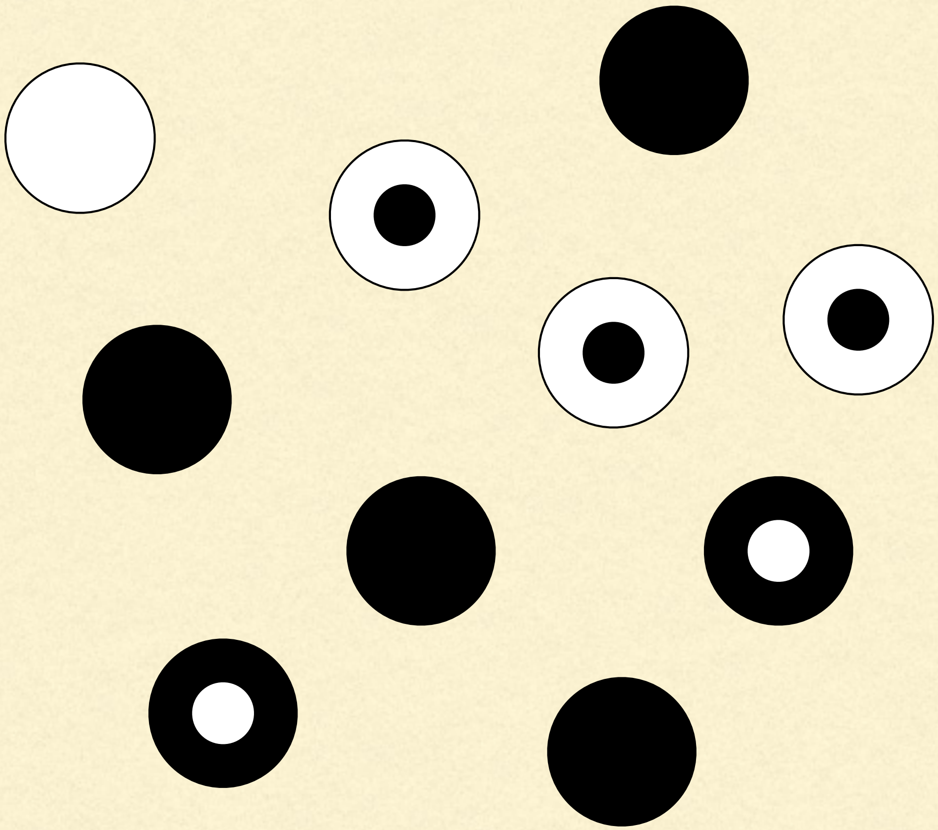
Equate the two ways of writing Pr(B,D)

$$\Pr(B|D)\,\Pr(D) = \Pr(D|B)\,\Pr(B)$$

Divide both sides by Pr(D)

$$\frac{\Pr(B|D)\,\cancel{\Pr(D)}}{\cancel{\Pr(D)}} = \frac{\Pr(D|B)\,\Pr(B)}{\Pr(D)}$$

Bayes' rule



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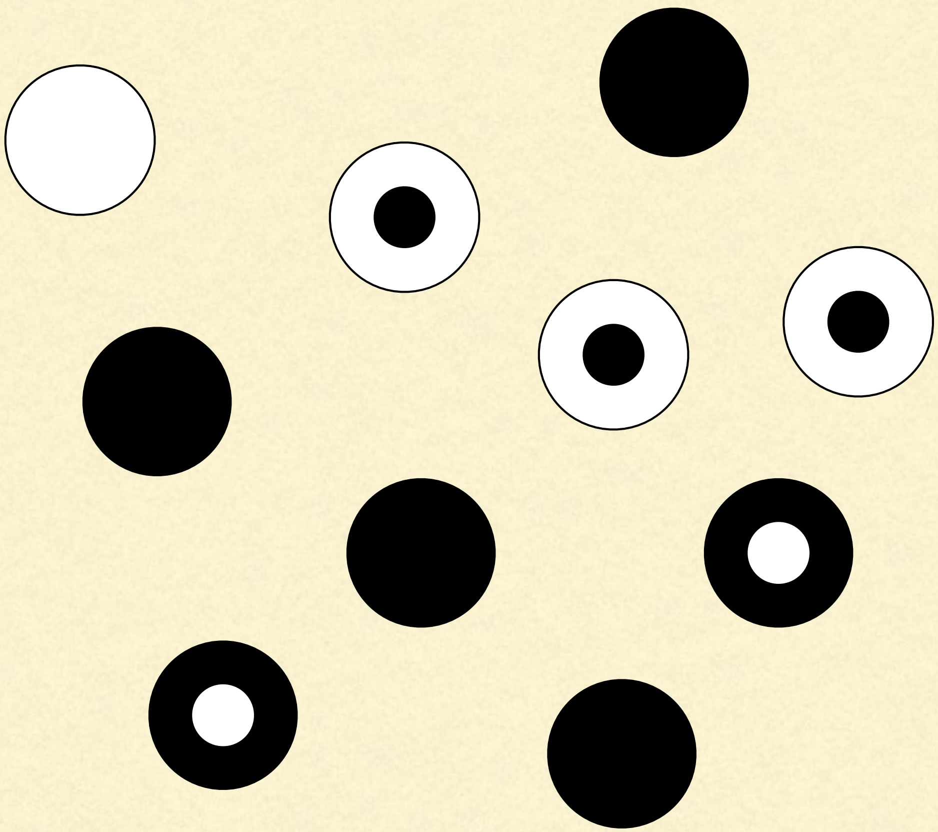
$$\frac{\Pr(B|D)\,\cancel{\Pr(D)}}{\cancel{\Pr(D)}} = \frac{\Pr(D|B)\,\Pr(B)}{\Pr(D)}$$

Bayes' rule

$$\Pr(B|D) = \frac{\Pr(D|B)\,\Pr(B)}{\Pr(D)}$$

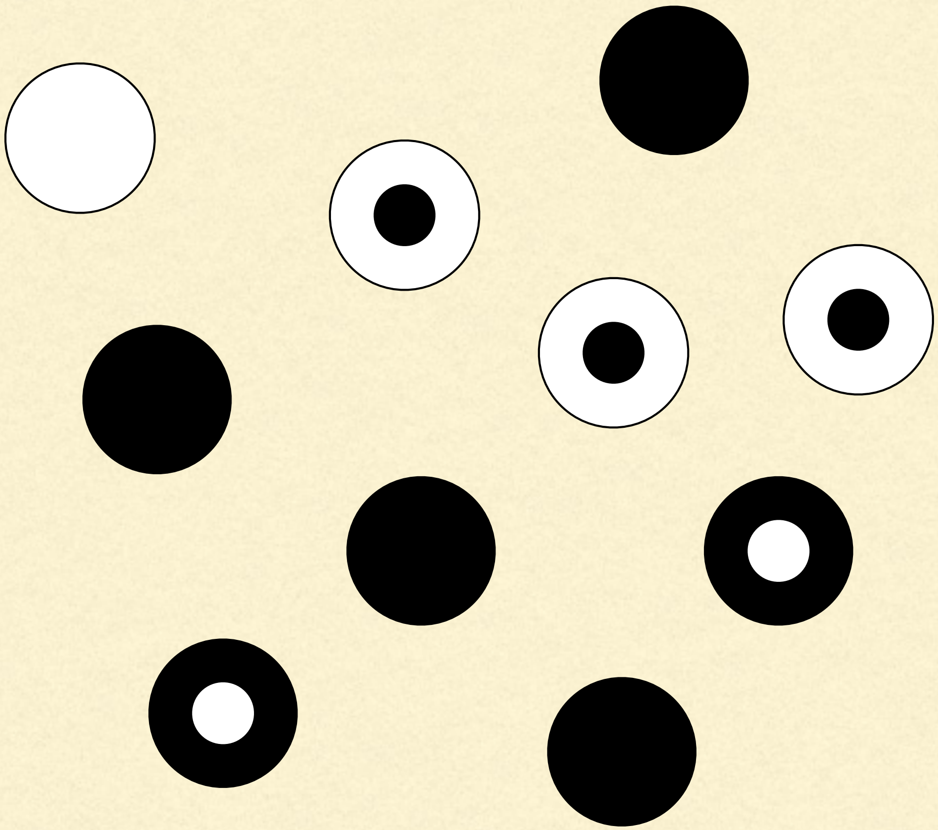
Bayes' rule



Bayes' rule

$$\Pr(B|D) = \frac{\Pr(D|B)\ \Pr(B)}{\Pr(D)}$$

Bayes' rule



Bayes' rule

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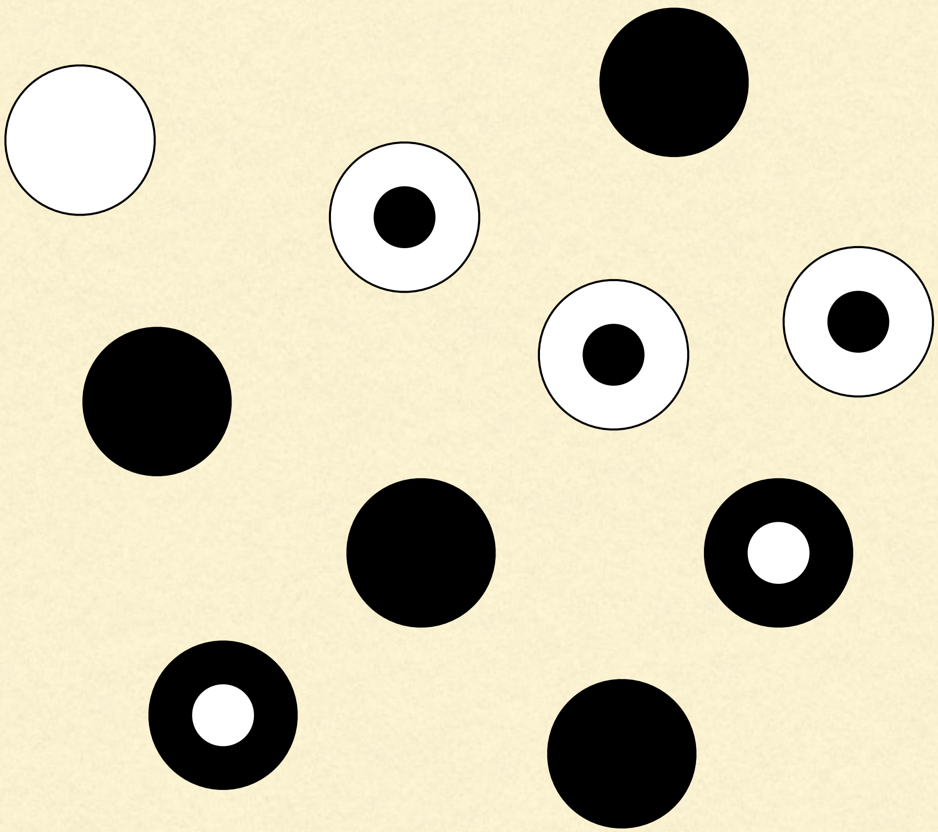
Bayes' rule

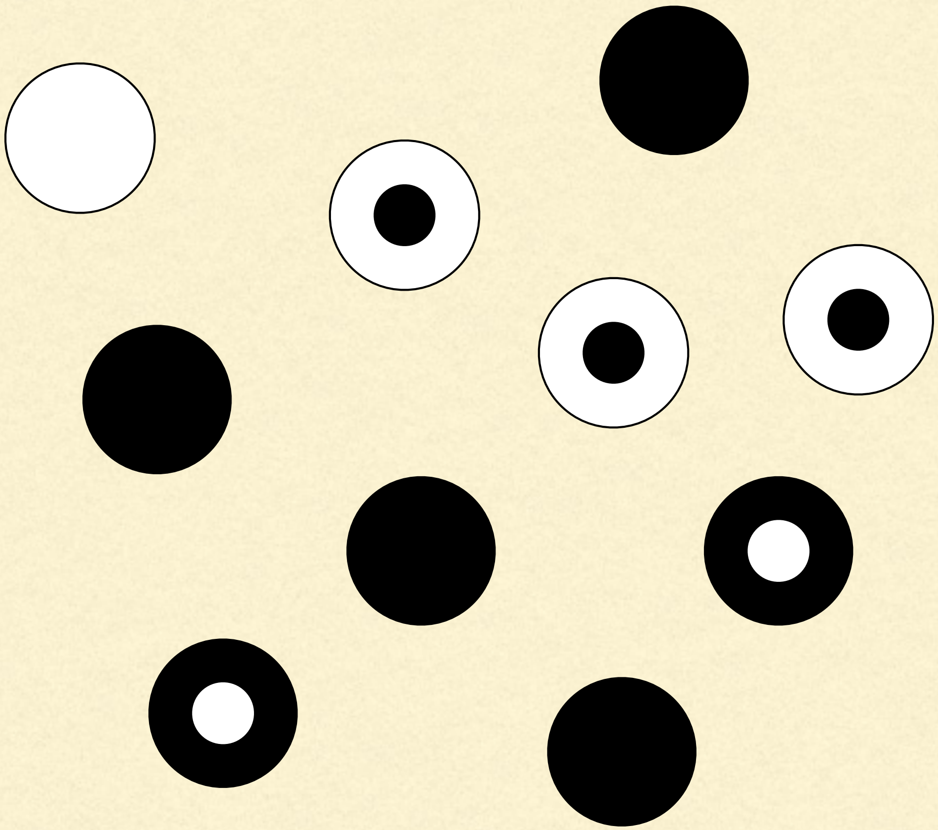


Bayes' rule

$$\Pr(B|D) = \frac{\Pr(D|B)\,\Pr(B)}{\Pr(D)}$$

$$\frac{2}{5} = \frac{\frac{1}{\cancel{3}} \times \frac{\cancel{3}}{5}}{\frac{1}{2}}$$

Bayes' rule



Bayes' rule

$$\Pr(B|D) = \frac{\Pr(D|B)\,\Pr(B)}{\Pr(D)}$$

$$\frac{2}{5} = \frac{\frac{1}{\cancel{3}} \times \frac{\cancel{3}}{5}}{\frac{1}{2}}$$

$$\frac{2}{5} = \frac{2}{5}$$

Bayes' rule (variations)

$$\Pr(B|D) = \frac{\Pr(B)\Pr(D|B)}{\Pr(D)}$$

$$= \frac{\Pr(D, B)}{\Pr(D, B) + \Pr(D, W)}$$

Bayes' rule (variations)

$$\Pr(B|D) = \frac{\Pr(B)\Pr(D|B)}{\Pr(D)}$$

$$= \frac{\Pr(D,B)}{\boxed{\Pr(D,B) + \Pr(D,W)}}$$

Pr(*D*) is the **marginal probability** of being dotted
To compute it, we **marginalize over colors**

Normalizing constant

It is easy to see that Pr(*D*) serves as a *normalization constant*, ensuring that Pr(*B*|*D*) + Pr(*W*|*D*) = 1.0

$$\Pr(B|D) = \frac{\boxed{\Pr(D,B)}}{\boxed{\Pr(D,B)} + \Pr(D,W)} \quad \longleftarrow \Pr(D)$$

$$\Pr(W|D) = \frac{\boxed{\Pr(D,W)}}{\Pr(D,B) + \boxed{\Pr(D,W)}} \quad \longleftarrow \Pr(D)$$

$$\Pr(B|D) + \Pr(W|D) = \frac{\cancel{\Pr(D,B) + \Pr(D,W)}}{\cancel{\Pr(D,B) + \Pr(D,W)}} = 1$$

Bayes' rule (variations)

$$\Pr(B|D) = \frac{\Pr(D|B)\Pr(B)}{\Pr(B,D) + \Pr(W,D)}$$

Bayes' rule (variations)

$$\Pr(B|D) = \frac{\Pr(D|B)\Pr(B)}{\Pr(B,D) + \Pr(W,D)}$$

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Bayes' rule (variations)

$$\Pr(B|D) = \frac{\Pr(D|B)\Pr(B)}{\Pr(B,D) + \Pr(W,D)}$$

$$= \frac{\Pr(D|B)\Pr(B)}{\Pr(D|B)\Pr(B) + \Pr(D|W)\Pr(W)}$$

$$= \frac{\Pr(D|B)\Pr(B)}{\sum_{\theta \in \{B,W\}} \Pr(D|\theta)\Pr(\theta)}$$

Bayes' rule in statistics

Likelihood of hypothesis θ

Prior probability of hypothesis θ

$$\Pr(\theta|D) = \frac{\Pr(D|\theta)\,\Pr(\theta)}{\sum_\theta \Pr(D|\theta)\,\Pr(\theta)}$$

Posterior probability of hypothesis θ

Marginal probability of the data (marginalizing over hypotheses)

Paternity example

(father) A- aa (mother)

Aa (child)

$\Pr(\theta \mid D) = \dfrac{\Pr(D \mid \theta)\Pr(\theta)}{\sum_\theta \Pr(D \mid \theta)\Pr(\theta)}$	θ_1	θ_2	Row sum
Genotypes	AA	Aa	---
Prior	1/2	1/2	1
Likelihood	1	1/2	---
Prior X Likelihood	1/2	1/4	3/4
Posterior	2/3	1/3	1

Bayes' rule: continuous case

Likelihood

Prior probability ***density***

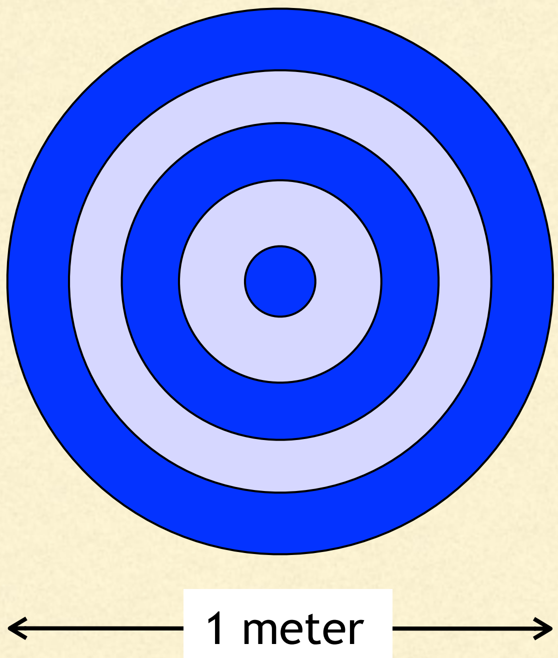
$$p(\theta \mid D) = \frac{p(D \mid \theta)\,p(\theta)}{\int p(D \mid \theta)\,p(\theta)\,d\theta}$$

Posterior probability ***density***

Marginal probability of the data

If you had to guess...

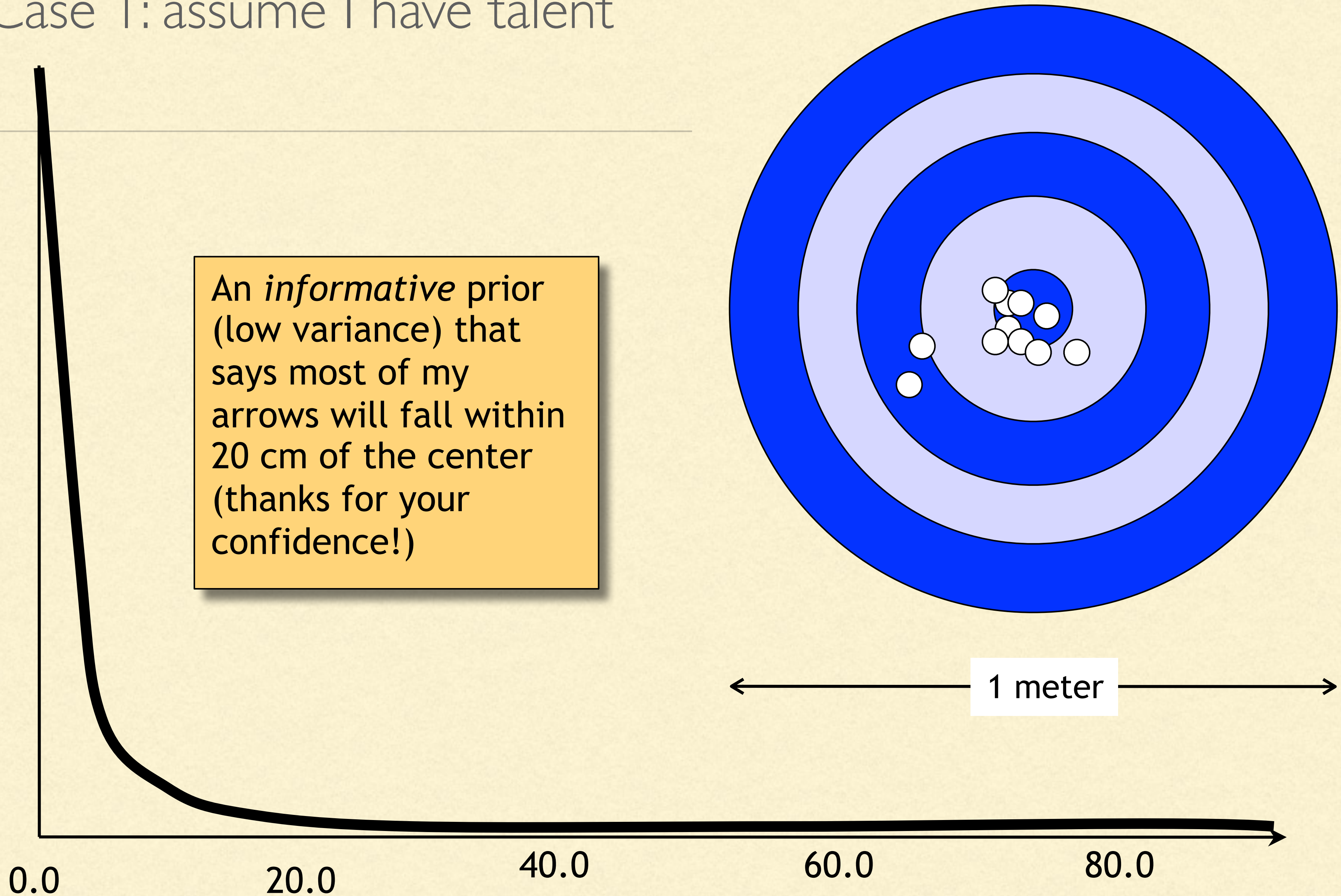
Photo by Tracy Heath



Not knowing anything about my archery abilities, draw a curve representing your view of the chances of my arrow landing a distance *d* centimeters from the center of the target (if it helps, I'm standing 50 meters away from the target)

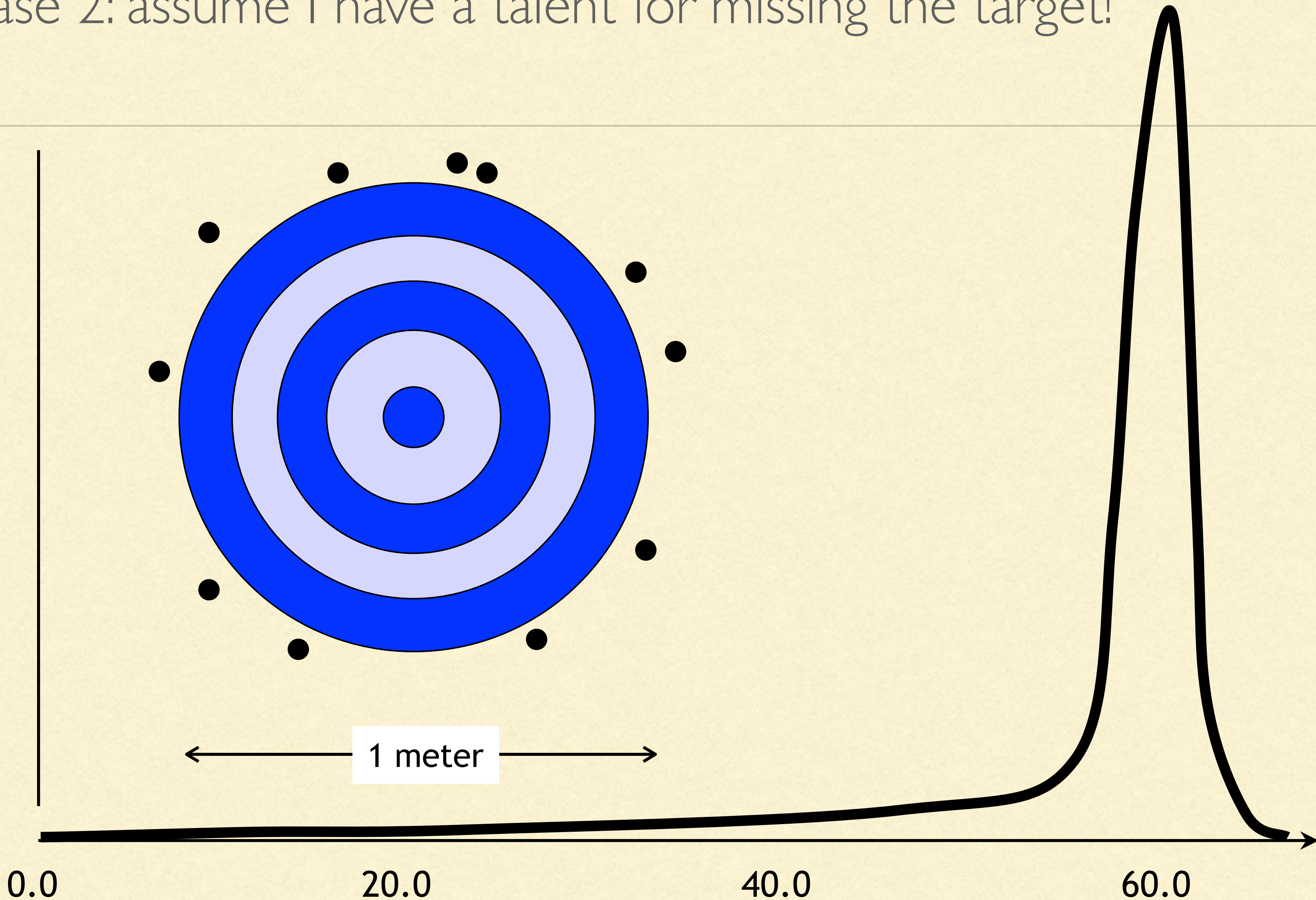
0.0 d ∞

Case 1: assume I have talent

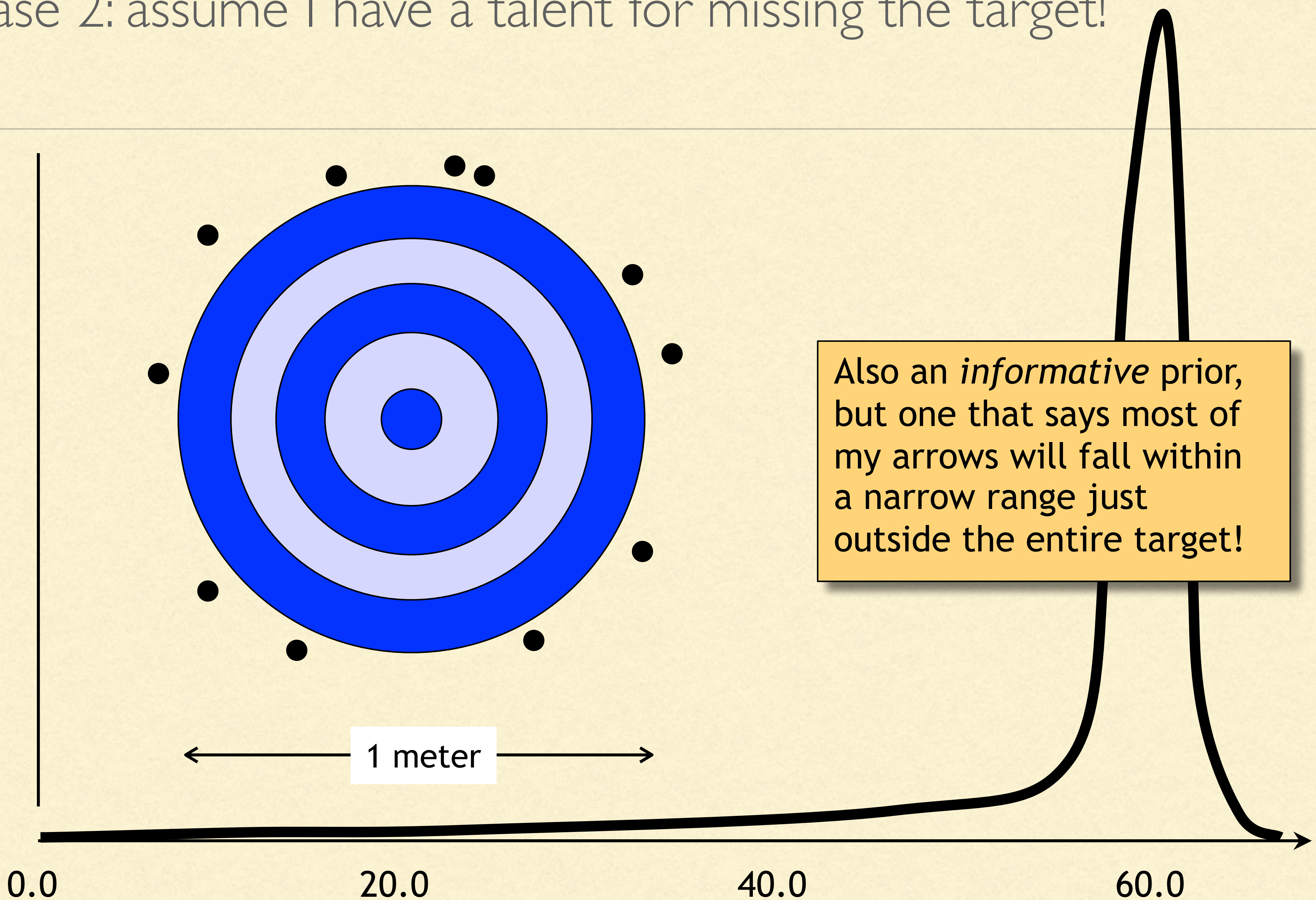


An *informative* prior (low variance) that says most of my arrows will fall within 20 cm of the center (thanks for your confidence!)

Case 2: assume I have a talent for missing the target!

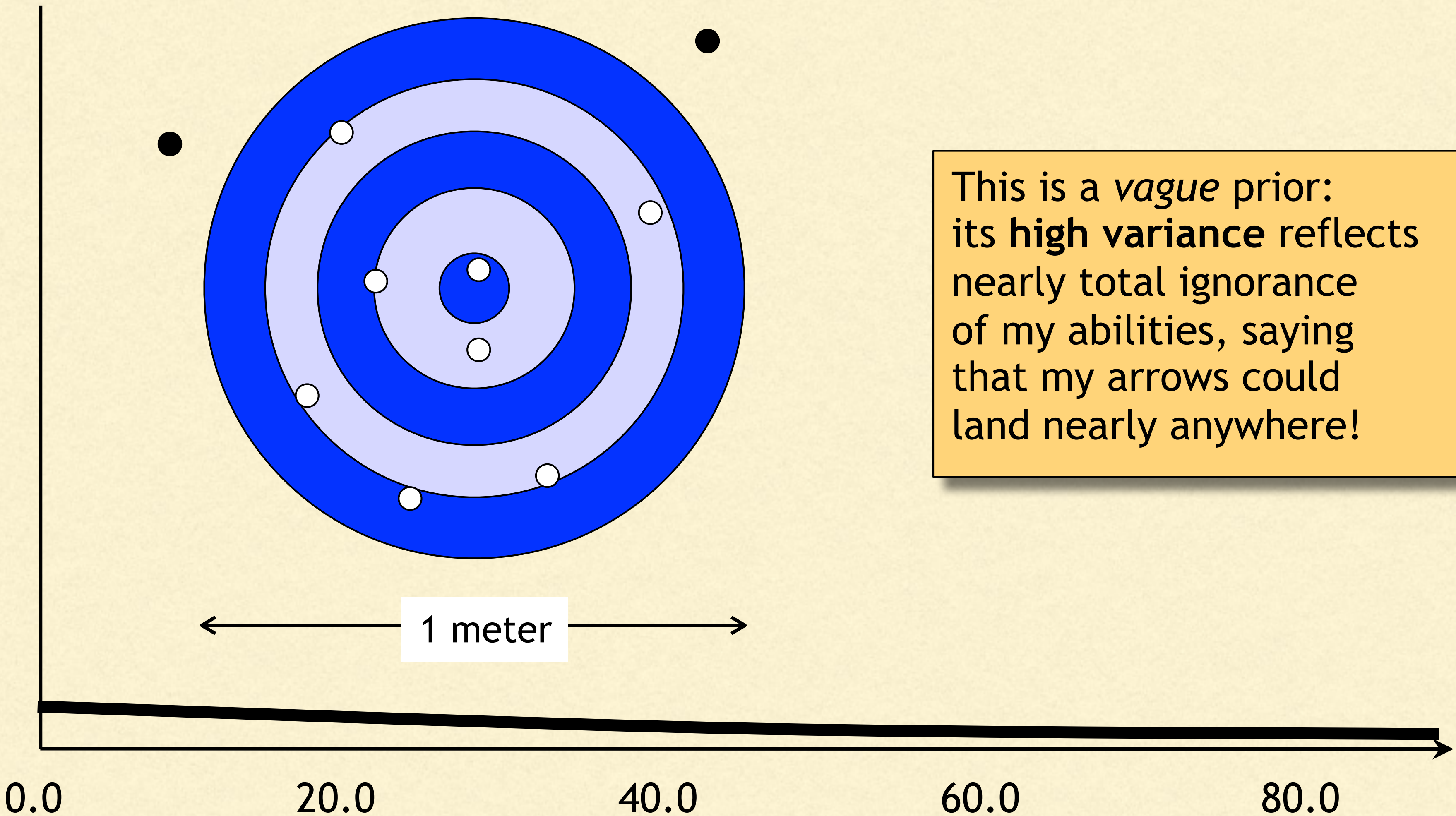


Case 2: assume I have a talent for missing the target!



Also an *informative* prior, but one that says most of my arrows will fall within a narrow range just outside the entire target!

Case 3: assume I have no talent



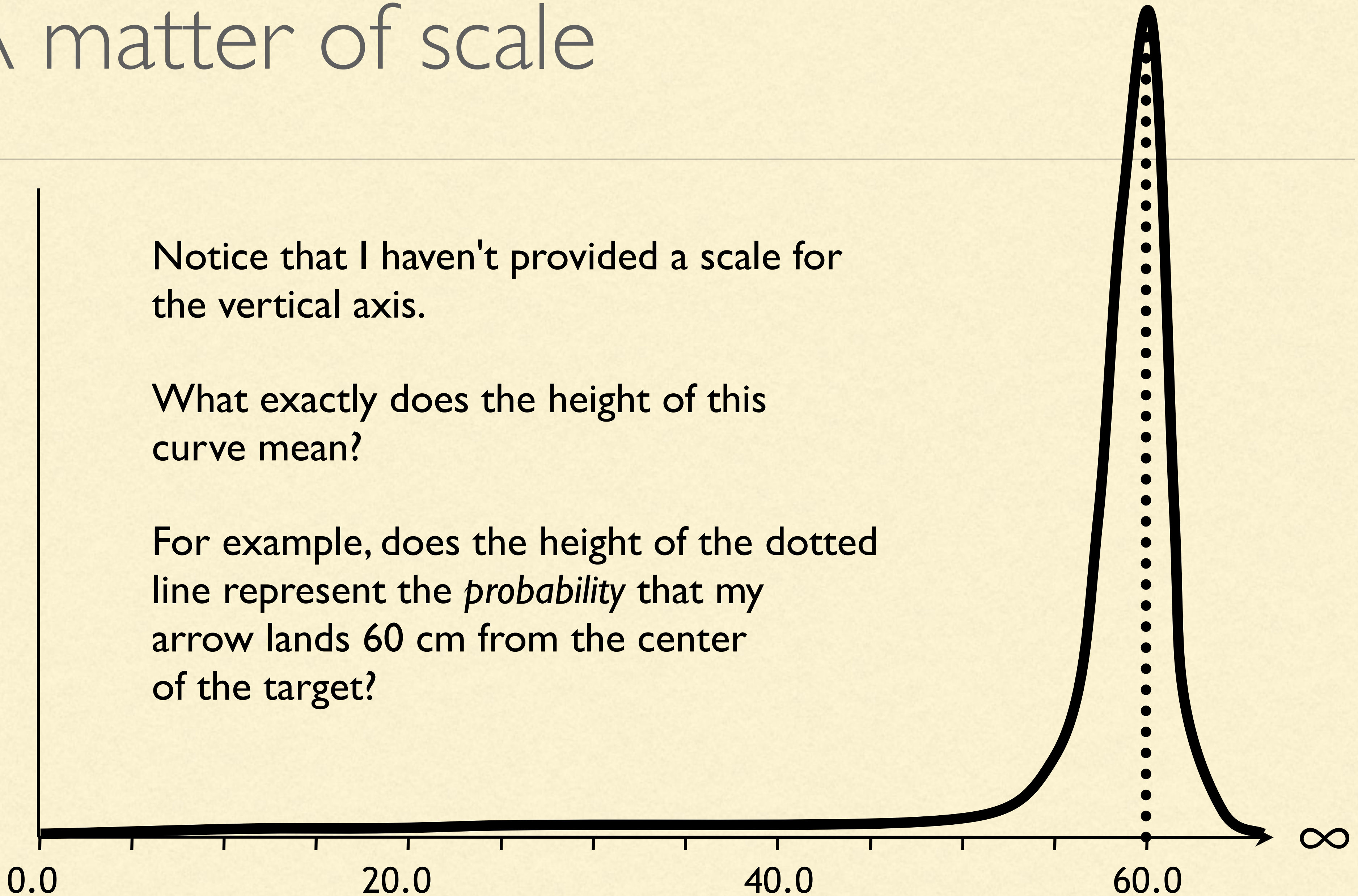
This is a *vague* prior: its **high variance** reflects nearly total ignorance of my abilities, saying that my arrows could land nearly anywhere!

A matter of scale

Notice that I haven't provided a scale for the vertical axis.

What exactly does the height of this curve mean?

For example, does the height of the dotted line represent the *probability* that my arrow lands 60 cm from the center of the target?

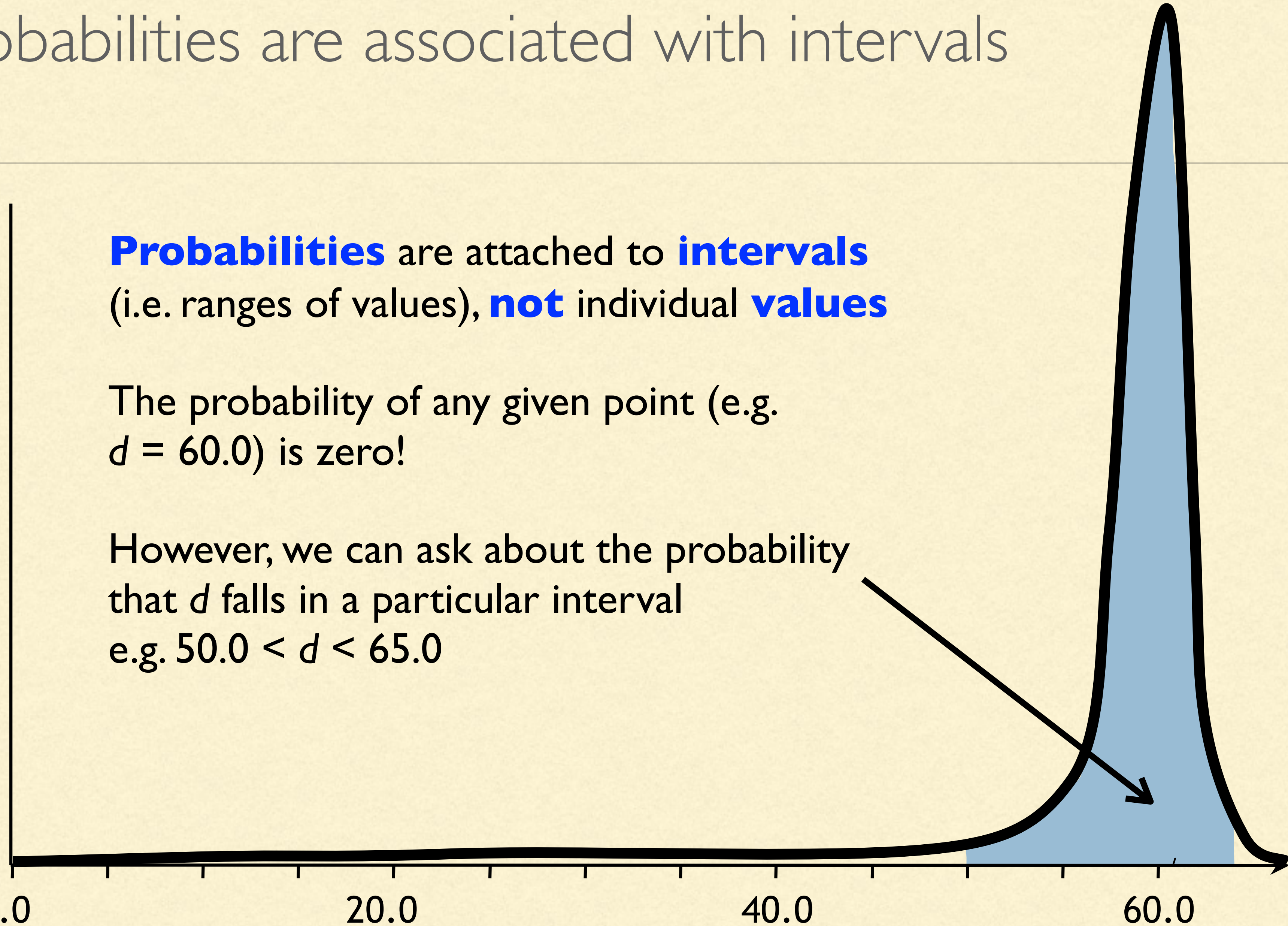


Probabilities are associated with intervals

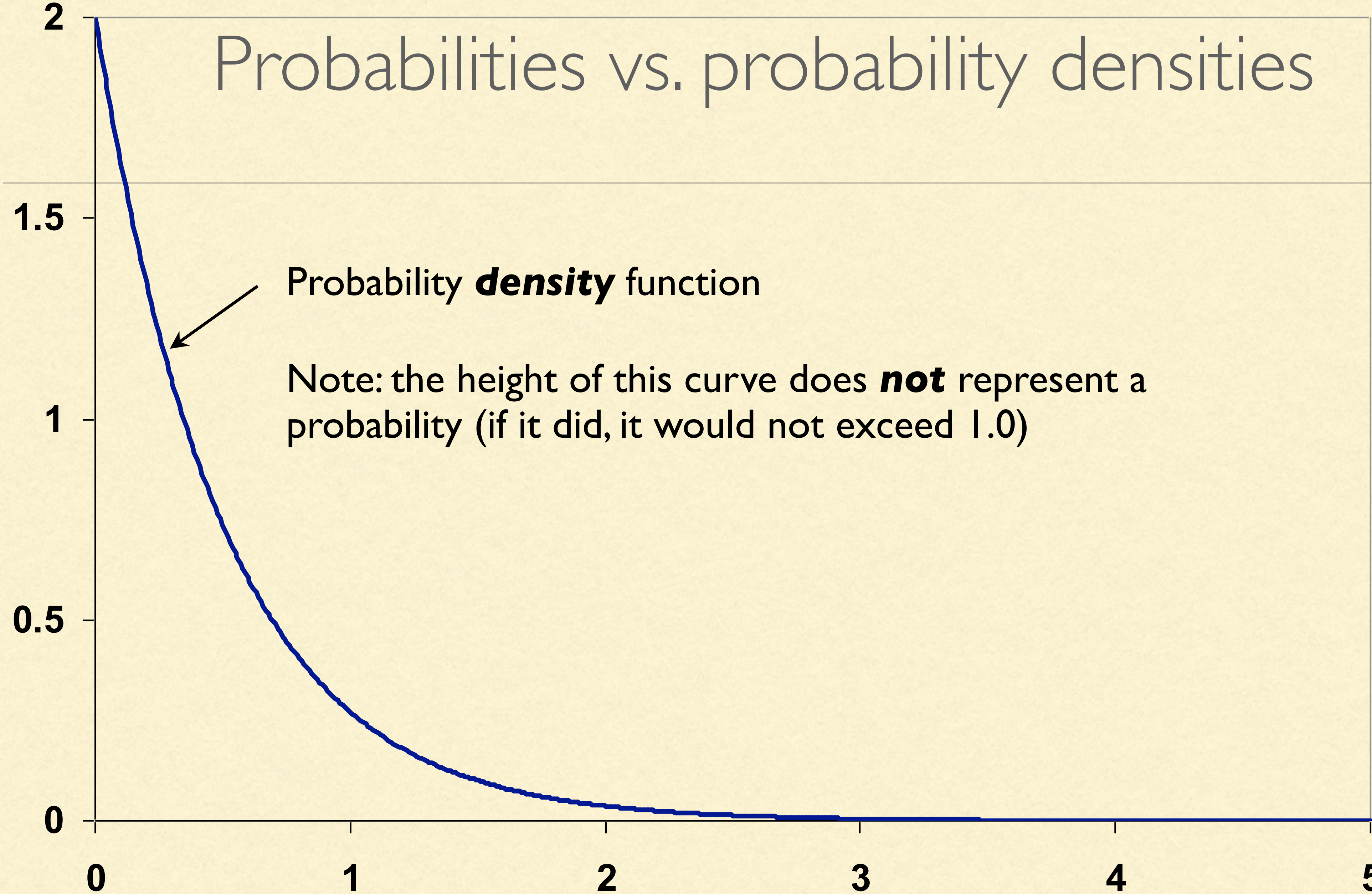
Probabilities are attached to **intervals** (i.e. ranges of values), **not** individual **values**

The probability of any given point (e.g. *d* = 60.0) is zero!

However, we can ask about the probability that *d* falls in a particular interval e.g. 50.0 < *d* < 65.0



Probabilities vs. probability densities

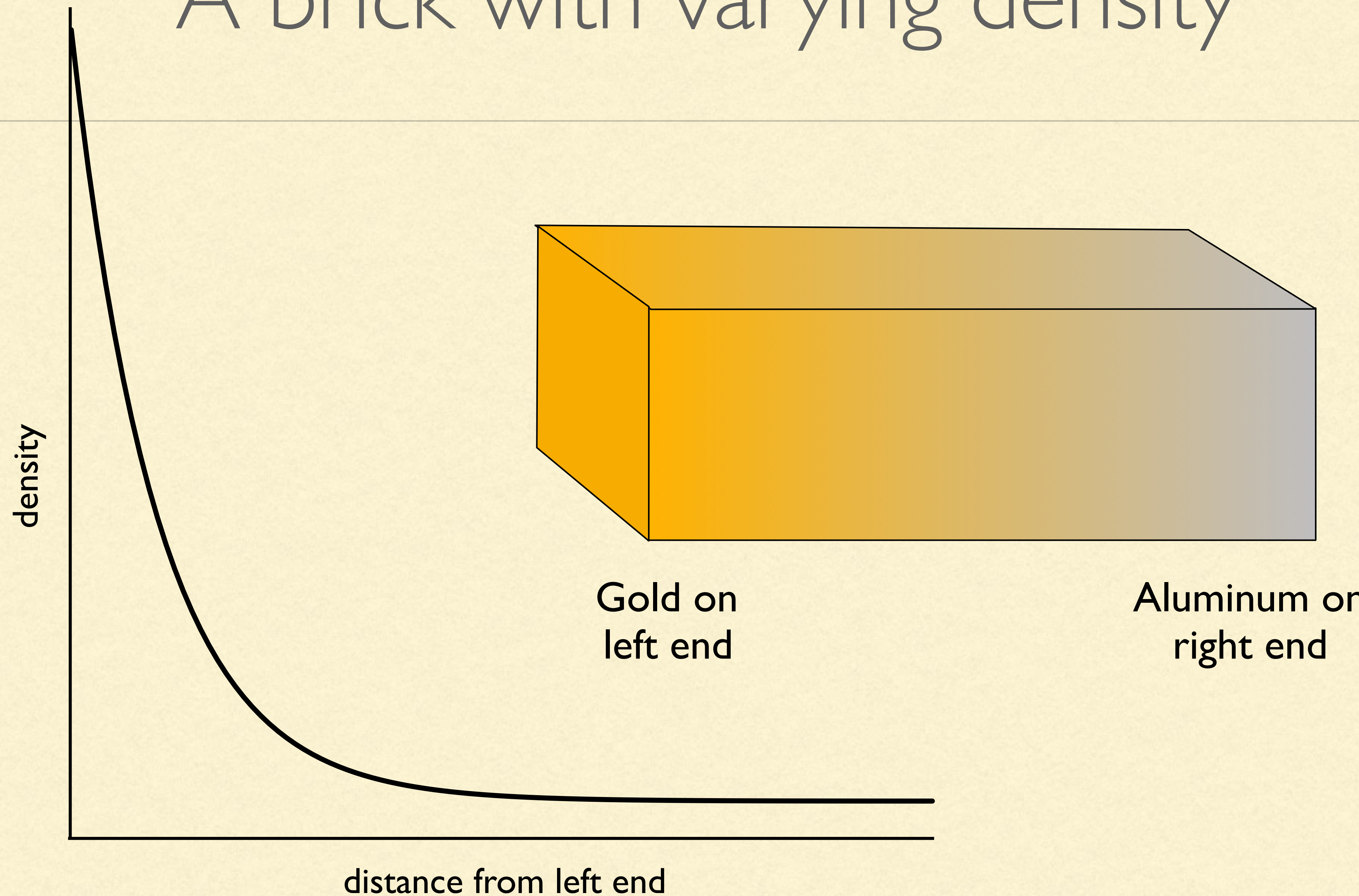


Densities of various substances

Substance	Density (g/cm^3)
Cork	0.24
Aluminum	2.7
Gold	19.3

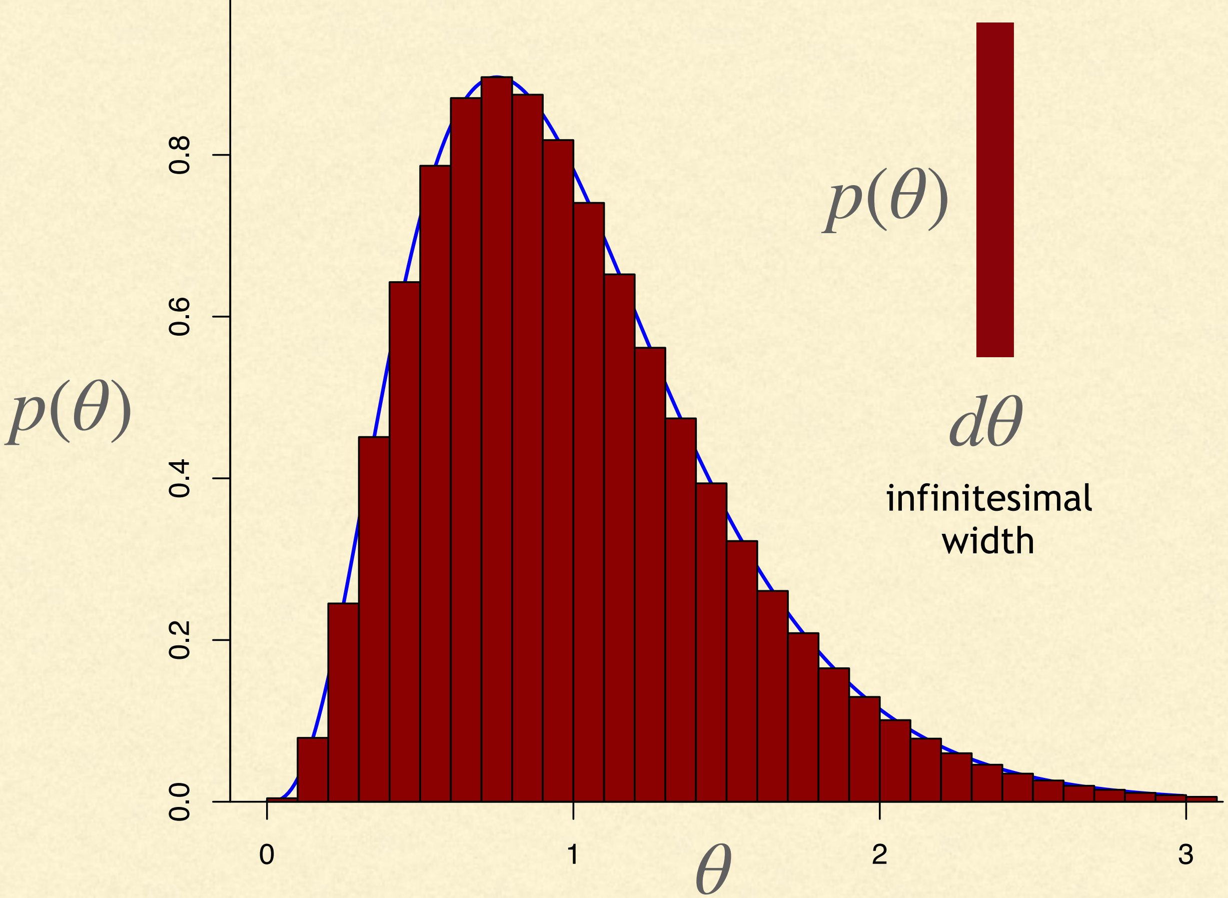
Density does not equal mass
mass = density × volume

A brick with varying density



Integrating a density yields a probability

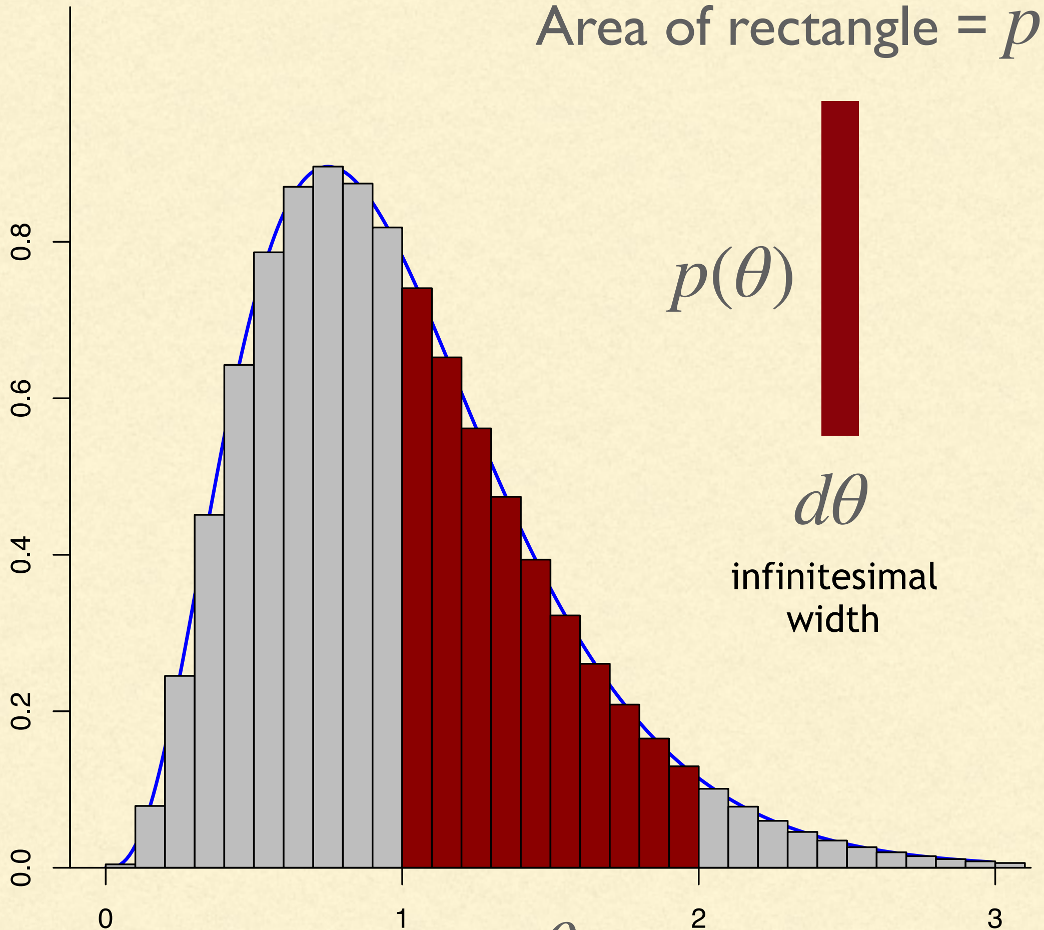
Area of rectangle = $p(\theta)d\theta$



$$1.0 = \int p(\theta)d\theta$$

The density curve is scaled so that the value of this integral (i.e. the total area) equals 1.0

Integrating a density yields a probability



$p(\theta)$

θ

Area of rectangle = $p(\theta)d\theta$

$p(\theta)$

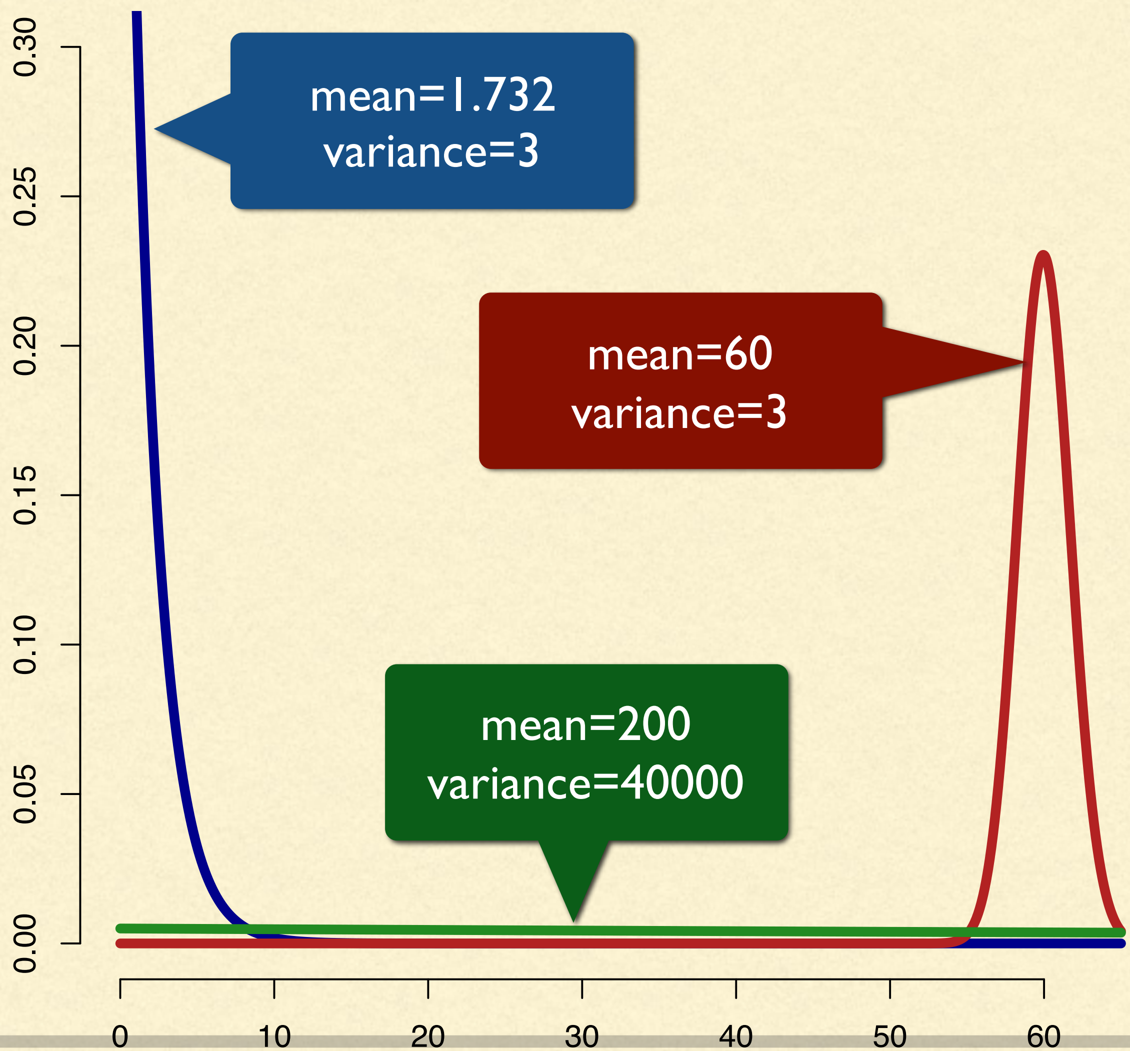
$d\theta$

infinitesimal width

$$1.0 = \int_1^2 p(\theta)d\theta$$

The **area** under the density curve from 1 to 2 is the **probability** that θ is between 1 and 2

Archery priors revisited



These density curves are all variations of a **gamma probability distribution**. We could have used a gamma distribution to specify each of the prior probability distributions for the archery example. Note that **higher variance** means **less informative**

Archery Prior Applet

https://phylogeny.uconn.edu/archery-priors/

Usually there are many parameters...

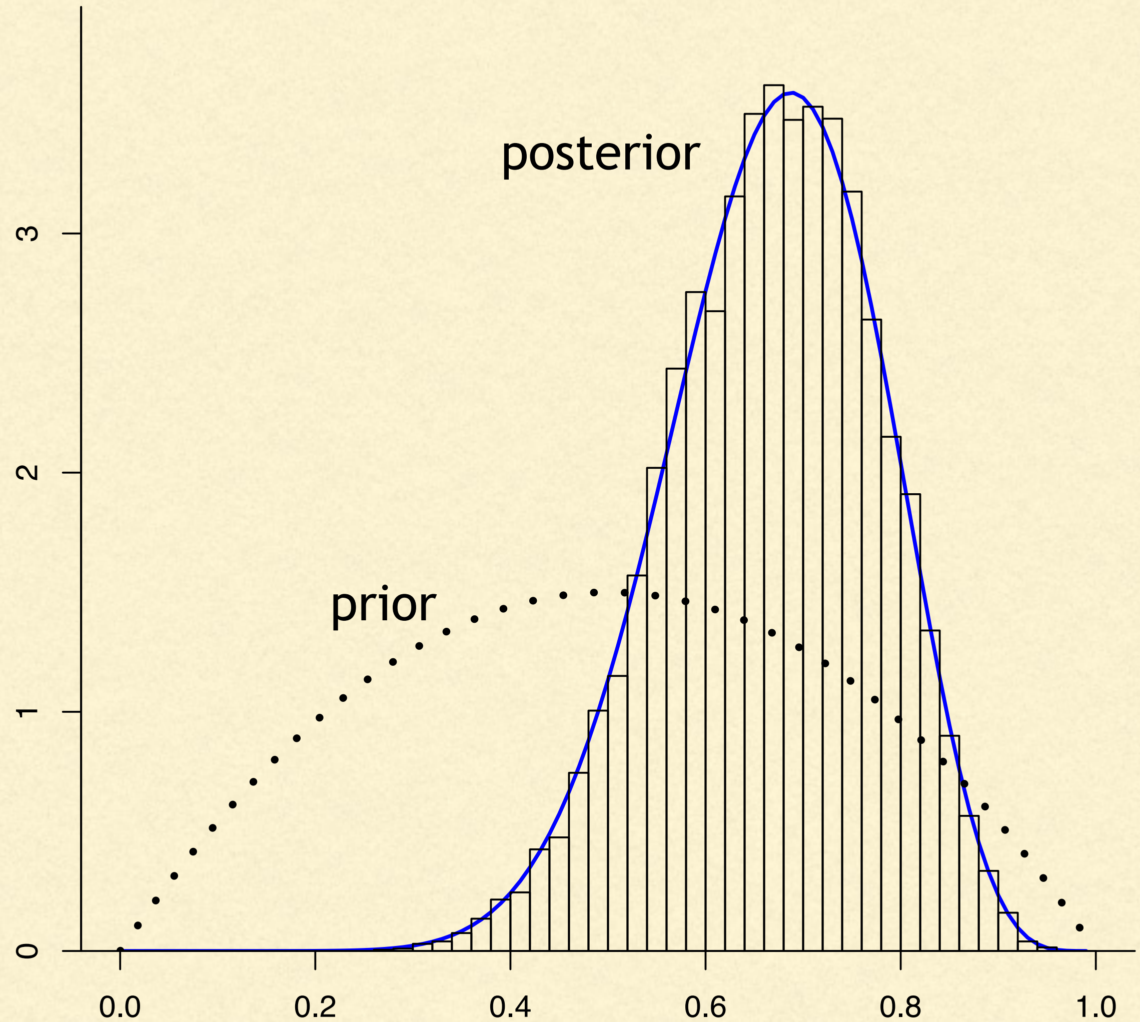
A 2-parameter example

$$\underbrace{p(\theta,\phi\,|\,D)}_{\text{Posterior probability density}} = \frac{\overbrace{p(D\,|\,\theta,\phi)}^{\text{Likelihood}}\;\overbrace{p(\theta)\;p(\phi)}^{\text{Prior density}}}{\underbrace{\int_\theta\int_\phi p(D\,|\,\theta,\phi)\;p(\theta)\;p(\phi)\;d\phi\;d\theta}_{\text{Marginal probability of data}}}$$

An analysis of **100 sequences** under the simplest model (JC69) requires 197 branch length parameters.
The denominator would require a **197-fold integral** inside a sum over **all possible tree topologies**!
It would thus be nice to avoid having to calculate the marginal probability of the data...

Markov chain Monte Carlo (MCMC)

Markov chain Monte Carlo (MCMC)

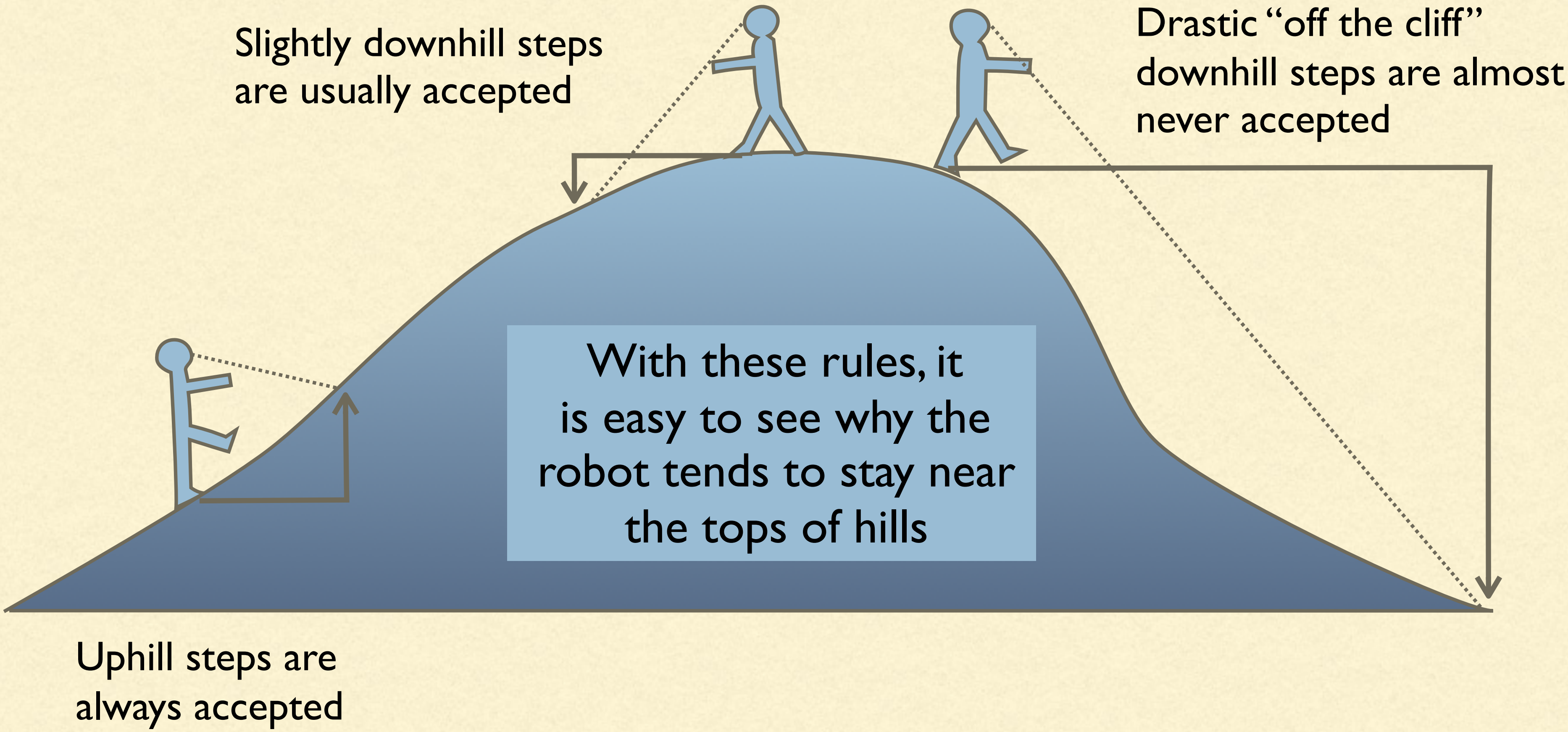


For more complex problems, we might settle for a

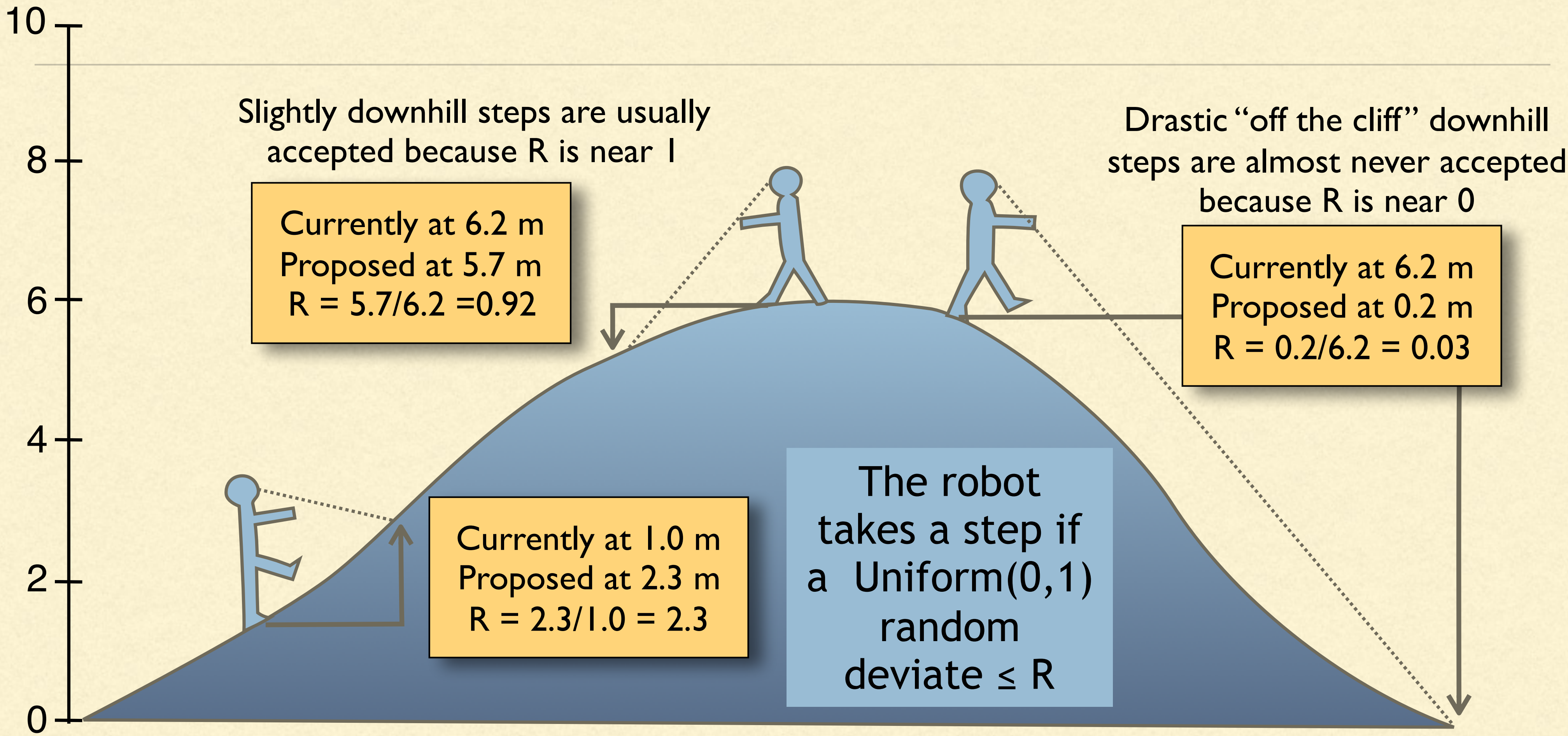
good approximation

to the posterior distribution

MCMC robot's rules



Actual rules (Metropolis algorithm)



Uphill steps are always accepted because R > 1

Metropolis et al. 1953. Equation of state calculations by fast computing machines. *J. Chem. Physics* 21(6):1087-1092.

Cancellation of marginal likelihood

When calculating the ratio (R) of posterior densities, the marginal probability of the data cancels.

$$\frac{p(\theta^* \,|\, D)}{p(\theta \,|\, D)} = \frac{\dfrac{p(D \,|\, \theta^*)\; p(\theta^*)}{\cancel{p(D)}}}{\dfrac{p(D \,|\, \theta)\; p(\theta)}{\cancel{p(D)}}} = \frac{p(D \,|\, \theta^*)\; p(\theta^*)}{p(D \,|\, \theta)\; p(\theta)}$$

Posterior odds

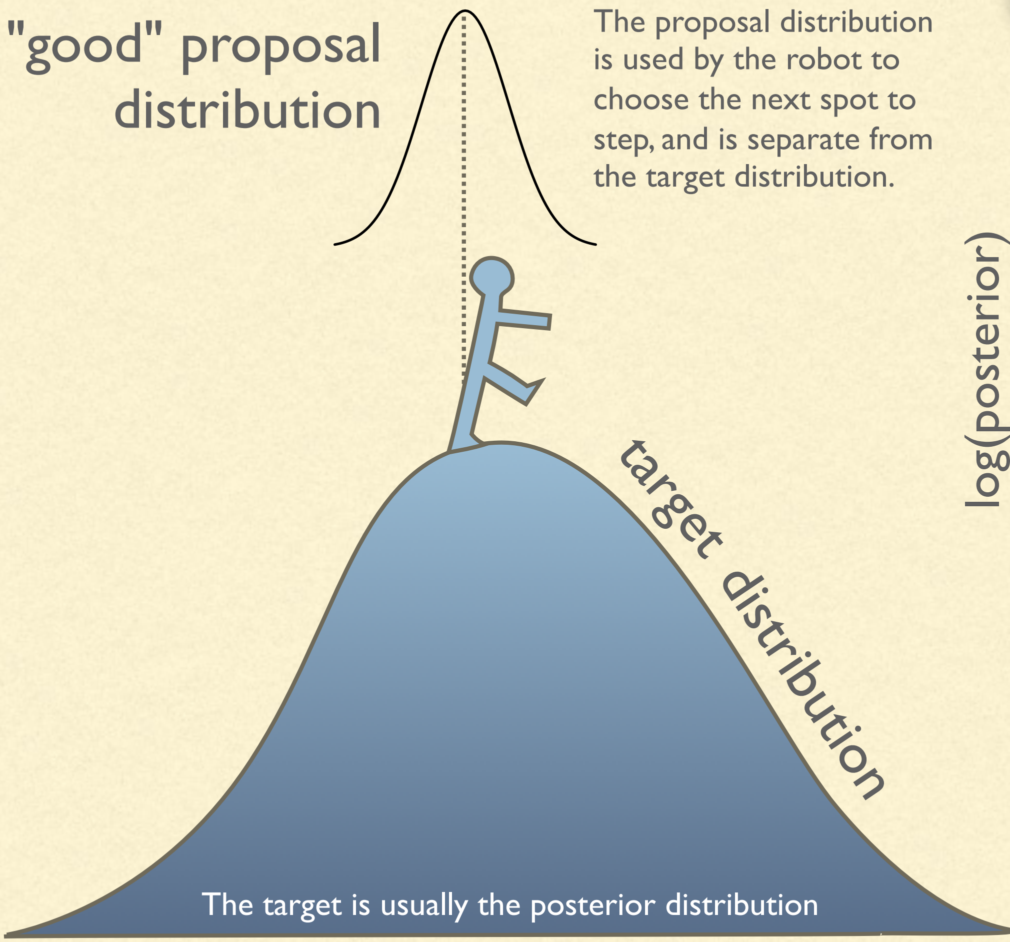
Apply Bayes' rule to both top and bottom

Likelihood ratio

Prior odds

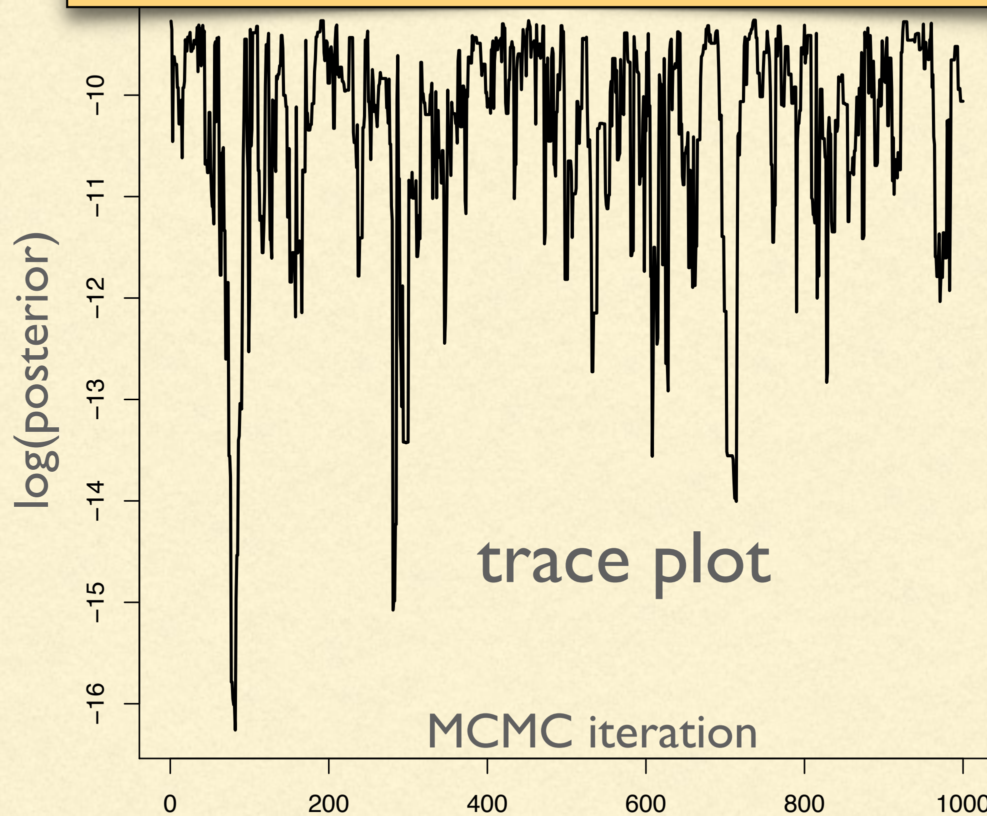
Target vs. Proposal Distributions

"good" proposal distribution



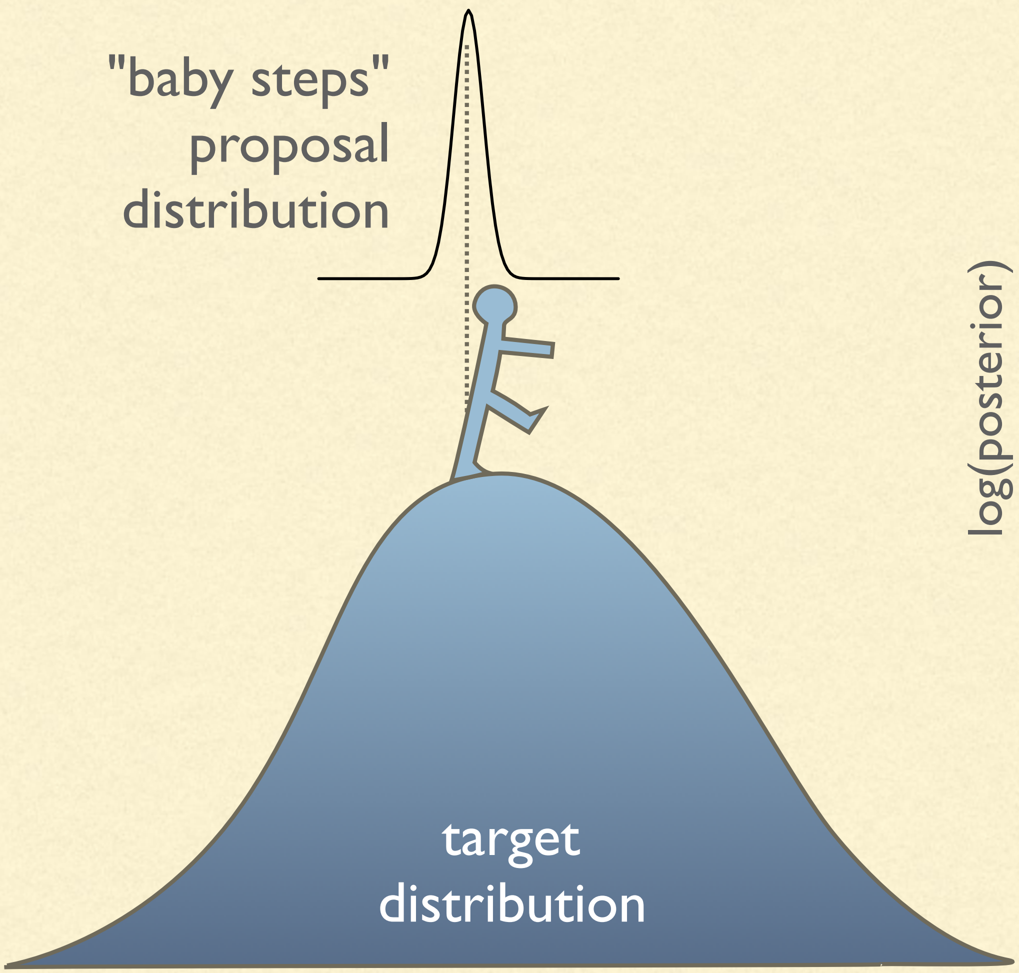
The proposal distribution is used by the robot to choose the next spot to step, and is separate from the target distribution.

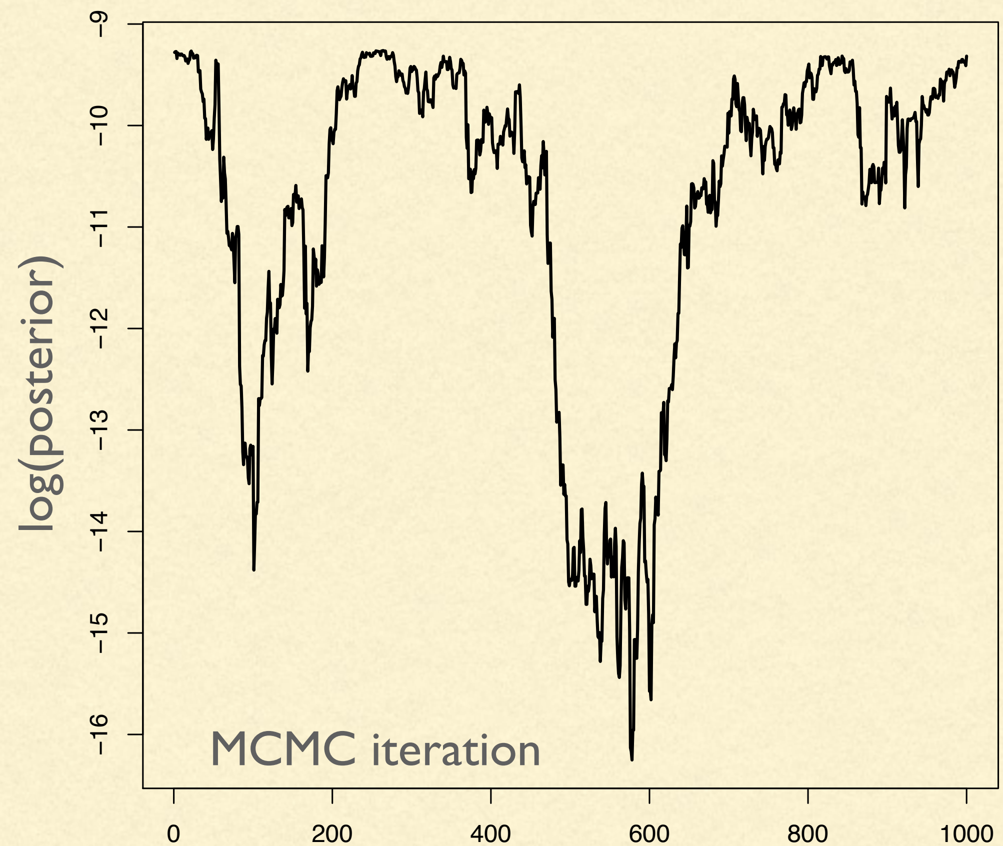
Tracer (app for generating trace plots from MCMC output):
http://tree.bio.ed.ac.uk/software/tracer/



White noise appearance is a sign of good mixing

Target vs. Proposal Distributions

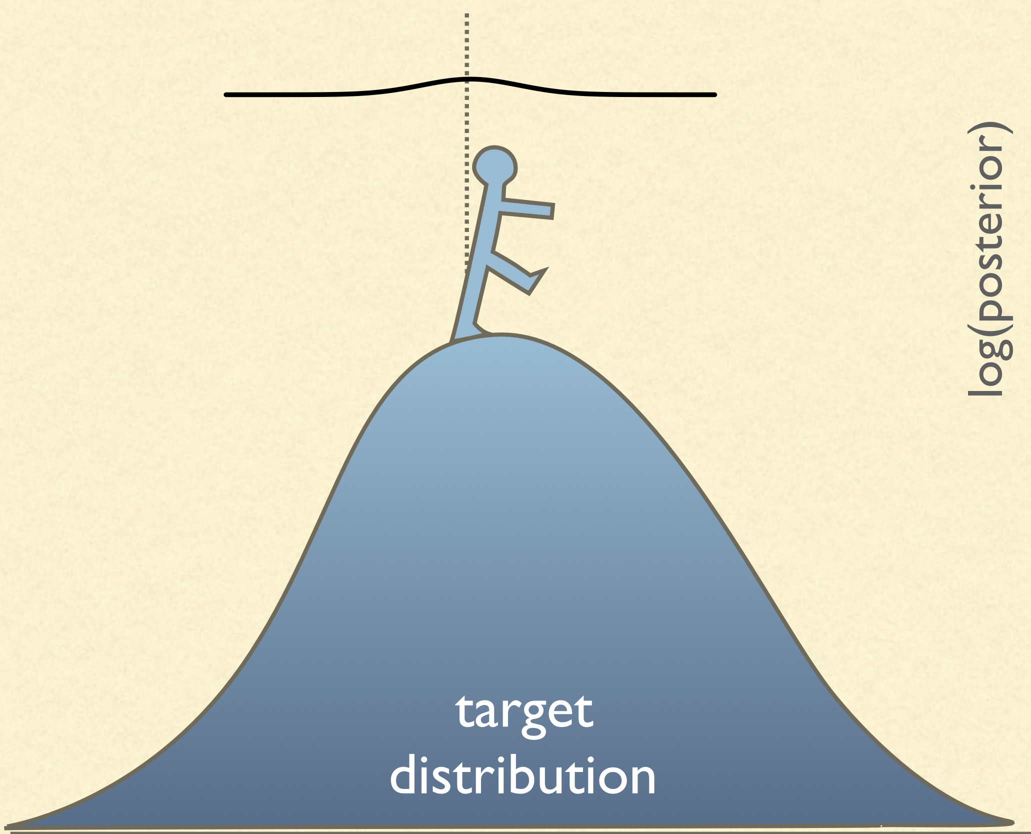


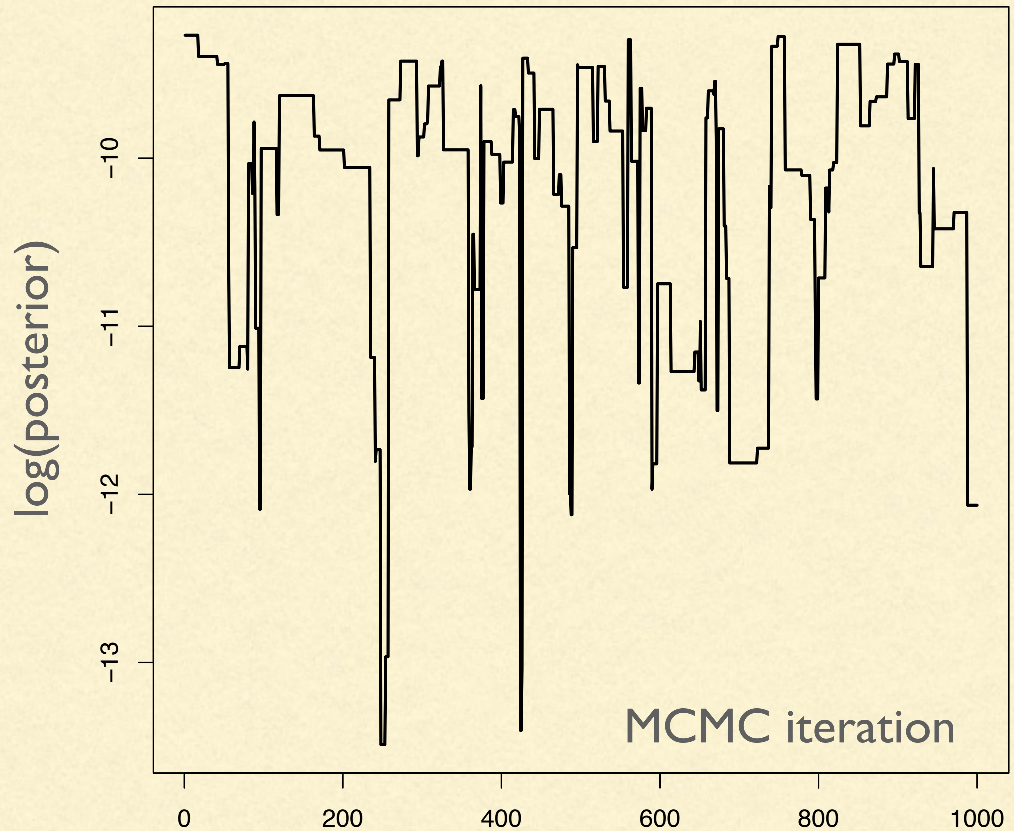


Big waves in trace plot indicate robot is crawling around

Target vs. Proposal Distributions

"overly bold" proposal distribution





Plateaus in trace plot indicate robot is often stuck in one place

MCRobot (or "MCMC Robot")

Javascript version used today will run in most web browsers and is available here:

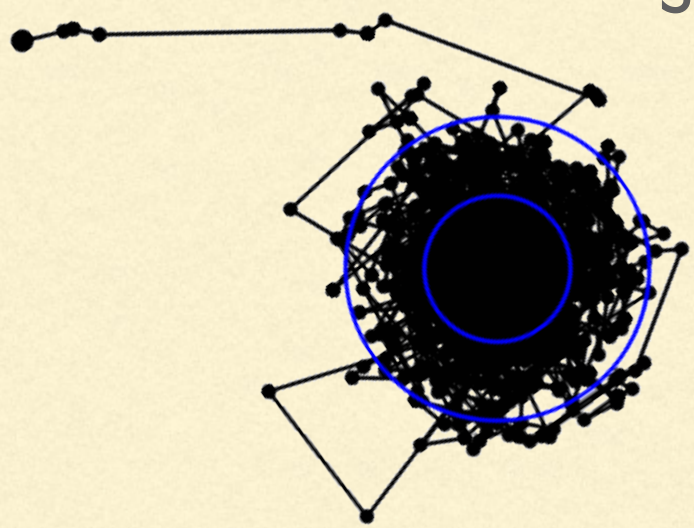
https://phylogeny.uconn.edu/mcmc-robot/

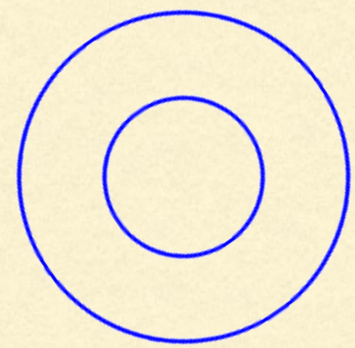
Free app for **Windows** or **iPhone/iPad** available from http://mcmcrobot.org/

(also see John Huelsenbeck's iMCMC app for MacOS: http://cteg.berkeley.edu/software.html)

Metropolis-coupled Markov chain Monte Carlo (MCMCMC)

Sometimes the robot needs some help,

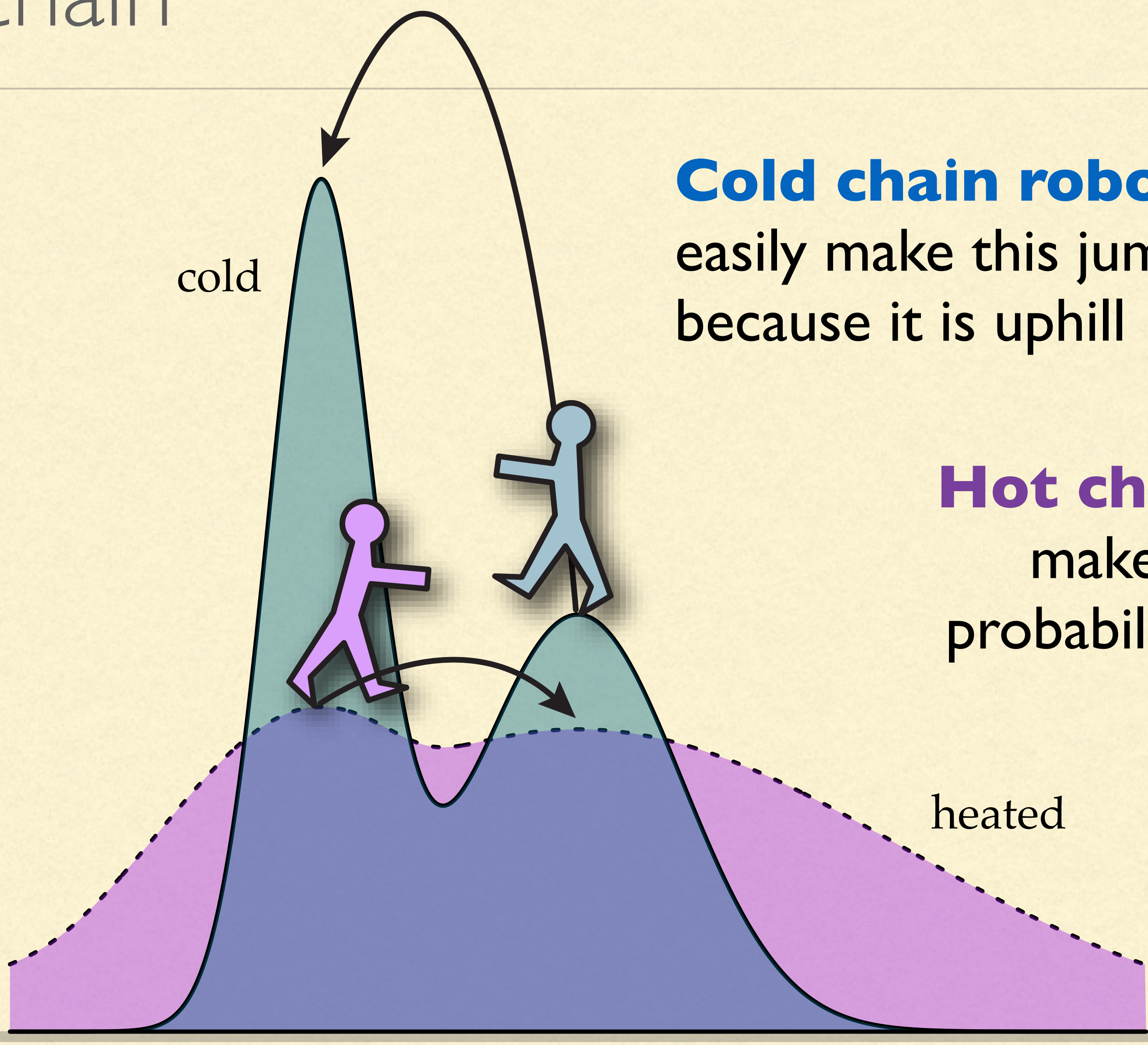




MCMCMC introduces helpers in the form of "heated chain" robots that can act as scouts.

Geyer, C. J. 1991. Markov chain Monte Carlo maximum likelihood for dependent data. Pages 156-163 *in* Computing Science and Statistics (E. Keramidas, ed.).

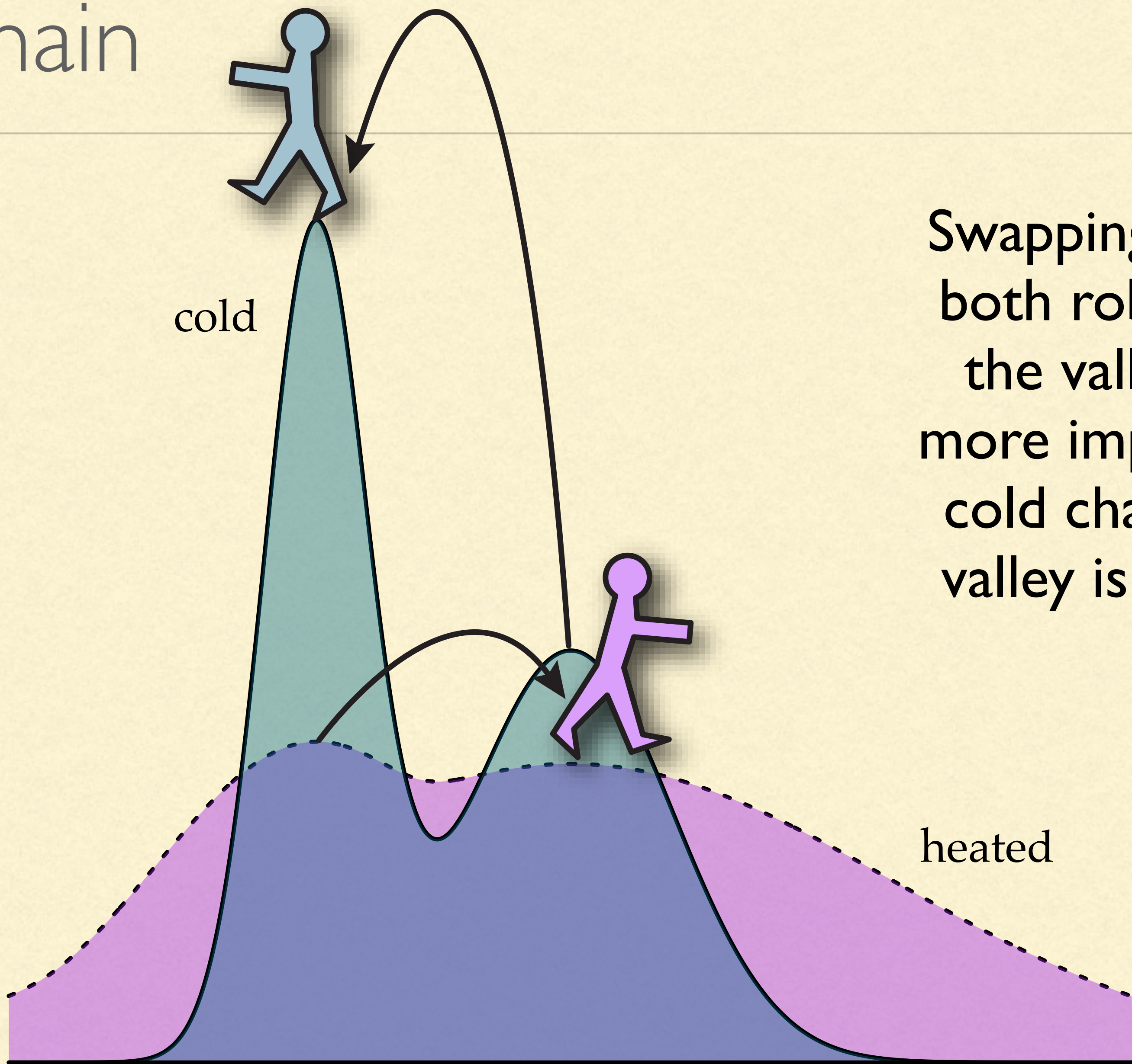
Heated chains act as scouts for the cold chain



Cold chain robot can easily make this jump because it is uphill

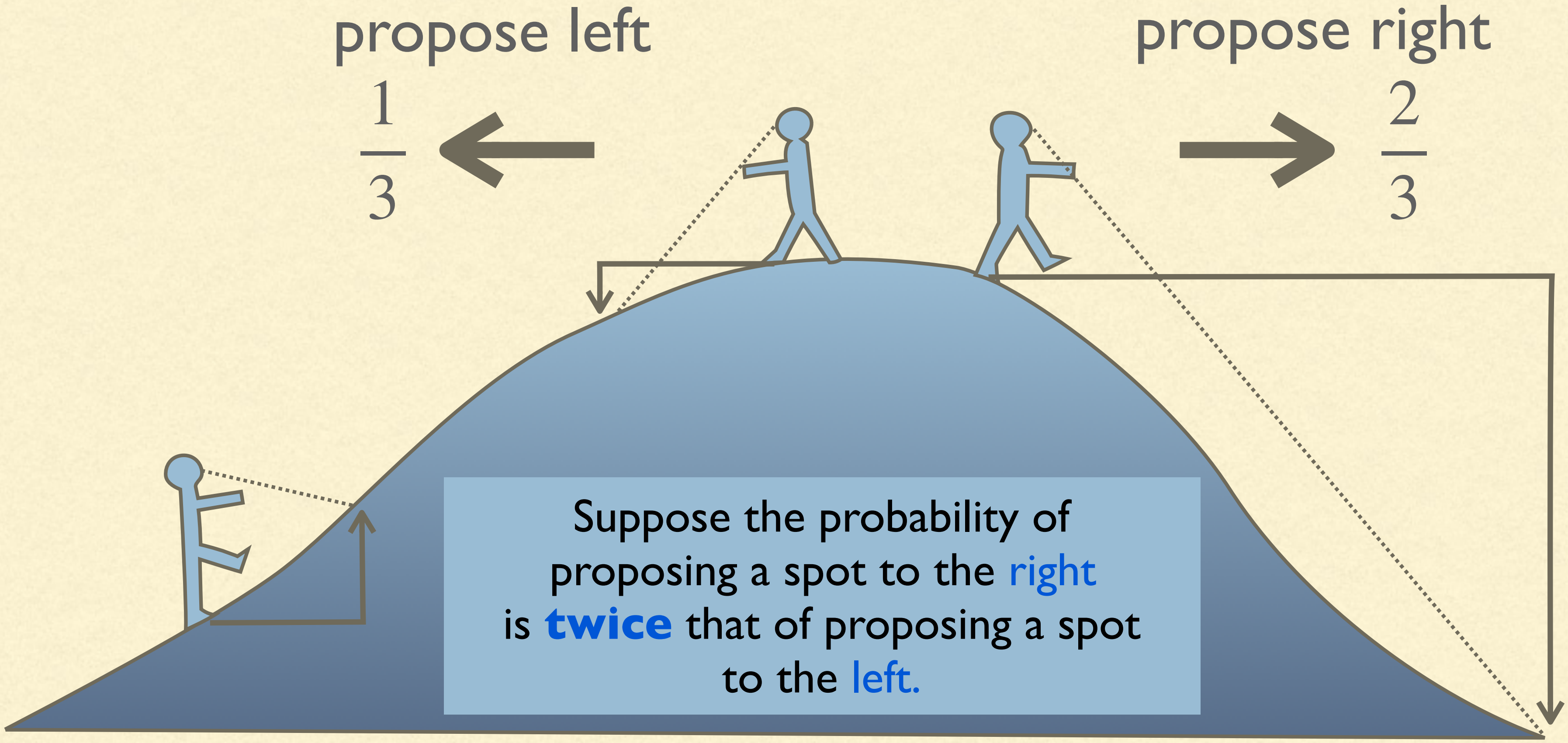
Hot chain robot can also make this jump with high probability because it is only slightly downhill

Heated chains act as scouts for the cold chain



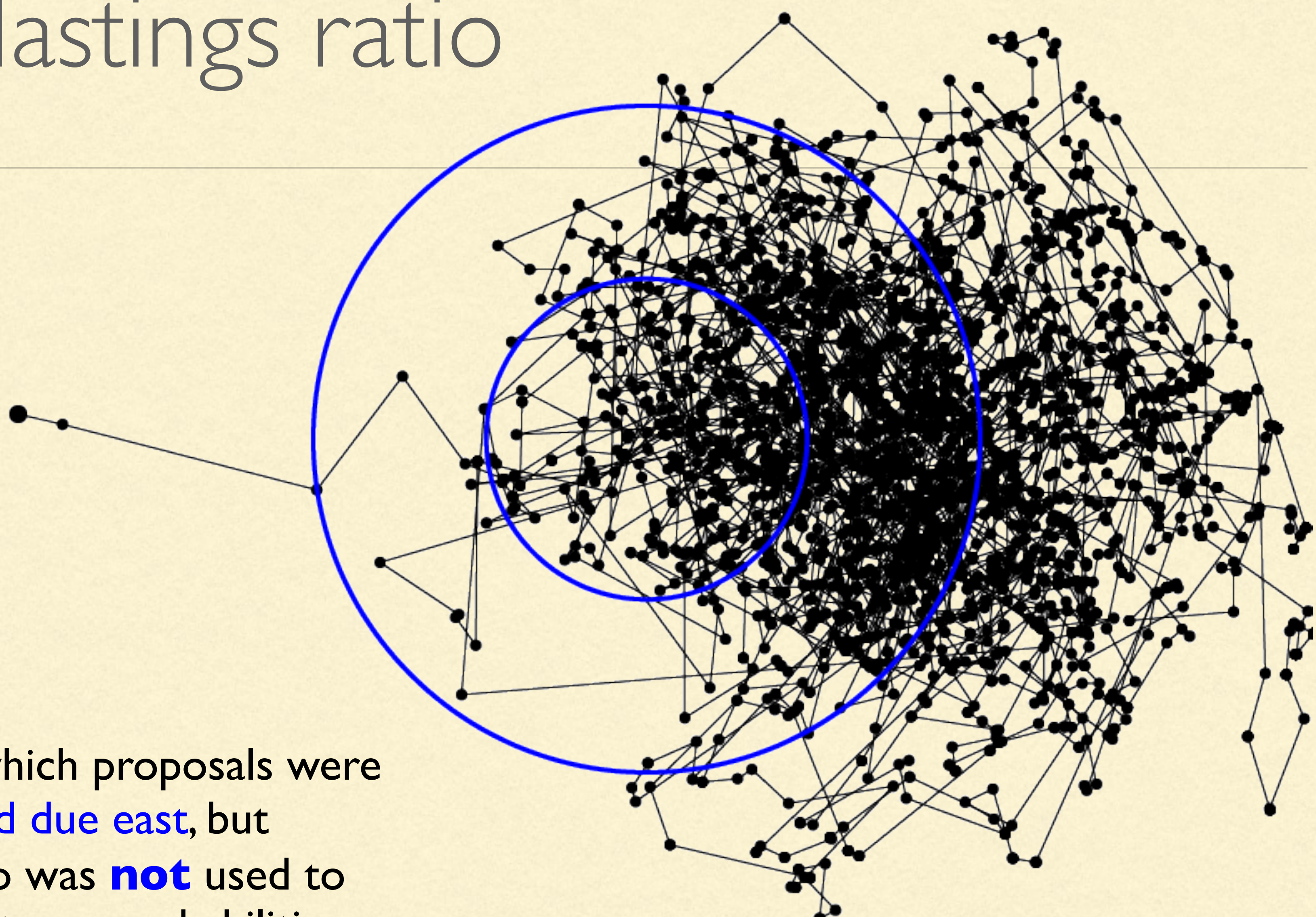
Swapping places means both robots can cross the valley, but this is more important for the cold chain because its valley is much deeper.

The Hastings ratio



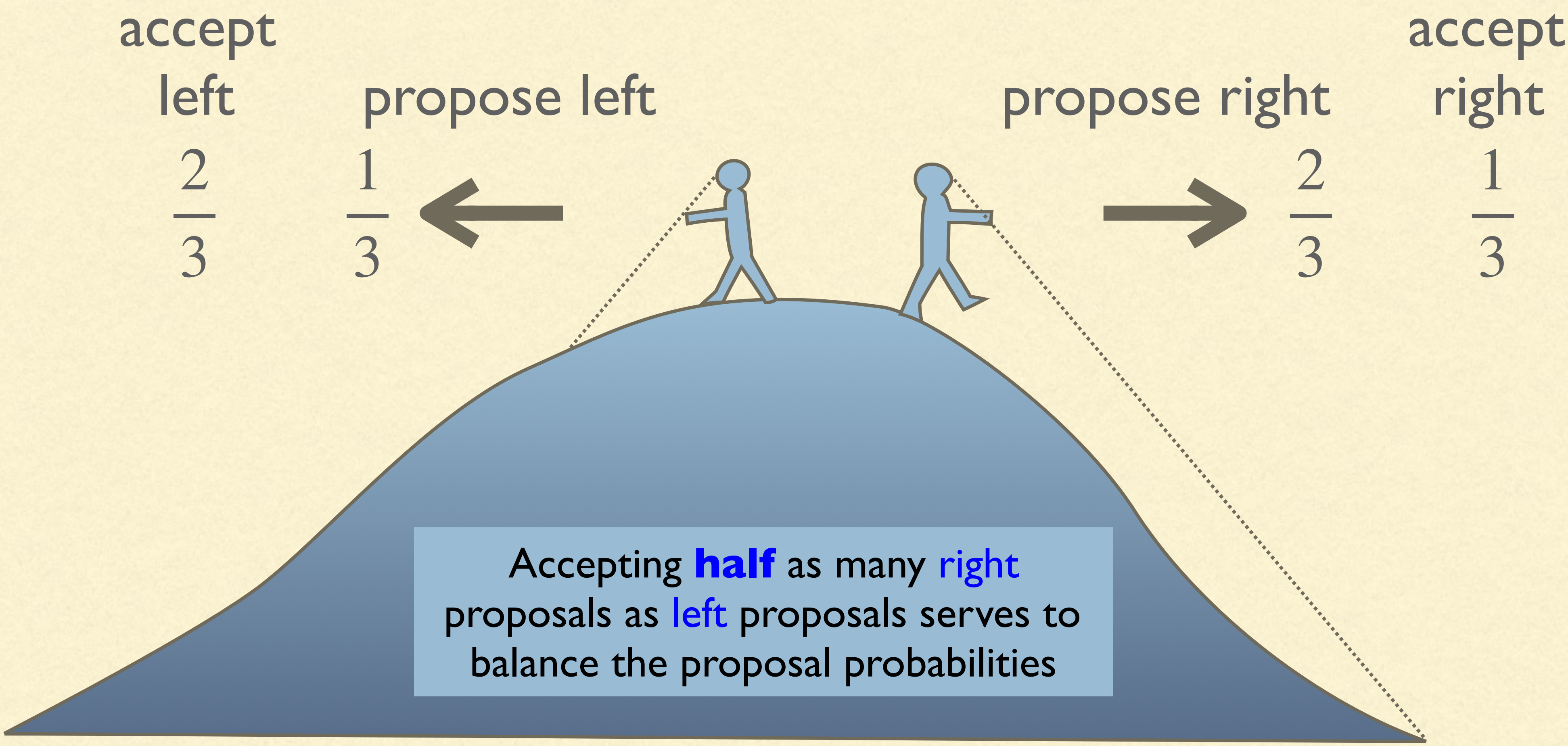
Hastings, W. K. 1970. Monte Carlo sampling methods using Markov chains and their applications. Biometrika 57:97-109.

The Hastings ratio



Example in which proposals were biased toward due east, but Hastings ratio was **not** used to modify acceptance probabilities

The Hastings ratio



Hastings, W. K. 1970. Monte Carlo sampling methods using Markov chains and their applications. Biometrika 57:97-109.

Hastings Ratio

$$R = \left[\frac{p(D\,|\,\theta^*)\;p(\theta^*)}{p(D\,|\,\theta)\;p(\theta)}\right]\left[\frac{q(\theta\,|\,\theta^*)}{q(\theta^*\,|\,\theta))}\right]$$

posterior ratio Hastings ratio

Note that the Hastings ratio is 1.0 if $q(\theta^*\,|\,\theta) = q(\theta\,|\,\theta^*)$

End of Part 3a

Upcoming Part 3b topics: MCMC proposals, prior distributions, hierarchical models, and Bayes factors