

## Fundamentals of Biostatistical Inference I

Meets: Tuesday and Thursday 1:25-3:20 in Mayo D327

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- Textbook (required): *Mathematical Statistics and Data Analysis* (3<sup>rd</sup> edition) by John A. Rice

- Some homework solutions in back of book.

- Grade: 80% homework (assigned each week) + 20% final exam.

- Course webpage: <http://www.biostat.umn.edu/~hanson>.

## Chapter 1: Introduction to Probability

- Read sections 1.1, 1.2, 1.3, 1.4, 1.5, 1.6.
- Supplemental reading (if needed): Sheldon Ross' *A First Course in Probability*.
- Lots of nice typed notes from courses taught elsewhere on the web.

## 1.1 History of Probability

- Modern study of probability begins with gambling.
- Dice found in Egyptian tombs early as 2000 B.C.
- Mathematical study begins with Blaise Pascal and Pierre Fermat in 1600's.
- Goal in applications of probability is usually to quantify chance of certain outcomes.
- Leads to ideas of experiment, sample space, and events.

## 1.2 Sample spaces and set theory

We term anything that results in an outcome that cannot be predicted beforehand as an **experiment**. Any set of possible outcomes of interest is termed an **event**.

The collection of possible outcomes of an experiment is called the **sample space** and is denoted by  $S$ .  $S$  is a *set* whose *elements*  $s$  are experimental outcomes. We write this  $s \in S$ , “ $s$  is an element of  $S$ .” Your book uses  $\Omega$  to denote a sample space and  $\omega$  to denote an element instead of  $S$  and  $s$ .

**Note:** curly brackets  $\{\dots\}$  are used to denote a set (a collection of elements). The symbol “:” is read “such that” and provides a condition that must be met for inclusion. For example  $\{x \in \mathbb{R} : x \leq 10\}$ , or simply  $\{x : x \leq 10\}$ , is the interval  $(-\infty, 10]$ . Recall  $\mathbb{R} = (-\infty, \infty)$ .

## Examples:

- A randomly selected full-blooded Navajo is tested for blood type.  $S = \{O, A\}$ . All possible blood types for full-blooded Navajos are  $O$  and  $A$ .
- e.g. Pulling balls from an urn. Say the urn has 3 white balls and 2 black balls. The experiment is to pull one randomly drawn ball from the urn. The sample space is  $S = \{\bigcirc, \bullet\}$ . Equivalently  $S = \{W, B\}$ . Note that the sample space *is not* denoted  $S = \{\bigcirc, \bigcirc, \bigcirc, \bullet, \bullet\}$  or  $S = \{W, W, W, B, B\}$  as these are redundant; there are only two possible outcomes to the experiment!

- Roll a 6-sided die.  $S = \left\{ \begin{array}{|c|} \hline \cdot \\ \hline \end{array}, \begin{array}{|c|} \hline \cdot \\ \cdot \\ \hline \end{array}, \begin{array}{|c|} \hline \cdot \\ \cdot \\ \cdot \\ \hline \end{array}, \begin{array}{|c|} \hline \cdot \\ \cdot \\ \cdot \\ \cdot \\ \hline \end{array}, \begin{array}{|c|} \hline \cdot \\ \cdot \\ \cdot \\ \cdot \\ \cdot \\ \hline \end{array}, \begin{array}{|c|} \hline \cdot \\ \cdot \\ \cdot \\ \cdot \\ \cdot \\ \cdot \\ \hline \end{array} \right\}$ . Equivalently  $S = \{1, 2, 3, 4, 5, 6\}$ . These are all possible outcomes of rolling a 6-sided die.
- e.g. The experiment is to record the age of a randomly selected individual from the mall. If age is recorded in years then  $S = \{0, 1, 2, 3, \dots\}$  or perhaps  $S = \{0, 1, 2, 3, \dots, 120\}$  would suffice. If age is recorded *exactly* then might be  $S = [0, 120]$  or equivalently  $S = \{s \in \mathbb{R} : 0 \leq s \leq 120\}$ .

An **event** is a subset of  $S$  and is a collection of outcomes that may or may not occur. Shortly, we will assign *probability* to events happening.

An event may be a single outcome, e.g.  $\left\{ \begin{array}{|c|} \hline \bullet \\ \hline \bullet \\ \hline \end{array} \right\}$ , or it may be a larger subset of  $S$ , e.g.  $\left\{ \begin{array}{|c|} \hline \bullet \\ \hline \bullet \\ \hline \end{array}, \begin{array}{|c|} \hline \bullet \\ \hline \bullet \\ \hline \end{array} \right\}$ .

The empty set  $\emptyset$  is a special set that contains no elements. It functions sort of like zero does for integers. The event  $S$  always happens and the event  $\emptyset$  never happens.

## Restated:

- An event, often generically denoted  $A$ ,  $B$ , etc., is a collection of experimental outcomes. After the experiment is over, an event has either *occurred* or *not occurred*.
- An event  $A$  is a *subset* of  $S$ . This is denoted  $A \subset S$  and does not preclude  $A = S$ .

## Examples:

- Rolling a 6-sided die. Let  $S = \{1, 2, 3, 4, 5, 6\}$ . Some events are  $A = \{2, 4, 6\}$ ,  $B = \{1, 3, 5\}$ ,  $C = \{4\}$ ,  $D = \{2, 3\}$ ,  $S$ , and  $\emptyset$ .
- The experiment is to record the time in months to remission or death of a randomly selected cancer patient receiving a new type of chemotherapy treatment. For simplicity we'll take  $S = (0, \infty)$ . Some events are  $A = [6, 12]$ ,  $B = [12, \infty]$ , and  $C = (0, 1)$ .

## Set operations

- Union:  $A \cup B = \{s \in S : s \in A \text{ or } s \in B\}$ .
- Intersection:  $A \cap B = \{s \in S : s \in A \text{ and } s \in B\}$ .
- Compliment:  $A^C = \{s \in S : s \notin A\}$

Two sets  $A$  and  $B$  are **disjoint** if they have no elements in common, i.e. if  $A \cap B = \emptyset$ . A collection of sets  $\{A_1, A_2, A_3, \dots\}$  is **mutually disjoint** if  $A_i \cap A_j = \emptyset$  for  $i \neq j$ .

If  $A \cap B = \emptyset$  then if  $A$  happens  $B$  cannot happen and vice-versa.

Recapping:

- $A \subset B$  if and only if  $B$  contains every element in  $A$ .
- $A \cup B$  are all the elements in  $S$  that are in either  $A$  or  $B$ .
- $A \cap B$  are those elements in  $S$  that  $A$  and  $B$  have in common.
- $A^C$  are those elements in  $S$  not in  $A$ .
- Also:  $A = B$  only if  $A$  and  $B$  have the same elements.

**Venn diagrams** are graphical tools to illustrate set operations. For example  $A \subset B$  nicely illustrated with Venn diagram.

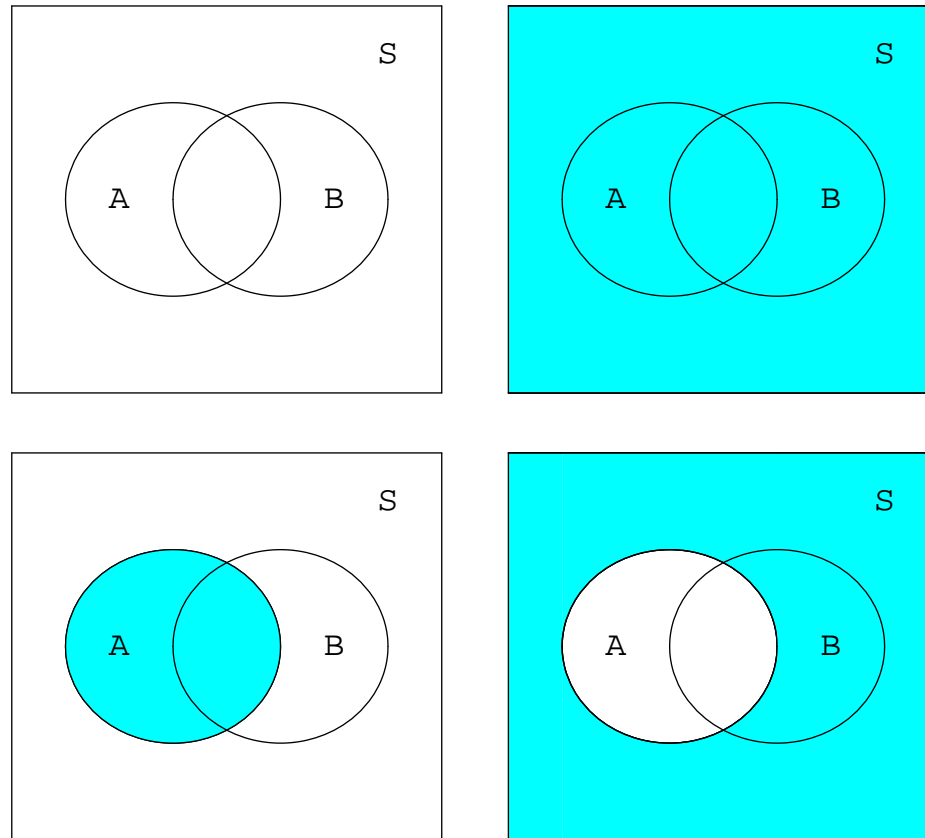


Figure 1: Upper left:  $\emptyset$ , upper right:  $S$ , lower left:  $A$ , lower right  $A^C$ .

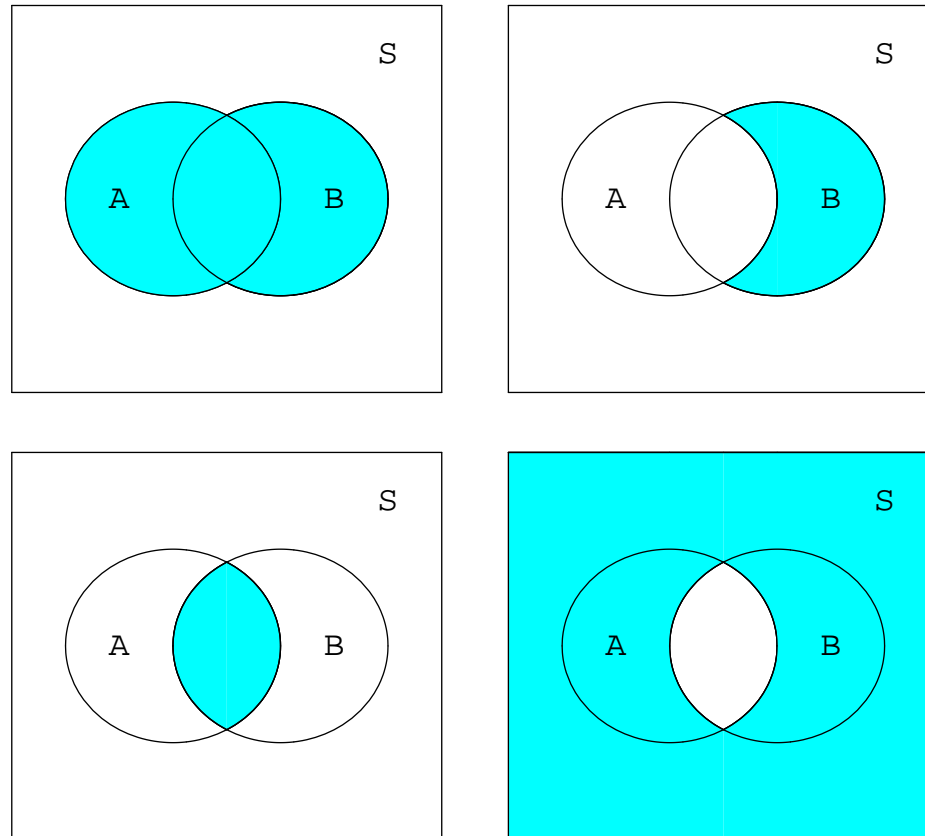


Figure 2: Upper left:  $A \cup B$ , upper right:  $A^C \cap B$ , lower left:  $A \cap B$ , lower right  $(A \cap B)^C = A^C \cup B^C$ .

Example: Let  $S = \{O, A, B, AB\}$  be blood types. Let  $C_1 = \{O, A, B\}$ ,  $C_2 = \{A, B, AB\}$ ,  $C_3 = \{O, B\}$ , and  $C_4 = \{A, AB\}$ .

- $C_1 \cap C_2 = \{A, B\}$ .
- $C_3 \cap C_4 = \emptyset$ .  $C_3$  and  $C_4$  are disjoint.
- $C_1 \cup C_2 = S$ .
- $C_1 \cup C_3 = C_1$ .
- $C_1 \cap C_3 = C_3$ .
- $C_3 \cup C_4 = S$ .
- $C_1^C = \{AB\}$ .
- Is  $C_4 \subset C_2$ ? Answer: yes.
- Is  $C_3 \subset C_1$ ? Answer: yes.
- Is  $C_2^C \subset C_3$ ? Answer: yes.

Example: The experiment is measuring the lifetime of a chemotherapy patient in years. Let  $S = \mathbb{R}^+ = [0, \infty)$  be the positive real numbers. Let  $C_1 = (0, 5)$ ,  $C_2 = (2, 10)$ ,  $C_3 = [5, 10)$ .

- $C_1 \cap C_2 = (2, 5)$ .
- $C_2 \cap C_3 = [5, 10) = C_3$ .
- $C_1 \cap C_3 = \emptyset$ .
- $C_2 \cap C_1^C = C_3$ .
- $C_1 \cup C_2 = (0, 10)$ .
- Is  $C_3 \subset C_2$ ? Answer: yes.
- Is  $C_3 \subset C_1$ ? Answer: no.
- Are  $C_1$  and  $C_3$  disjoint? Yes.

## Some laws of set theory:

Commutative:

$$A \cup B = B \cup A$$

$$A \cap B = B \cap A$$

Associative:

$$(A \cup B) \cup C = A \cup (B \cup C)$$

$$(A \cap B) \cap C = A \cap (B \cap C)$$

Distributive:

$$(A \cup B) \cap C = (A \cap C) \cup (B \cap C)$$

$$(A \cap B) \cup C = (A \cup C) \cap (B \cup C)$$

Sometimes we will need the union or intersection of lots of (maybe infinity many) events. The union of an infinite number of events is denoted

$$A_1 \cup A_2 \cup A_3 \cup A_4 \cup \dots = \bigcup_{i=1}^{\infty} A_i.$$

An infinite intersection is denoted

$$A_1 \cap A_2 \cap A_3 \cap A_4 \cap \dots = \bigcap_{i=1}^{\infty} A_i.$$

Finite versions are given by

$$A_1 \cup A_2 \cup A_3 \cup \dots \cup A_n = \bigcup_{i=1}^n A_i,$$

$$A_1 \cap A_2 \cap A_3 \cap \dots \cap A_n = \bigcap_{i=1}^n A_i.$$

### 1.3: Probability functions

A probability is a function from the set of all events (subsets of  $S$ ) to  $[0, 1]$ . We denote the probability of event  $A$  as  $P(A)$ . Three axioms (statements we assume to be true at the outset) provide various properties we expect probabilities to have:

1. For every event  $A$ ,  $P(A) \geq 0$ .
2.  $P(S) = 1$ .
3. For every infinite sequence of mutually disjoint events  $A_1, A_2, A_3, \dots$

$$P\left(\bigcup_{i=1}^{\infty} A_i\right) = \sum_{i=1}^{\infty} P(A_i).$$

Recall “summation notation.” In general, for a sequence of numbers  $a_1, a_2, \dots, a_n$ ,

$$\sum_{i=1}^n a_i = a_1 + a_2 + \dots + a_n.$$

For example,

$$\sum_{i=1}^5 i^2 = 1^2 + 2^2 + 3^2 + 4^2 + 5^2 = 55.$$

An infinite version is given by

$$\sum_{i=1}^{\infty} a_i = \lim_{n \rightarrow \infty} \sum_{i=1}^n a_i.$$

Axiom 3 is also written

$$P(A_1 \cup A_2 \cup A_3 \cup \dots) = P(A_1) + P(A_2) + P(A_3) + \dots$$

where  $\{A_1, A_2, A_3, \dots\}$  are mutually disjoint.

**Property:**  $P(\emptyset) = 0$ .

Proof:  $S$  and  $\emptyset$  are disjoint ( $S \cap \emptyset = \emptyset$ ) and two empty sets are disjoint ( $\emptyset \cap \emptyset = \emptyset$ ). Let  $A_1 = S$  and  $A_j = \emptyset$  for  $j \geq 2$ . then axiom 3 tells us

$$1 = 1 + \sum_{j=2}^{\infty} P(\emptyset).$$

Axiom 1 implies the result.

**Property:** For an *finite* number of disjoint sets  $A_1, A_2, \dots, A_n$ ,

$$P\left(\bigcup_{i=1}^n A_i\right) = \sum_{i=1}^n P(A_i).$$

Proof: assign  $A_{n+1} = \emptyset$ ,  $A_{n+2} = \emptyset$  and so on and use axiom 3.

In particular, if  $A \cap B = \emptyset$  then  $P(A \cup B) = P(A) + P(B)$ .

**Property:**  $P(A^C) = 1 - P(A)$ .

Proof:  $A^C$  and  $A$  are disjoint and  $S = A \cup A^C$ . So  
 $1 = P(S) = P(A \cup A^C) = P(A) + P(A^C)$

**Property:** If  $A \subset B$  then  $P(A) \leq P(B)$ .

Proof: stems from identity  $B = A \cup (B \cap A^C)$  where  $A$  and  $B \cap A^C$  are disjoint, and fact that  $P(B \cap A^C) \geq 0$ .

**Property** (addition law):  $P(A \cup B) = P(A) + P(B) - P(A \cap B)$ .

Proof: involves chopping  $A \cup B$  into disjoint pieces, see book page 5.

Example: A fair coin is thrown twice. The sample space is  $S = \{hh, ht, th, tt\}$ , all of which are equally likely. Let  $A = \{hh, ht\}$  and  $B = \{hh, th\}$  be the events of heads on the first toss and heads on the second toss respectively. The probability that heads comes up on either toss is

$$\begin{aligned} P(A \cup B) &= P(A) + P(B) - P(A \cap B) \\ &= P(\{hh, ht\}) + P(\{hh, th\}) - P(\{hh\}) \\ &= 0.5 + 0.5 - 0.25 = 0.75. \end{aligned}$$

Or could consider complimentary event that heads does not come up on either toss  $\{tt\}$ . The probability that heads comes up on either toss is one minus the probability that heads does not come up on either toss:  $1 - P(\{tt\}) = 1 - 0.25 = 0.75$ .

## Section 1.4: probability through counting

Let  $S$  have a finite number  $N$  of outcomes  $S = \{s_1, \dots, s_N\}$ . Let  $P(s_i) = p_i$  for  $i = 1, \dots, N$ .

- Let  $A$  be an event. The probability of  $A$  is the sum of probabilities associated with each outcome in  $A$ :

$$P(A) = \sum_{i:s_i \in A} p_i.$$

This is from axiom 3 and noting that  $\{s_i\} \cap \{s_j\} = \emptyset$  for  $i \neq j$  because elements in  $S$  are unique. Also

$$A = \bigcup_{i:s_i \in A} \{s_i\},$$

the union of disjoint simple events each comprised of one outcome in  $A$ .

- Then  $p_1 + p_2 + \cdots + p_N = 1$ . This is because  $P(S) = 1$  and  $S = \{s_1, s_2, \dots, s_N\} = \{s_1\} \cup \{s_2\} \cup \cdots \cup \{s_N\}$ , the union of  $N$  simple disjoint sets each comprised of one element.

Computing probabilities is simplified when all elements in  $S$  have the same probability of occurring,  $p_i = P(s_i) = \frac{1}{N}$ . Then

$$P(A) = \frac{\text{number of elements in } A}{\text{number of elements in } S} = \frac{n}{N},$$

where  $n$  is the number of outcomes in  $A$ .

- Rolling a 6-sided die. A die roll has outcomes  $S = \{1, 2, 3, 4, 5, 6\}$ . If the die is fair then  $p_j = P(j) = \frac{1}{6}$  where  $j = 1, 2, 3, 4, 5, 6$ . Then the probability of a roll that is a prime number is  $P(A)$  where  $A = \{2, 3, 5\}$ . Since  $A$  has 3 elements,  $P(A) = \frac{3}{6} = \frac{1}{2}$ .
- Consider a bag holding the 26 letters  $\{A, B, C, \dots, X, Y, Z\}$ . If we randomly pull one letter from the bag and all letters are equally likely, what is the probability of getting a vowel?

$$P(\{A, E, I, O, U\}) = \frac{5}{26}.$$

The probability of getting a consonant is then

$$1 - P(\{A, E, I, O, U\}) = \frac{21}{26}.$$

## Multiplication principle

If one experiment has  $m$  outcomes and another experiment has  $n$  outcomes, then there are  $mn$  outcomes for the combined experiment.

Example: Playing cards have 13 face values

$\{A, 2, 3, 4, 5, 6, 7, 8, 9, 10, J, Q, K\}$  and 4 suits  $\{\clubsuit, \spadesuit, \heartsuit, \diamondsuit\}$ , so there are  $13 \times 4 = 52$  possible outcomes to the experiment “face value & suit,” i.e. 52 different cards

$\{A\clubsuit, A\spadesuit, A\heartsuit, A\diamondsuit, 2\clubsuit, 2\spadesuit, 2\heartsuit, 2\diamondsuit, \dots, K\clubsuit, K\spadesuit, K\heartsuit, K\diamondsuit\}$ .

The multiplication principle naturally extends to more than two experiments.

## Permutations and combinations

A **permutation** is an ordered arrangement of objects. For example  $ACB$  is one (of 6 possible) permutations of the letters  $\{A, B, C\}$ .

Now think of a bag with all 26 letters  $\{A, B, C, D, \dots, X, Y, Z\}$ . We wish to choose  $r$  letters from the bag; how many unique words can we make?

In general, let  $\mathcal{C} = \{c_1, c_2, \dots, c_n\}$  be  $n$  unique objects.

**Proposition:** For a sample of size  $r$  from  $n$  objects  $\{c_1, c_2, \dots, c_n\}$ , there are  $n^r$  different permutations when sampling with replacement and  $n(n-1)(n-2)\cdots(n-r+1)$  different permutations when sampling without replacement.

Let  $\mathcal{C} = \{A, B, C\}$  so  $n = 3$ . Let's sample  $r = 2$  letters both with and without replacement.

- Sampling with replacement yields  $n^r = 3^2 = 9$  possible words: AA, AB, AC, BA, BB, BC, CA, CB, CC.
- Sampling without replacement eliminates those words with repeated letters giving  
 $n(n - r + 1) = n(n - 2 + 1) = n(n - 1) = 3 \times 2 = 6$  words: AB, AC, BA, BC, CA, CB.

Let's reconsider the bag with 26 letters  $\mathcal{C} = \{A, B, C, D, \dots, X, Y, Z\}$ .

- Assuming each word is equally likely, what is the probability of randomly choosing the word *PERMUTATION* when sampling  $r = 11$  letters with replacement? Answer: There are  $n^r = 26^{11} = 3,670,344,486,987,776$  unique words possible, of which this is one, so  $\frac{1}{3,670,344,486,987,776}$ .
- Trick question: what is this probability when sampling without replacement?

**Birthday problem:** Suppose that a room contains  $n$  people. What is the probability that at least two of the  $n$  share the same birthday?

Answer: This is more easily answered by considering the complimentary event  $A^C$  that no two people share the same birthday. Think of a bag filled with the numbers  $\{1, 2, 3, \dots, 364, 365\}$ , all the days in a year. Assigning each of the  $n$  people their own unique day from the bag *without replacement* yields  $365 \times 364 \times 363 \times \dots \times (365 - n + 1)$  possible permutations of  $n$  numbers from 365. There are  $365^n$  permutations, or orderings, possible (i.e. with replacement) when people can share birthdays. So the probability is

$$P(A^C) = \frac{\text{number in } A^C}{\text{number in } S} = \frac{365 \times 364 \times 363 \times \dots \times (365 - n + 1)}{365^n}.$$

$P(A) = 1 - P(A^C)$ ; see page 11 for some concrete numbers.

**Combinations** are unordered groups of unique objects. In a permutation order mattered, in a combination it does not.

e.g. When choosing two letters from  $\mathcal{C} = \{A, B, C\}$  without replacement there are 6 permutations AB, AC, BA, BC, CA, CB, but only 3 combinations  $\{A, B\}$ ,  $\{A, C\}$ , and  $\{B, C\}$ .

From the multiplication principle the number of ordered samples of size  $r$  from  $n$  unique objects is the number of unordered samples, i.e.

combinations, denoted  $\binom{n}{r}$  and read “ $n$  choose  $r$ ,” times the number of ways to permute the  $r$  unordered objects within one sample:

$$\binom{n}{r} r(r-1)(r-2)\cdots 1 = n(n-1)(n-2)\cdots(n-r+1).$$

Solving for the number of combinations yields

$$\binom{n}{r} = \frac{n(n-1)(n-2)\cdots(n-r+1)}{r(r-1)(r-2)\cdots 1} = \frac{n!}{(n-r)!r!},$$

where we define “ $m$  factorial”

$$m! = m(m-1)(m-2)\cdots 2 \times 1,$$

for any integer  $m$ . Define  $0! = 1$  as well.

e.g.

$$5! = 5 \times 4 \times 3 \times 2 \times 1 = 120.$$

Note:  $m! = m \times (m-1)!$ .

e.g. From a team consisting of  $n = 24$  third grade children,  $r = 3$  will be chosen to keep goal on a soccer team (two alternates). How many different combinations of children are possible?

$$\binom{24}{3} = \frac{24 \times 23 \times 22}{3 \times 2 \times 1} = 2024.$$

An urn contains 3 red and 2 green balls in it. The balls are drawn one at a time without replacement and placed in a row. What is the probability that all 3 red balls are next to each other?

There are three ways this can happen:  $\{rrr gg, grrrg, ggrrr\}$ . How many different ways total can we order the balls? Since there's only 5 balls we *could* list them. A more clever approach that generalizes to lots of balls is to think instead of the number combinations from the slots  $\{1, 2, 3, 4, 5\}$  of size 3 in which the red balls are placed; here we can count them:  $\{123, 124, 125, 134, 135, 145, 234, 235, 245, 345\}$ . This corresponds to drawing

$\{rrr gg, rrgrg, rr ggr, rgrrg, rgrgr, rg grr, grrrg, grrgr, gr grr, ggrrr\}$ .

The number is succinctly given by  $\binom{5}{3} = 10$ .

So the probability is  $\frac{3}{10} = 0.3$ .

The result for counting combinations generalizes. The number of ways  $n$  distinct objects can be divided into  $r$  groups of sizes  $n_1, n_2, \dots, n_r$ , where  $n_1 + n_2 + \dots + n_r = n$ , is given by

$$\binom{n}{n_1 \ n_2 \ \dots \ n_r} = \frac{n!}{n_1!n_2!\dots n_r!}.$$

Note where  $n_1 + n_2 = n$  that

$$\binom{n}{n_1 \ n_2} = \binom{n}{n_1} = \binom{n}{n_2} = \frac{n!}{n_1!n_2!}.$$

Example (page 15): In how many ways can the set of nucleotides  $\{A, A, G, G, G, G, C, C, C\}$  be arranged in a sequence of 9 letters? We *cannot* tell the difference between the 3 *C*'s, the 4 *G*'s, or the 2 *A*'s; these 9 letters are not unique. However we *can* think of dividing the 9 unique slots  $\{1, 2, 3, 4, 5, 6, 7, 8, 9\}$  into three groups of sizes  $n_1 = 3$ ,  $n_2 = 4$ , and  $n_3 = 2$  representing the *C*'s, *G*'s, and *A*'s respectively.

$$\binom{9}{3 \ 4 \ 2} = \frac{9!}{3!4!2!} = 1260.$$

## Poker example:

Assuming each hand of 5 cards is equally likely, what is the probability of getting dealt a straight flush? A straight flush is 5 cards of the same suit whose face values form a sequence. Let  $E$  denote the event of obtaining a straight flush.

There are  $m = 4$  suits  $\{\clubsuit, \spadesuit, \heartsuit, \diamondsuit\}$  and  $n = 9$  ways of obtaining a straight

$\{A2345, 23456, 34567, 45678, 56789, 678910, 78910J, 8910JQ, 910JQK\}$ .

By the multiplication principle there are  $m \times n = 4 \times 9 = 36$  possible straight flushes.

There are  $\binom{52}{5} = 2,598,960$  unique poker hands, so

$$P(E) = \frac{36}{2,598,960} \approx 0.00001385.$$

Say there's 4 people playing poker. What is the probability that *each* player is dealt a straight flush?

$$\frac{\binom{36}{4}}{\binom{52}{5 \ 5 \ 5 \ 5 \ 32}} \approx 4 \times 10^{-20}.$$

Homework 1 (part A): 1, 2\*, 3, 4, 5, 9, 11, 12\*, 13, 14\*, 15, 16\*, 19, 20\*, 21, 22, 25, 27, 30\*, 31, 32, 33, 38\*, 41

\*due Sept. 11th.

Homework 1 (part B): 42\*, 45, 46\*, 47, 49, 50\*, 52, 53, 56\*, 60\*, 63, 67, 70\*, 78 & 79 (if interested).

Next time: Conditional probability, independence, law of total probability, Bayes rule.