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- Gusfield's book, chapters 5, 6, 7

# Entropy of a Distribution $p$

Let $X = (x_1, \ldots, x_n)$ be elements in a finite probability space, and $p(x_1), \ldots, p(x_n)$ be their probabilities ($\sum_{i=1}^{n} p(x_i) = 1$).

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- Informally, the entropy measures the amount of surprise (in bits) when observing a single occurrence of $X$.
- Let $p, q$ be two probability distributions on the same probability space, $X$. If $H(p) > H(q)$ then $p$ is more surprising than $q$. We also say that there is more randomness in $p$.

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- Entropy is a fundamental tool in Shannon's information theory.
- Also essential in communication, coding, probability, combinatorics, ...

# Entropy in Boolean Case

Suppose $X$ has just two elements $x_0, x_1$. Denote $p = p(x_1)$, then the probability of $x_0$ is $1 - p$.

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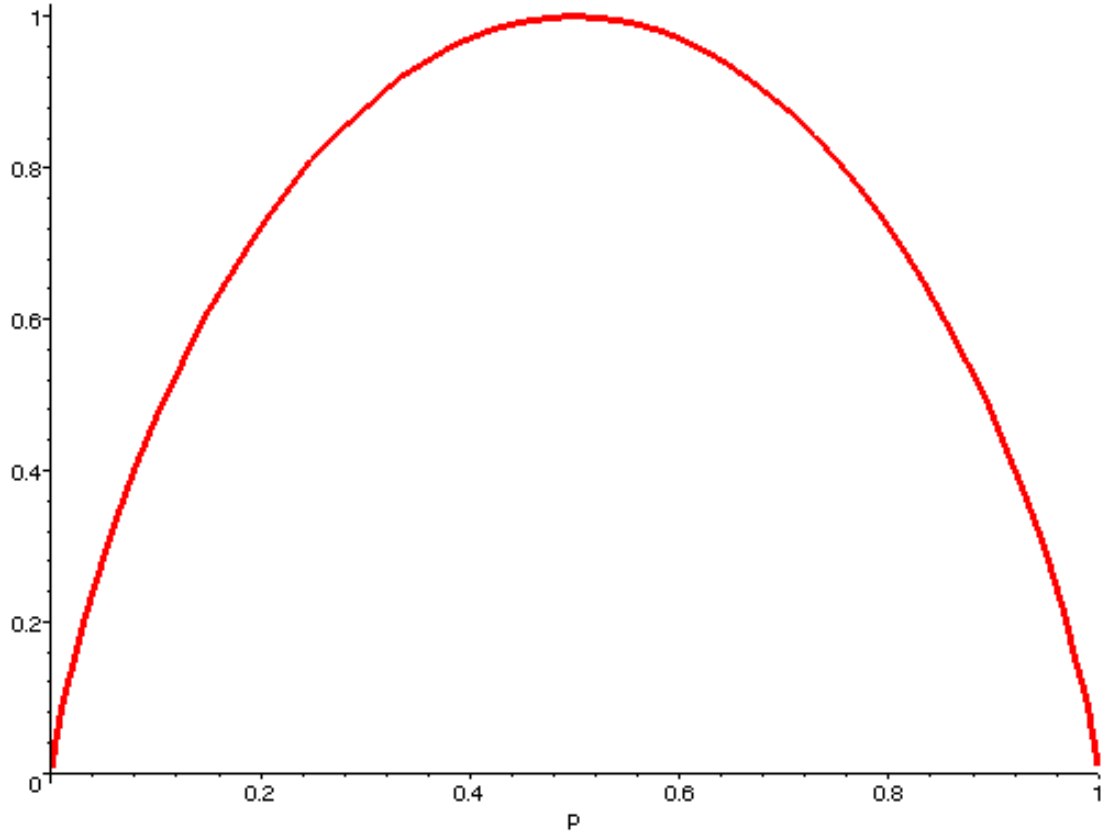
```
plot(-p*log[2](p)-(1-p)*log[2](1-p),p=0..1,thickness=3);
```



# Relative Entropy of Two Distributions

The Kullback-Leibler (KL) relative entropy of two distributions $p, q$ over the same probability space $X$ is defined as

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- Turns out the other direction holds too, *i.e.* $D(p \,||\, q) = 0 \Longrightarrow p = q$.

# Relative Entropy of Two Distributions (2)

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- In general $D$ is *not* a distance metric.
- Usually, $D(p \,||\, q) \neq D(q \,||\, p)$.
- In many cases, triangle inequality is violated: $D(p_1 \,||\, p_3) > D(p_1 \,||\, p_2) + D(p_2 \,||\, p_3)$ is possible.

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  Again, take $X = x_0, x_1$:
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  $p_2(x_0) = 1/4, p_2(x_1) = 3/4$,
  $p_3(x_0) = 1/3, p_3(x_1) = 2/3$.
  Calculation shows $\Delta$ inequality does not hold.

# Symmetric Relative Entropy

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- is clearly symmetric, $d(p,q) = d(q,p)$,
- tends to satisfy triangle inequality more often (still, not always),
- is more suitable as an "estimation" of distance between two distributions.

# Estimating Distances between Genomes

Given two genomes $g_1, g_2$ (each is a very long string over DNA alphabet, not necessarily of equal length), is there a way to define their distance?

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- Can get clues from information theory, if think of genomes as product of two distributions $G_1, G_2$.
- For example, can take $d(G_1, G_2)$ as desired "distance".

# Distances between Genomes (2)

Problems with approach:

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- Distributions $d(G_1, G_2)$ unknown.
- All we know is long samples of them, $g_1, g_2$.
- Should look for operators that approximate $d(G_1, G_2)$.

# Useful Notations

- Let $(g_1)_{i+1}^{i+k+1}$ denotes the substring of $g_1$ that starts in position $i+1$ and ends in position $i+k+1$.

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- What is $L_i(g_2, g_1)$?
- This is the longest substring of $g_1$, starting at $i$, that is also a substring of $g_2$.

# Intuition

$L_i(g_2, g_1) = \max_k((g_1)_{i+1}^{i+k+1} \subset g_2)$.

- Strings $g_2, g_1$ that are close by will tend to have long common substrings.

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- Strings $g_2, g_1$ that are close by will tend to have long common substrings.
- Strings $g_2, g_1$ that are far away will tend to have short common substrings.
- Maybe some average can lead to desired distance.

# The Distance Operator

Let $\bar{L}(g_2, g_1) = \frac{1}{|g_2|} \sum_i L_i(g_2, g_1)$ be the average over $i$'s of $L_i(g_2, g_1)$.

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A theorem of Weiner states that as the length of $g_2, g_1$ increases,

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This gives a theoretical justification for using the average common string method.

# Average Common String Algorithm

Given two strings $g_2, g_1$

- Use a suffix tree to efficiently compute $\sum_i L_i(g_2, g_1)$, $\sum_j L_j(g_2, g_1)$.

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- Average to estimate $d(g_1, g_2)$.

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- For real proteome and genome strings, triangle inequality satisfied for all pairs.

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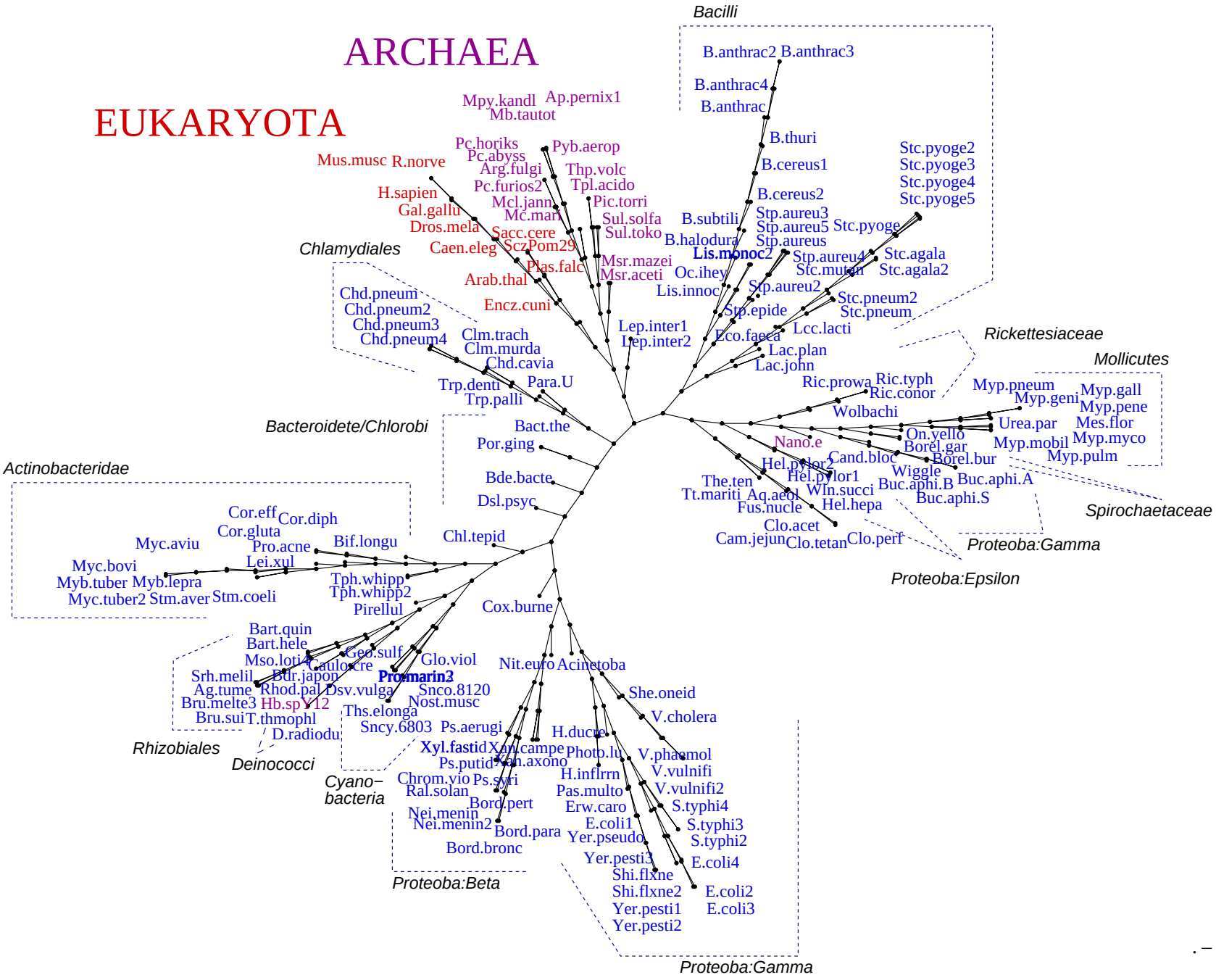
- For real proteome and genome strings, triangle inequality satisfied for all pairs.
- Joint work with Burstein, Ulitsky, Tuller (2004).

# Prot. Tree (average $1M$ long), 191 Taxa



# Retroid Virus Tree

Part of 1837 virus forest. Average genome length 5K.