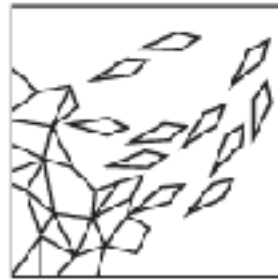
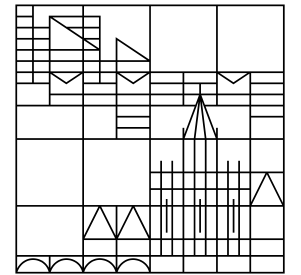


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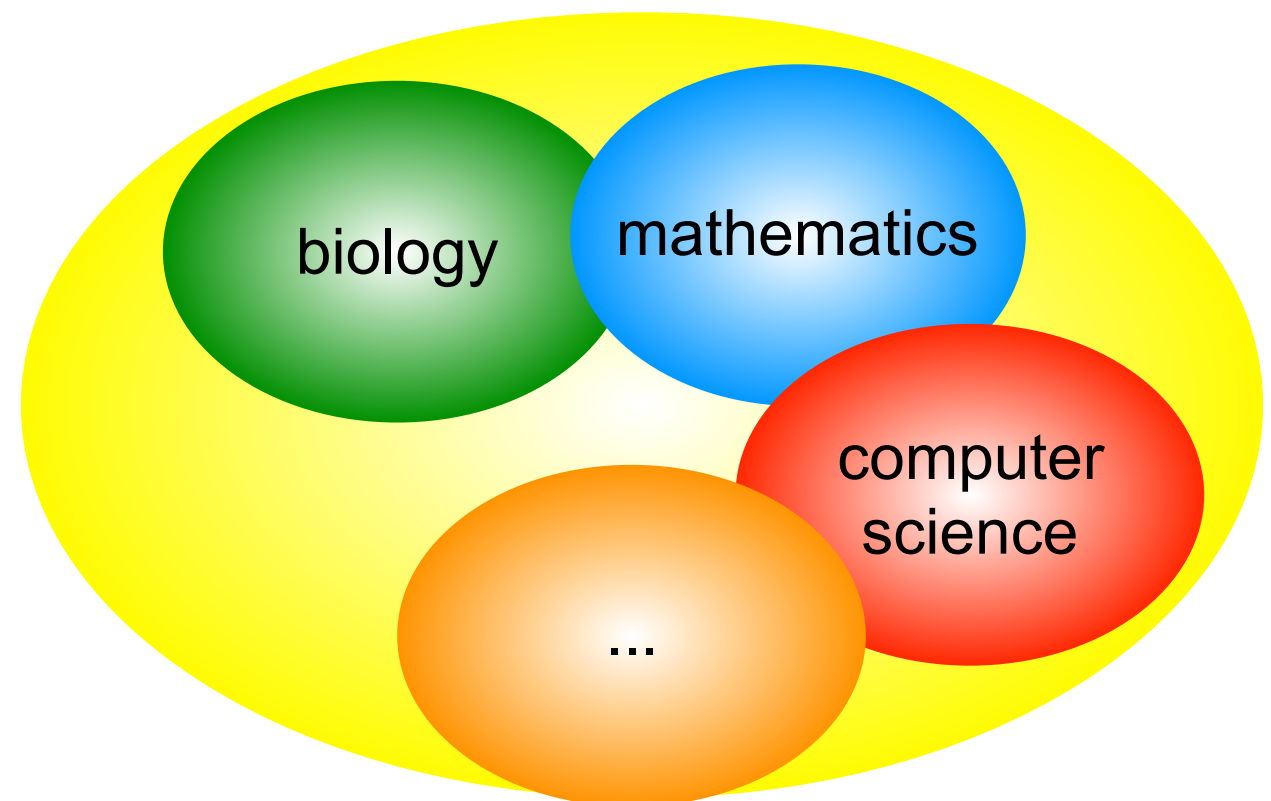


Universität  
Konstanz



# Probabilistic Modelling for Computer Scientists

**Tatjana Petrov**  
October 29th 2019,  
*Lecture 1*



# Probabilities...

*Probability is the most important concept in modern science,  
especially as nobody has the slightest notion what it means.*

— Bertrand Russell, 1929 Lecture  
(cited in Bell 1945, 587)

‘The Democrats will probably win the next election.’

‘The coin is just as likely to land heads as tails.’

‘There’s a 30% chance of rain tomorrow.’

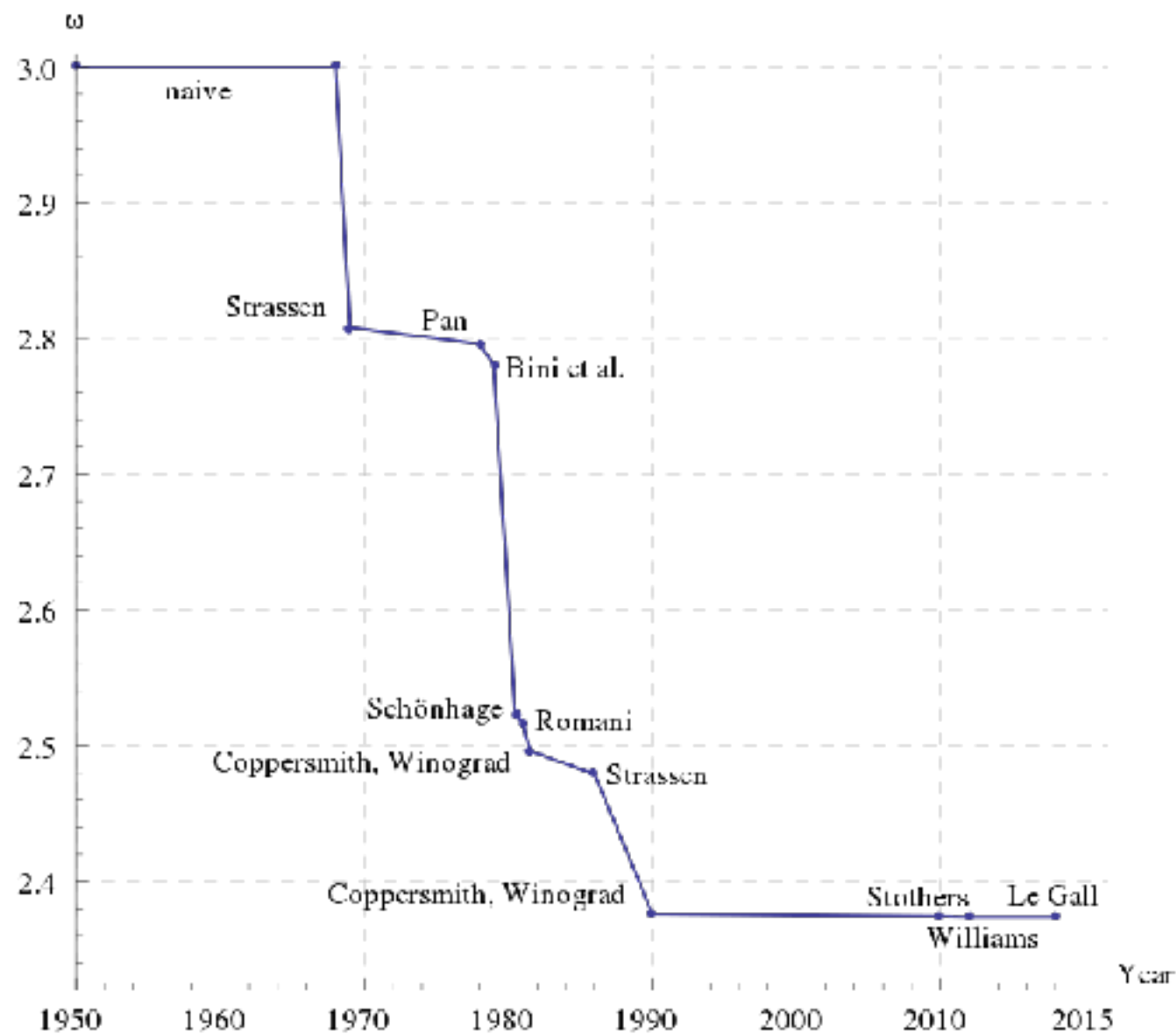
‘The probability that a radium atom decays in one year is roughly 0.0004.’

(source: <https://plato.stanford.edu/entries/probability-interpret/>)

# Probabilities...

- ... to facilitate rational reasoning
- ... to improve algorithms
- ... to model what we don't know precisely, or what is really computing with randomness

# Matrix multiplication

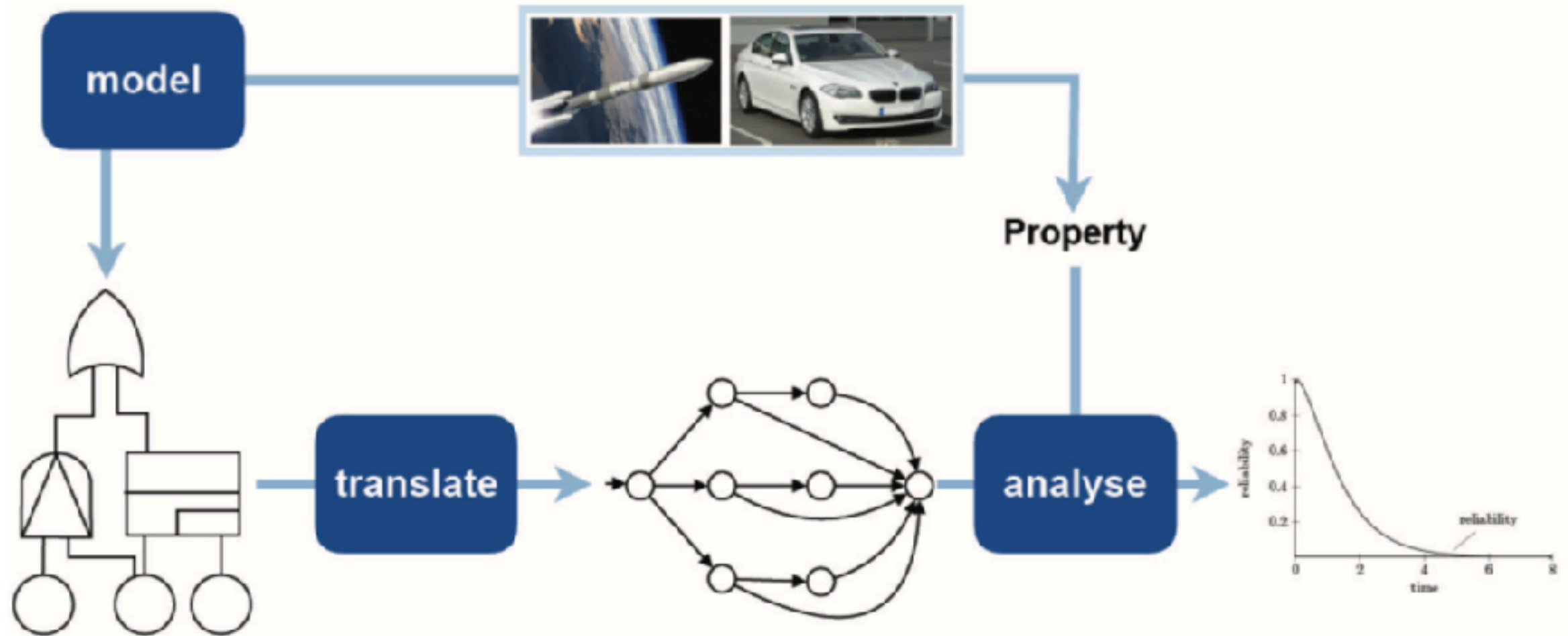


Freivald's (Monte Carlo) algorithm


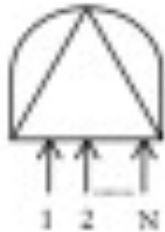
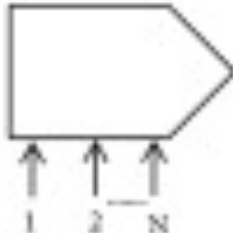
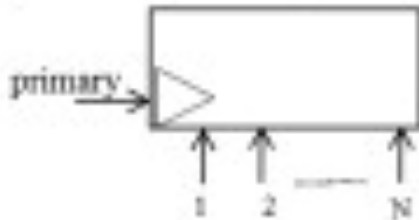
$O(kn^2)$

$P(n^{2.37})$

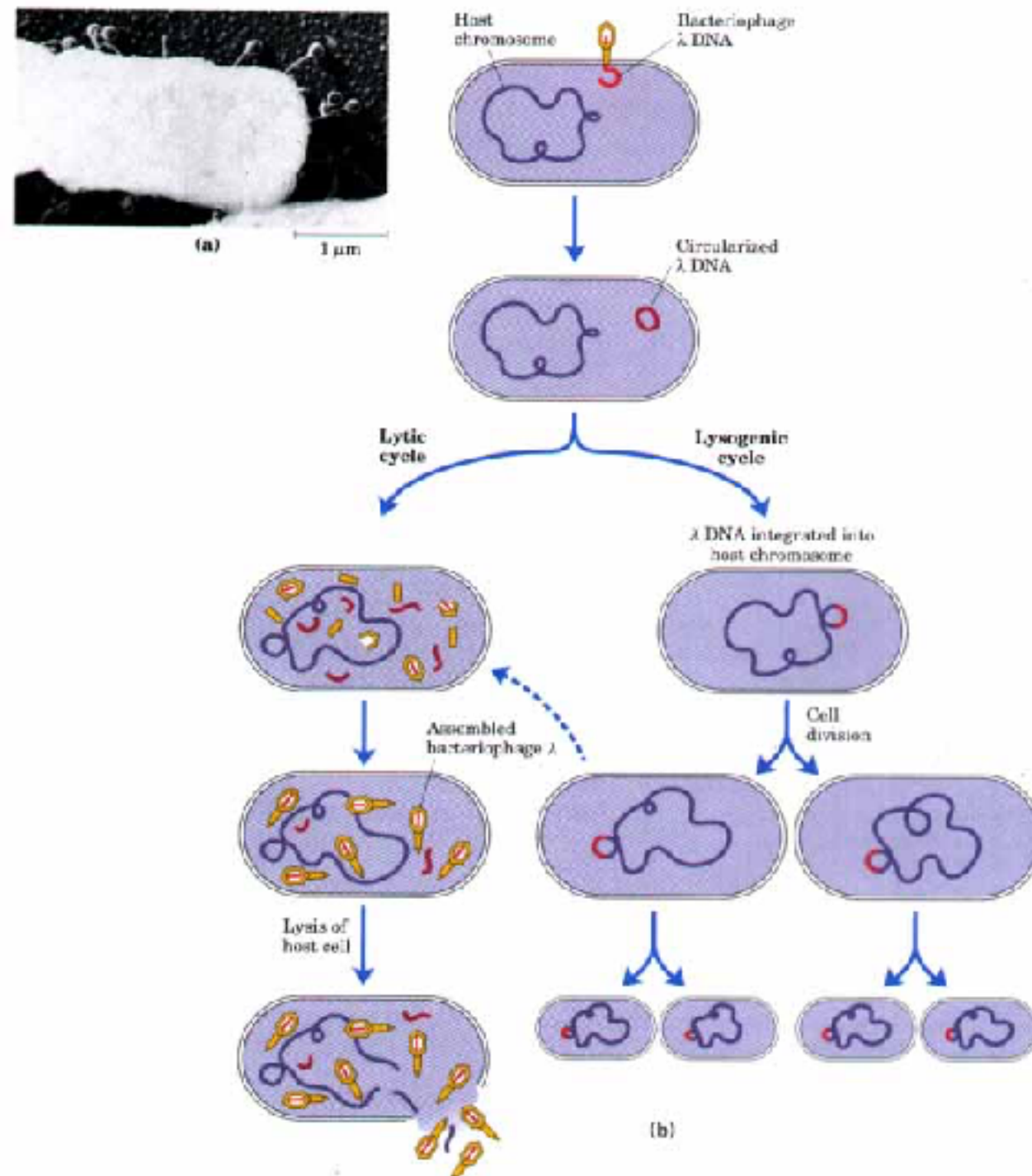
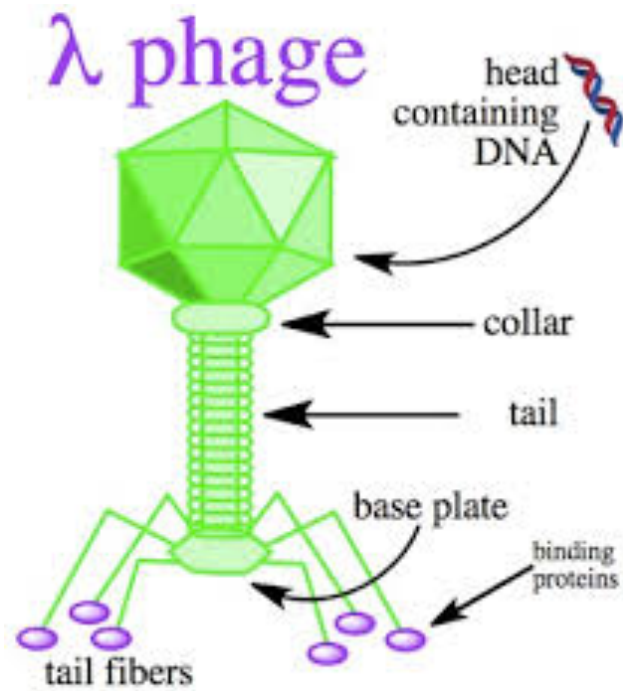
# Dynamic fault trees



# Dynamic fault trees

Name	Graphical Representation	Description (N input)
SPARE		It triggers only after the primary if all the N spares occur. Spares can be shared with other spare gate.
PAND		It behaves like an AND gate but it triggers only if the input events occur in the order from the left most to the right.
SEQ		It forces the input events to occur from the left to the right order. It can model the gradual degradation of a system.
FDEP		This gate models the failure of the dependent input events if the primary occurs. The output is a dummy or an input for other gates.

# Bacteriophage $\lambda$ : an Example of a Regulated Developmental Switch





# Stochasticity in biology: It's a noisy bussiness!

(McAdams, Arkin, 1999)

# It's a noisy bussiness!

Genetic regulation at the nanomolar scale

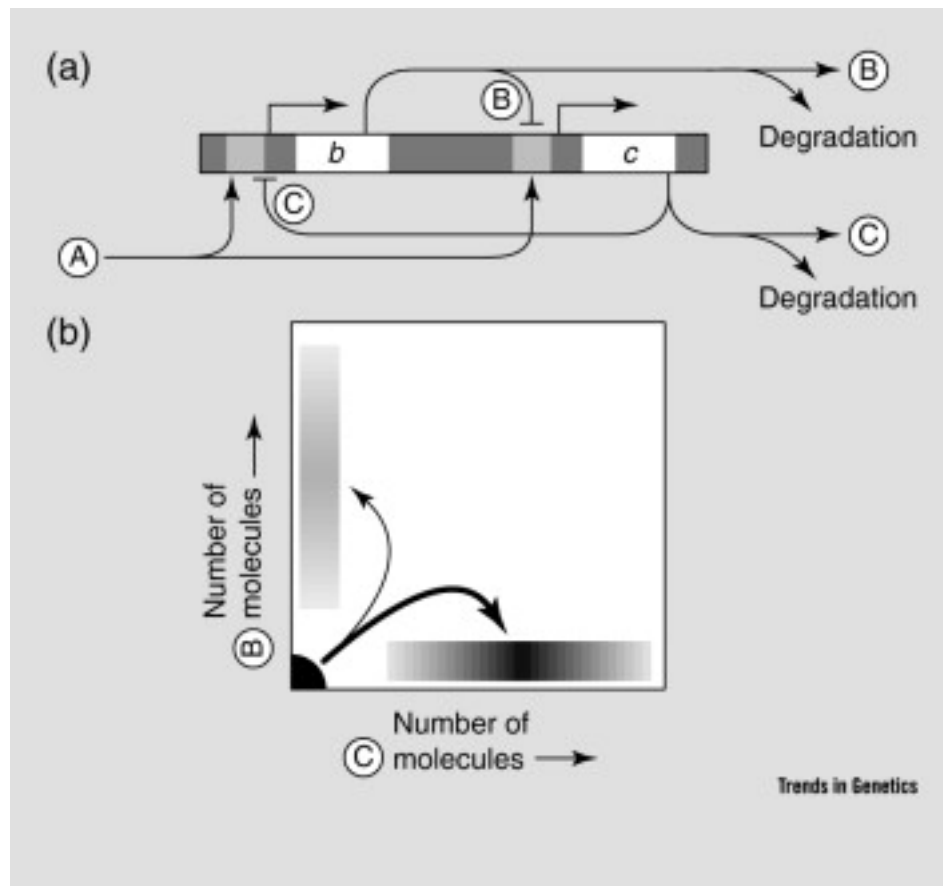
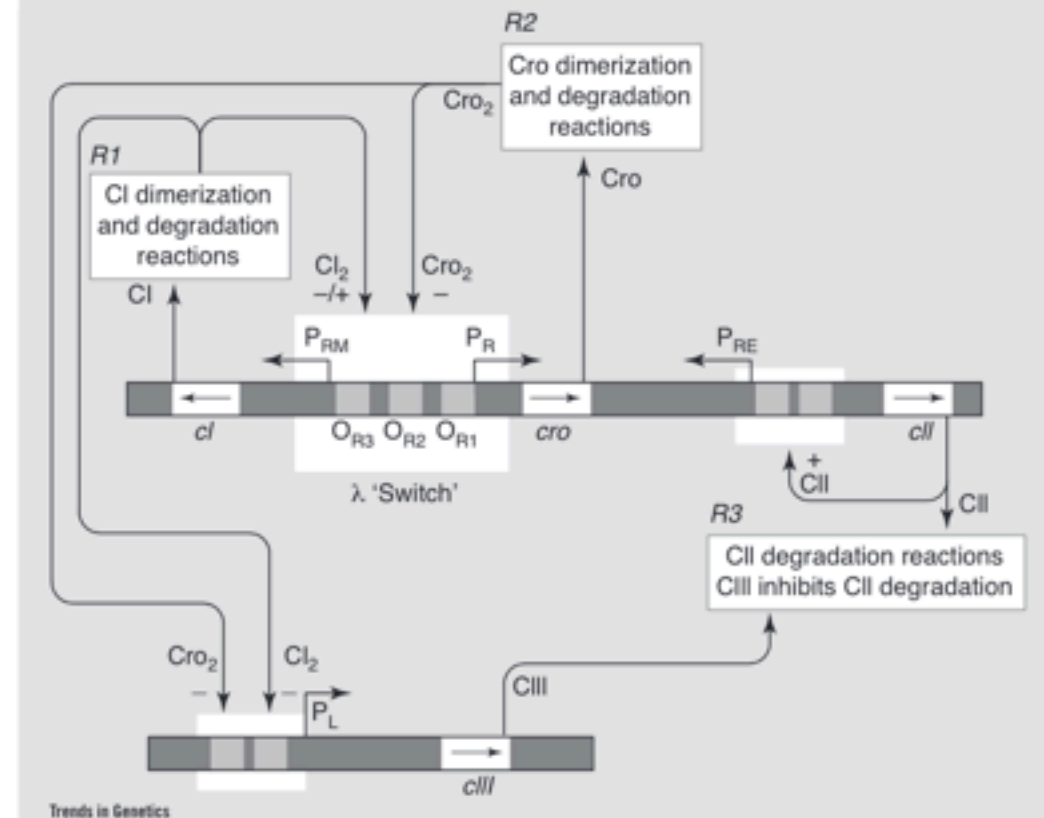


FIGURE 2. Phage  $\lambda$  lysis–lysogeny decision circuit

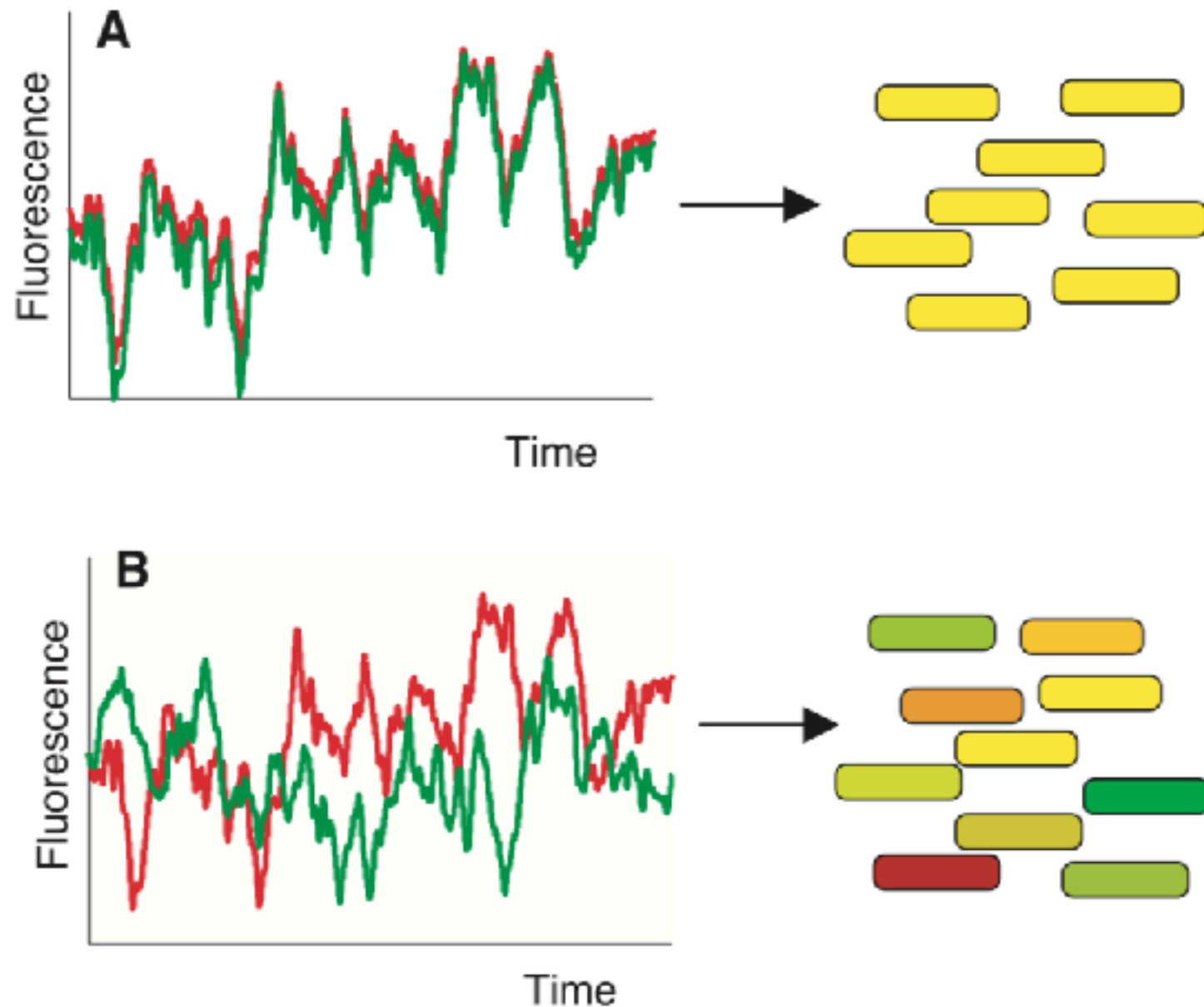


Simplified version of the phage  $\lambda$  decision circuit that determines whether infected *Escherichia coli* cells follow the lytic or lysogenic pathway. Bold horizontal lines indicate stretches of double-stranded DNA. Arrows in genes indicate the direction of transcription. The boxes R1–R3 indicate non-genetic protein reaction subsystems. The three operator sites,  $O_{R1-R3}$  of the ' $\lambda$  switch' implement a concentration-dependent 'logic', controlling promoters  $P_{RM}$  and  $P_R$ . Cro and Cl dimers bind to the three sites with different affinities and in opposite order to control the activation level of the  $P_{RM}$  and  $P_R$  promoters<sup>40,41</sup>. The Cl dimer acts as either a repressor or activator of promoter  $P_{RM}$ , depending on its concentration. The result is a mutually exclusive locking mechanism, so that either  $P_{RM}$  or  $P_R$  ends up being activated with the other promoter locked off. Strong production of Cl relatively soon after infection is necessary for locking on the  $P_{RM}$  loop to select the lysogenic pathway. This occurs only when the strong promoter  $P_{RE}$  is activated by CII to 'jump start' Cl production. Degradation of CII is inhibited by CIII, so production of CIII increases the probability of Cl 'winning' the race. Environmental signals influence the outcome by affecting the rate of CII degradation. Due to the stochastic character of protein production and the other reactions involved, both the lytic and the lysogenic outcome can occur with some probability, so that two alternative phenotypes result.

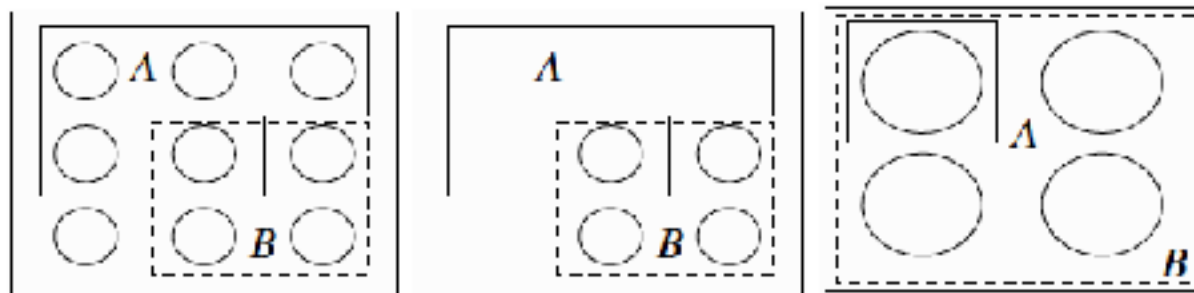


# Stochastic Gene Expression in a Single Cell (Elowitz et al., 2002)

**Fig. 1.** Intrinsic and extrinsic noise can be measured and distinguished with two genes (*cfp*, shown in green; *yfp*, shown in red) controlled by identical regulatory sequences. Cells with the same amount of each protein appear yellow, whereas cells expressing more of one fluorescent protein than the other appear red or green. **(A)** In the absence of intrinsic noise, the two fluorescent proteins fluctuate in a correlated fashion over time in a single cell (left). Thus, in a population, each cell will have the same amount of both proteins, although that amount will differ from cell to cell because of extrinsic noise (right). **(B)** Expression of the two genes may become uncorrelated in individual cells because of intrinsic noise (left), giving rise to a population in which some cells express more of one fluorescent protein than the other.



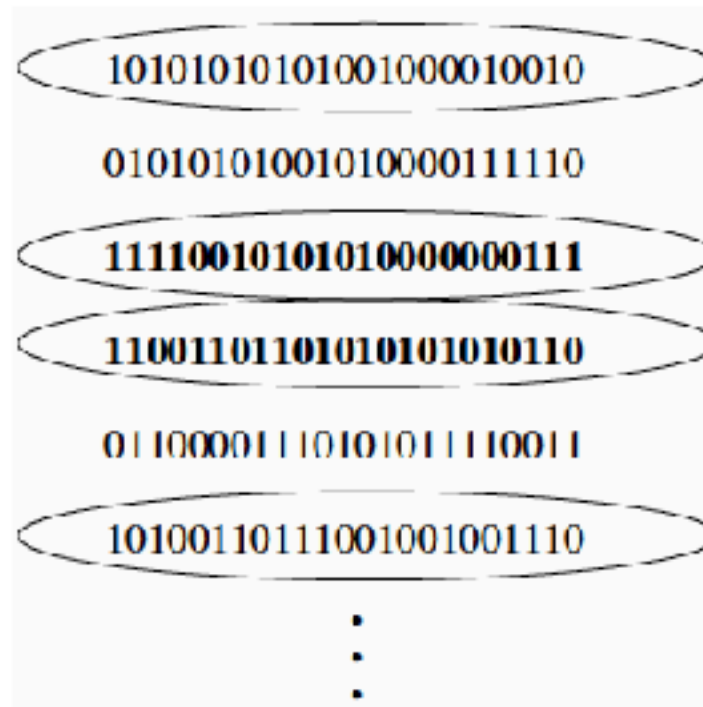
# Conditional probability



**FIGURE 2.1**

Pebble World intuition for  $P(A|B)$ . From left to right: (a) Events  $A$  and  $B$  are subsets of the sample space. (b) Because we know  $B$  occurred, get rid of the outcomes in  $B^c$ . (c) In the restricted sample space, renormalize so the total mass is still 1.

# Conditional probability



**FIGURE 2.2**

Frequentist intuition for  $P(A|B)$ . The repetitions where  $B$  occurred are circled; among these, the repetitions where  $A$  occurred are highlighted in bold.  $P(A|B)$  is the long-run relative frequency of the repetitions where  $A$  occurs, within the subset of repetitions where  $B$  occurs.

## Conditional probability

**Example 2.2.5** (Elder is a girl vs. at least one girl). A family has two children, and it is known that at least one is a girl. What is the probability that both are girls, given this information? What if it is known that the *elder* child is a girl?

## Conditional probability

**Example 2.2.5** (Elder is a girl vs. at least one girl). A family has two children, and it is known that at least one is a girl. What is the probability that both are girls, given this information? What if it is known that the *elder* child is a girl?

*Solution:*

Assume each child is equally likely to be a boy or a girl, independently.<sup>1</sup> Then

$$P(\text{both girls} | \text{at least one girl}) = \frac{P(\text{both girls, at least one girl})}{P(\text{at least one girl})} = \frac{1/4}{3/4} = 1/3,$$

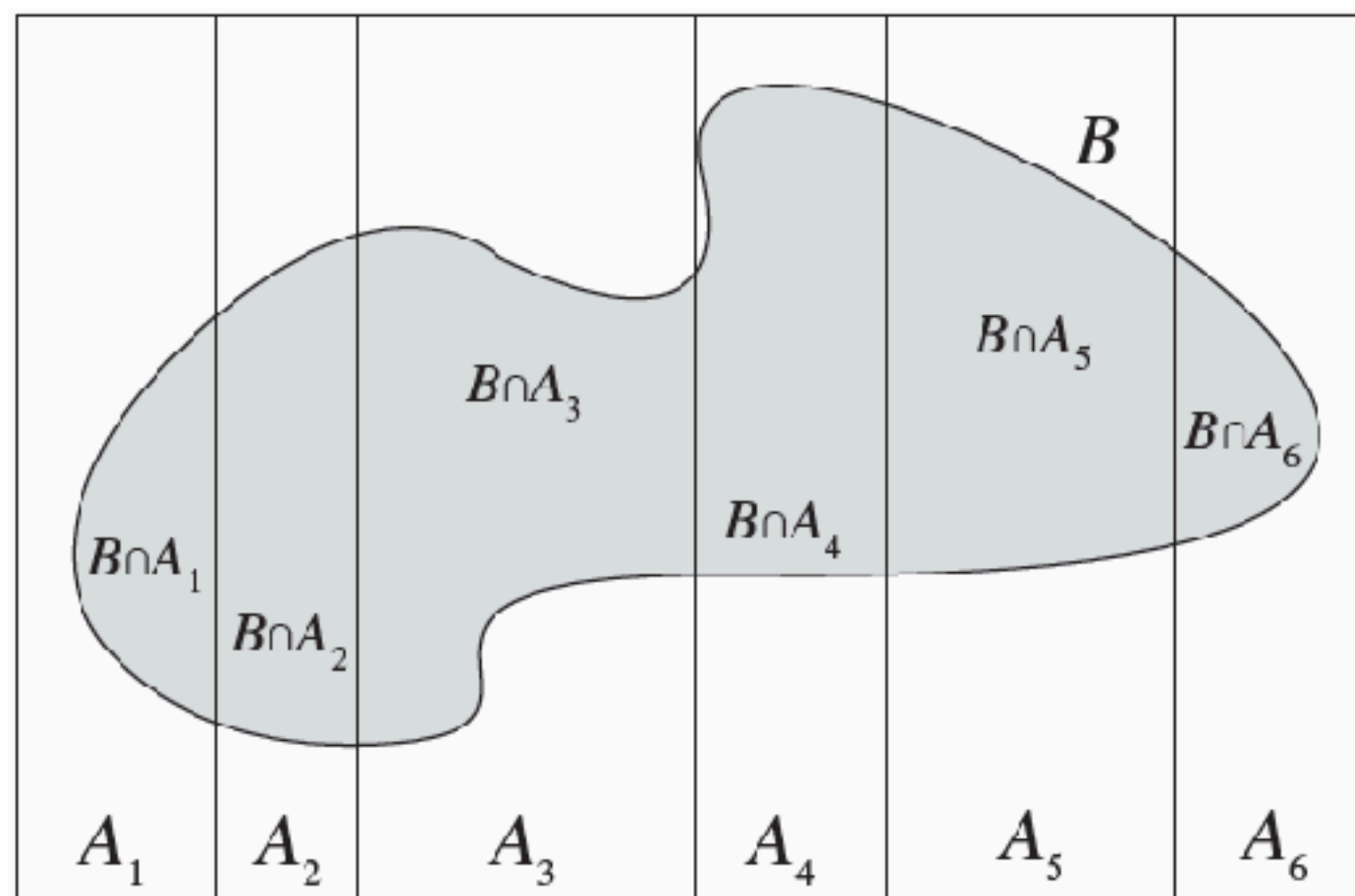
$$P(\text{both girls} | \text{elder is a girl}) = \frac{P(\text{both girls, elder is a girl})}{P(\text{elder is a girl})} = \frac{1/4}{1/2} = 1/2.$$

It may seem counterintuitive at first that the two results are different, since there is no reason for us to care whether the elder child is a girl as opposed to the younger child. Indeed, by symmetry,

$$P(\text{both girls} | \text{younger is a girl}) = P(\text{both girls} | \text{elder is a girl}) = 1/2.$$

## Law of total probability

$$P(B) = P(B|A_1)P(A_1) + \dots + P(B|A_n)P(A_n).$$

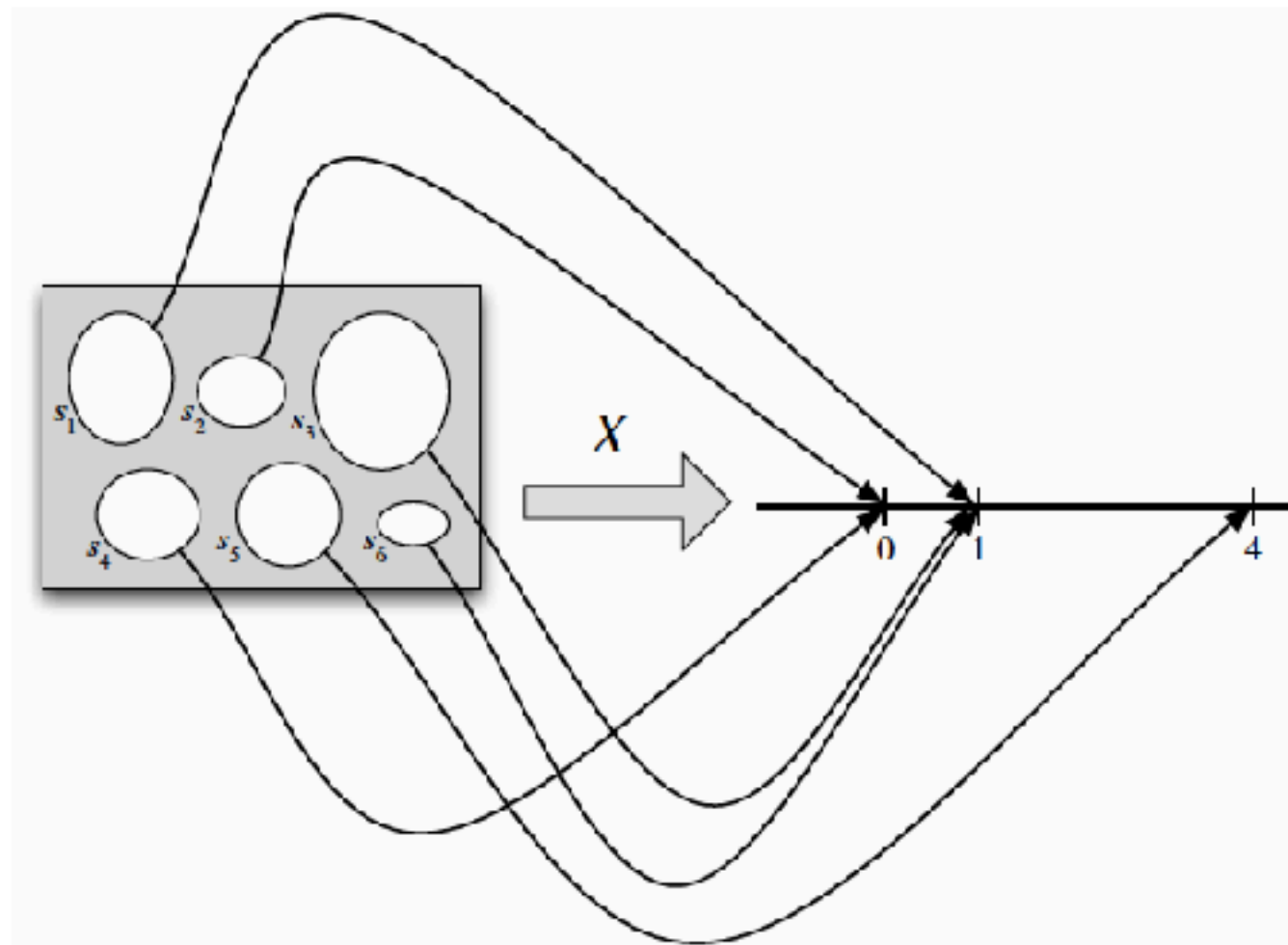


**FIGURE 2.3**

The  $A_i$  partition the sample space;  $P(B)$  is equal to  $\sum_i P(B \cap A_i)$ .



# Random Variables



**FIGURE 3.1**

A random variable maps the sample space into the real line. The r.v.  $X$  depicted here is defined on a sample space with 6 elements, and has possible values 0, 1, and 4. The randomness comes from choosing a random pebble according to the probability function  $P$  for the sample space.

# Random Variables

**Example 3.2.5** (Sum of die rolls). We roll two fair 6-sided dice. Let  $T = X + Y$  be the total of the two rolls, where  $X$  and  $Y$  are the individual rolls. The sample space of this experiment has 36 equally likely outcomes:

$$S = \{(1, 1), (1, 2), \dots, (6, 5), (6, 6)\}.$$

For example, 7 of the 36 outcomes  $s$  are shown in the table below, along with the corresponding values of  $X$ ,  $Y$ , and  $T$ . After the experiment is performed, we observe values for  $X$  and  $Y$ , and then the observed value of  $T$  is the sum of those values.

$s$	$X$	$Y$	$X + Y$
(1, 2)	1	2	3
(1, 6)	1	6	7
(2, 5)	2	5	7
(3, 1)	3	1	4
(4, 3)	4	3	7
(5, 4)	5	4	9
(6, 6)	6	6	12

# Random Variables

$$P(T = 2) = P(T = 12) = 1/36,$$

$$P(T = 3) = P(T = 11) = 2/36,$$

$$P(T = 4) = P(T = 10) = 3/36,$$

$$P(T = 5) = P(T = 9) = 4/36,$$

$$P(T = 6) = P(T = 8) = 5/36,$$

$$P(T = 7) = 6/36.$$

# Random Variables

$$P(T = 2) = P(T = 12) = 1/36,$$

$$P(T = 3) = P(T = 11) = 2/36,$$

$$P(T = 4) = P(T = 10) = 3/36,$$

$$P(T = 5) = P(T = 9) = 4/36,$$

$$P(T = 6) = P(T = 8) = 5/36,$$

$$P(T = 7) = 6/36.$$

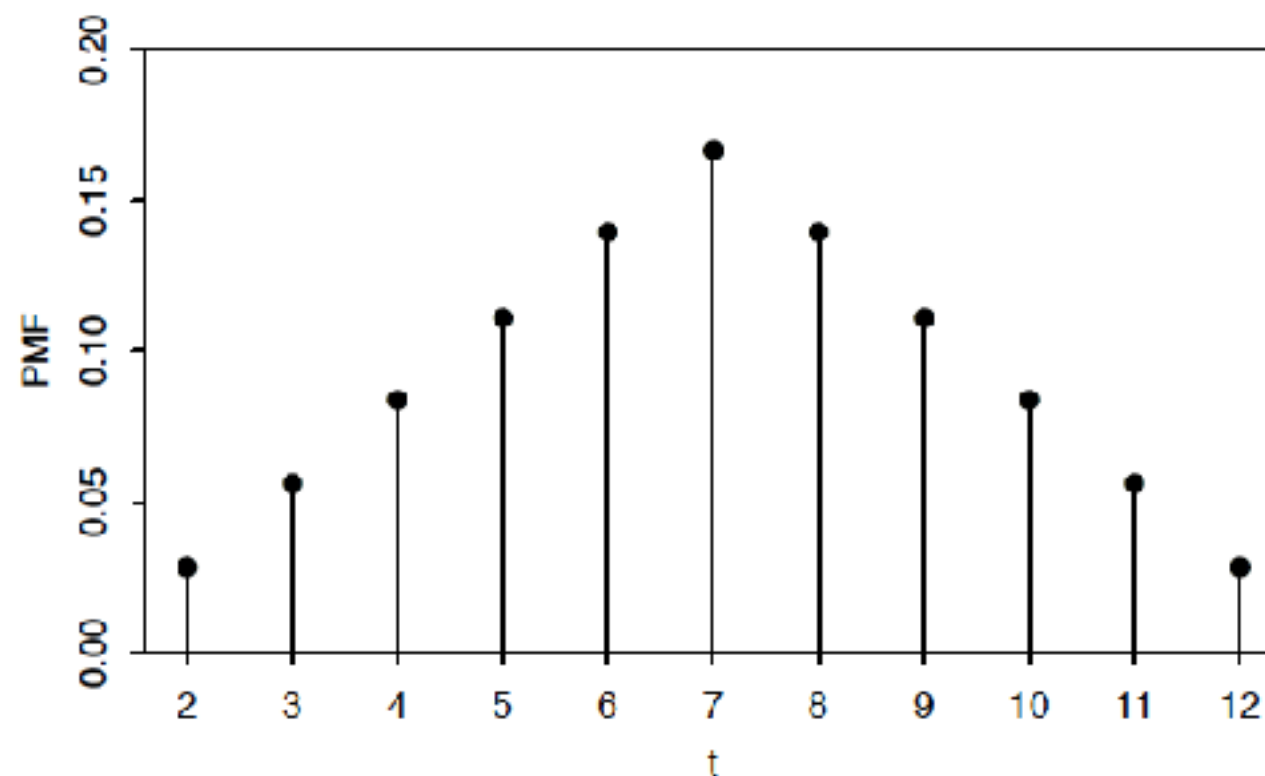


FIGURE 3.4

PMF of the sum of two die rolls.