Three Principles of Biological States: Ecology and Cancer

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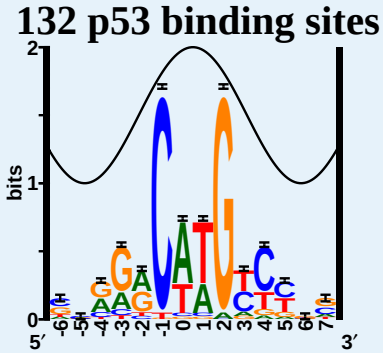
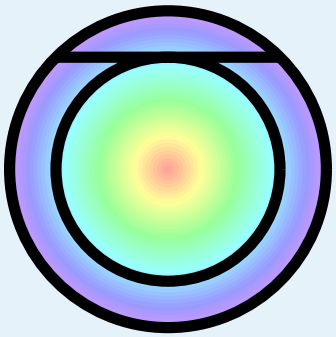
National Cancer Institute
Frederick, MD 21702-1201





Information Theory: One-Minute Lesson

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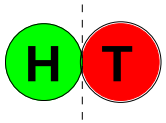
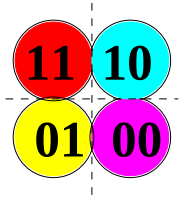
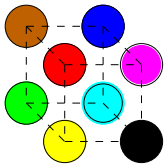
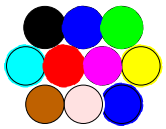
2	1	
4	2	
8	3	
$M=2^B$	$B=\log_2 M$	

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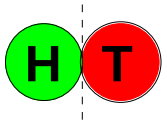
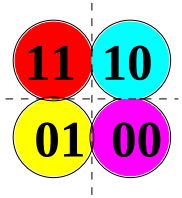
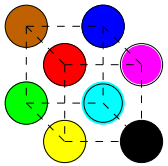
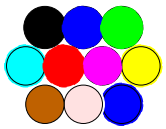
2	1	 
4	2	
8	3	
$M=2^B$	$B=\log_2 M$	

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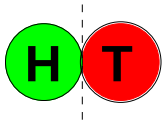
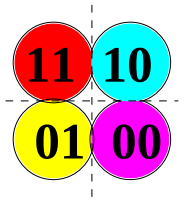
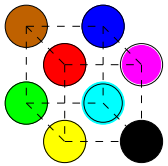
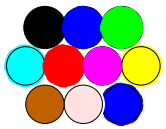
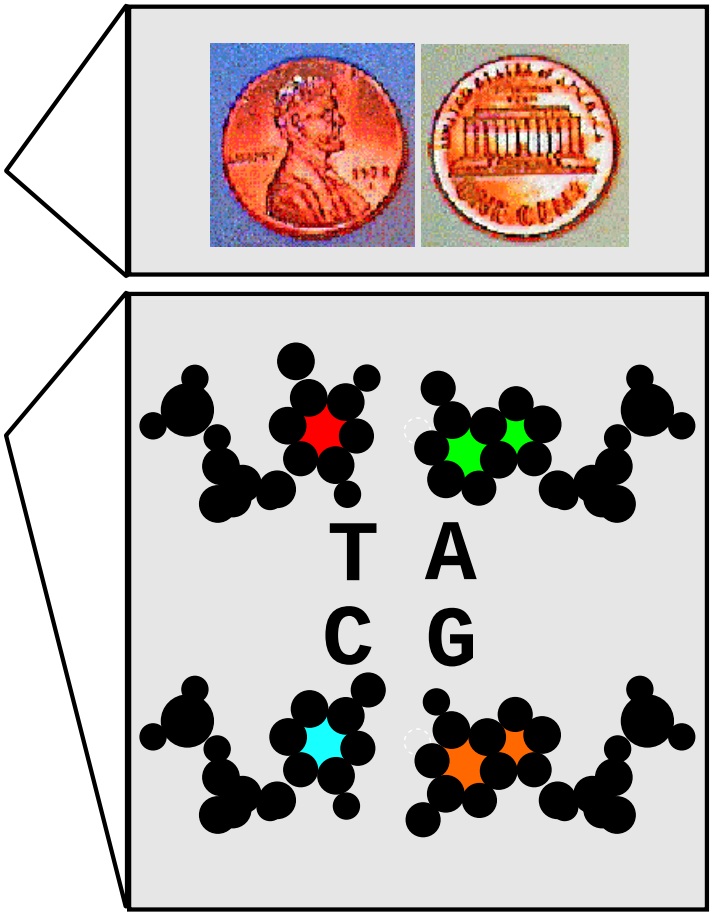
2	1	
4	2	
8	3	
$M=2^B$	$B=\log_2 M$	



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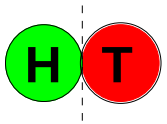
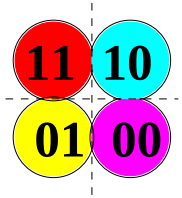
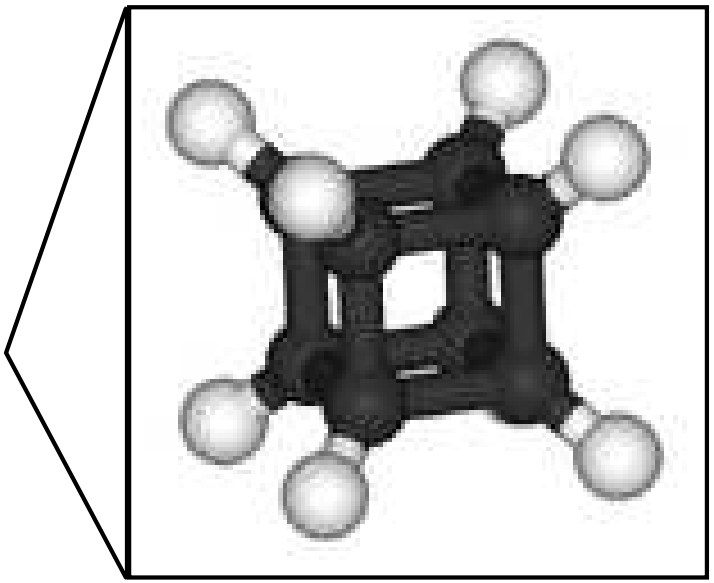
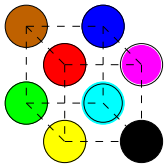
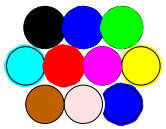
2	1	 
4	2	 
8	3	
$M=2^B$	$B=\log_2 M$	

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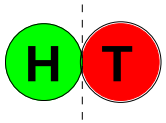
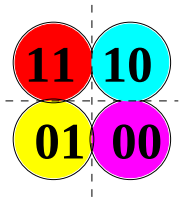
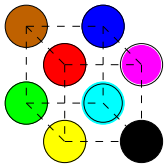
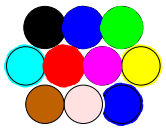
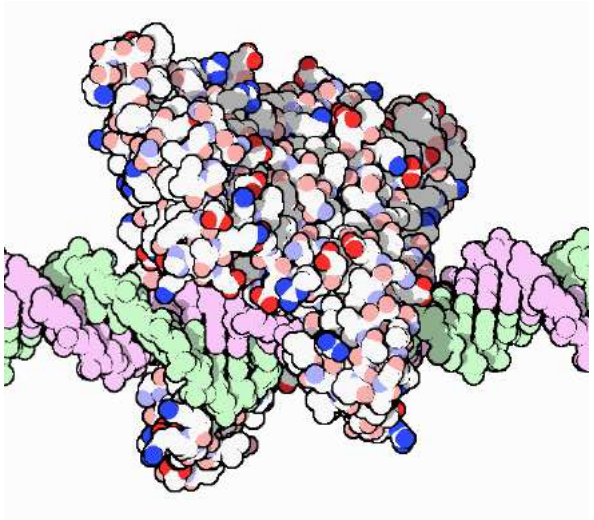
2	1	 
4	2	
8	3	
$M=2^B$	$B=\log_2 M$	 

Information of EcoRI DNA Binding

- EcoRI - restriction enzyme



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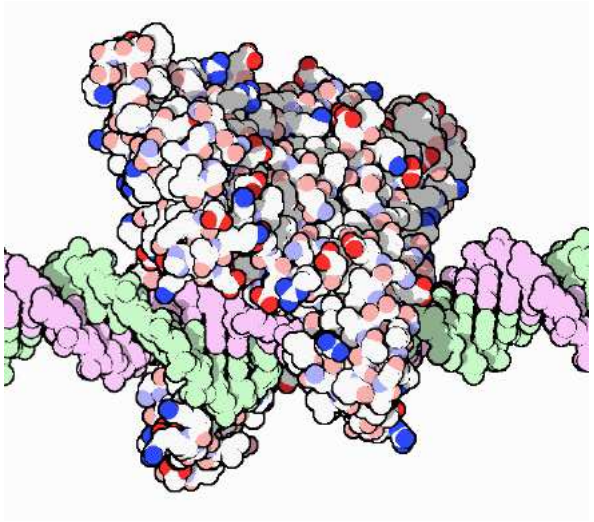

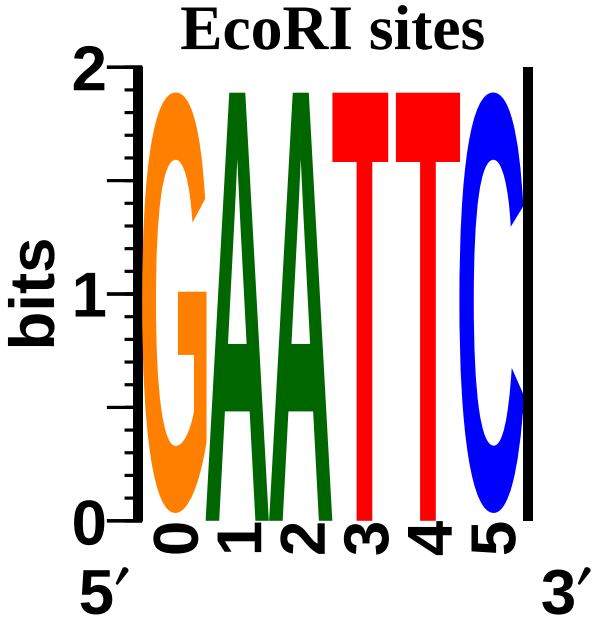

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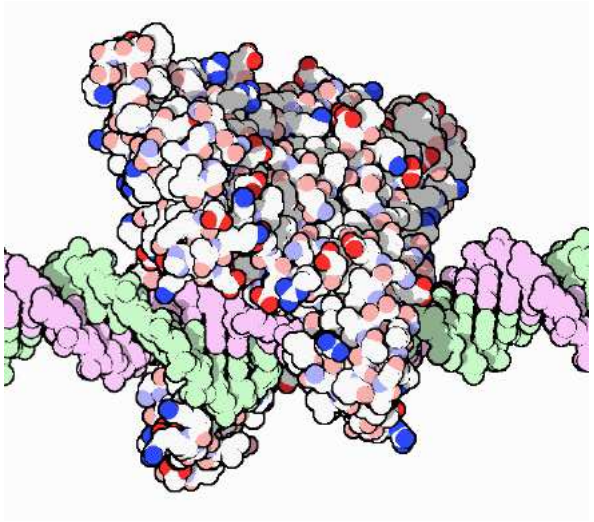

- EcoRI - restriction enzyme
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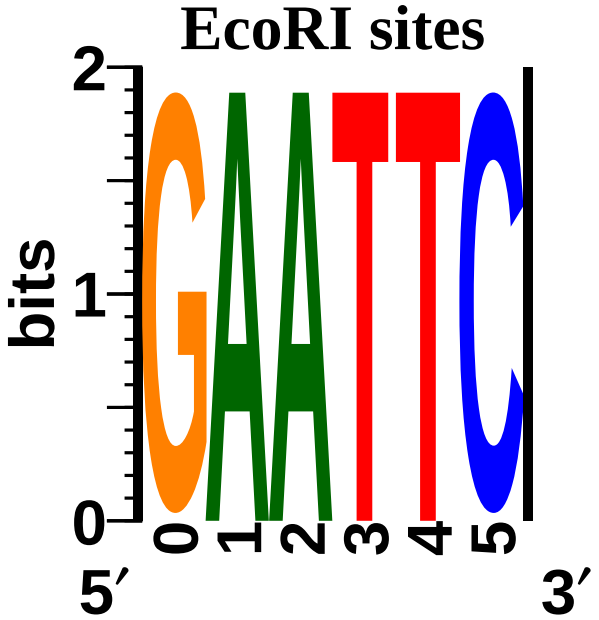
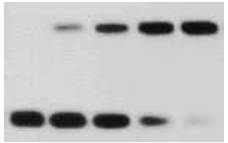
- information required:
  6 bases $\times$ 2 bits per base $=$ 12 bits



Energy Dissipation by EcoRI

- Measured specific binding constant:

$$K_{spec} = 1.6 \times 10^5$$



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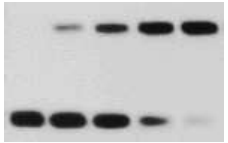

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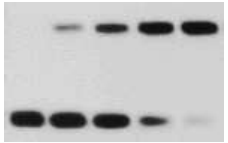

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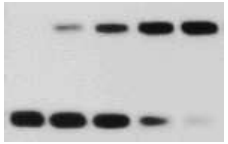

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- Number of bits that could have been selected:

$$\begin{aligned} R_{energy} &= -\Delta G^\circ / \mathcal{E}_{min} \\ &= k_\mathsf{B} T \ln K_{spec} / k_\mathsf{B} T \ln 2 \\ &= \log_2 K_{spec} \qquad \Leftarrow \text{SO SIMPLE!} \\ &= \boxed{\text{17.3 bits per binding}} \end{aligned}$$

Information/Energy = Efficiency of EcoRI

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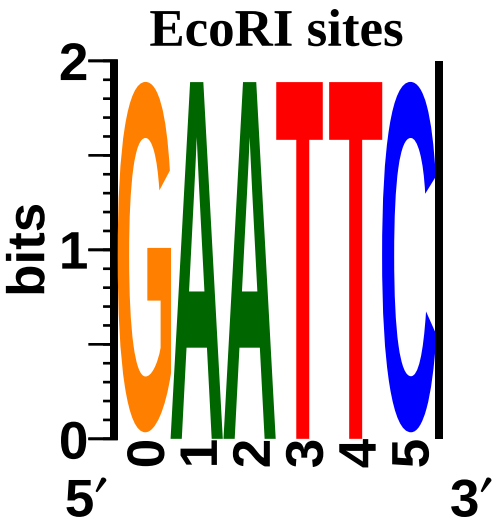

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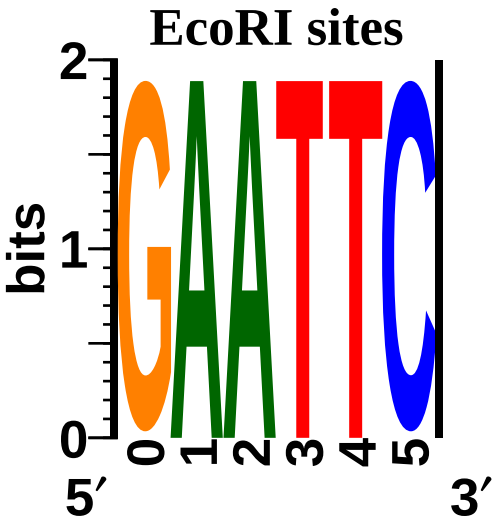

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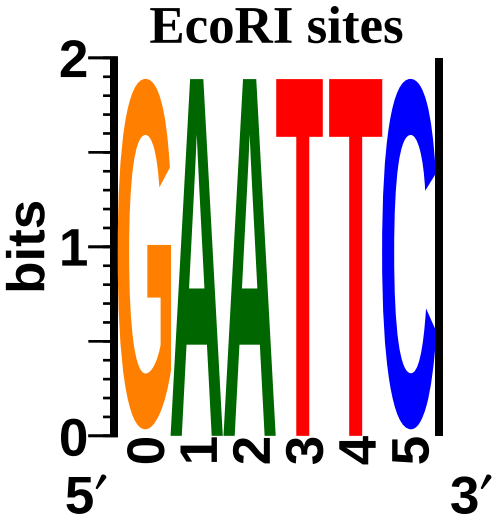

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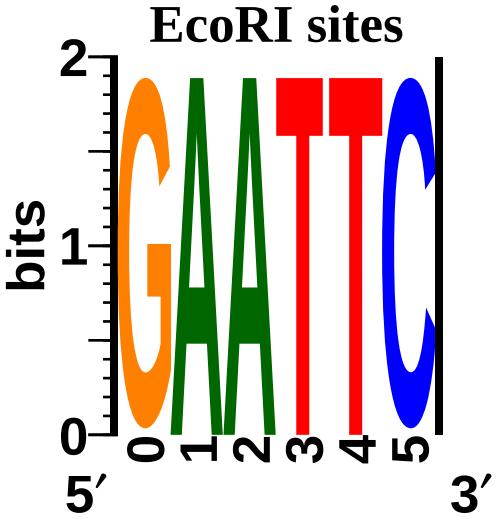

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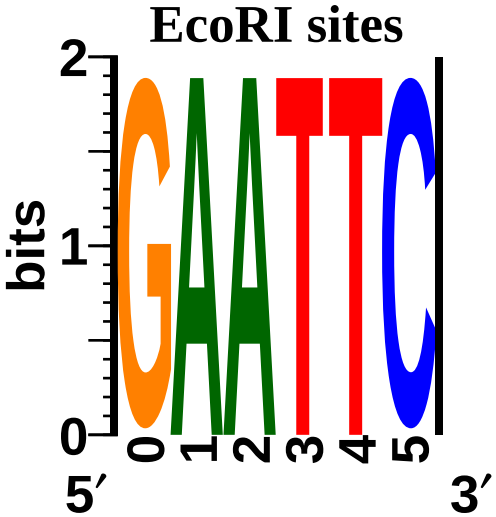

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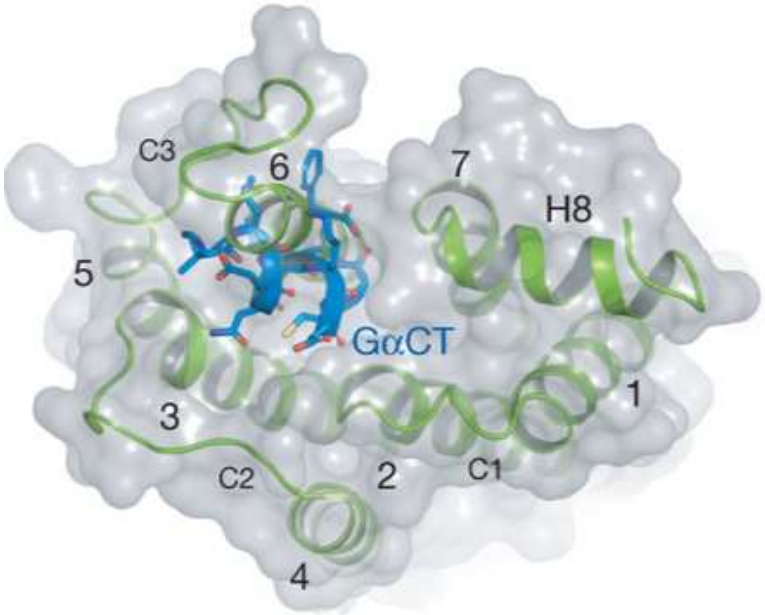
18 out of 19 DNA binding proteins give ∼70% efficiency.

Rhodopsin Shape Change

Dark State



P. Scheerer et al. Nature 455, 497-502(2008) doi:10.1038/nature07330

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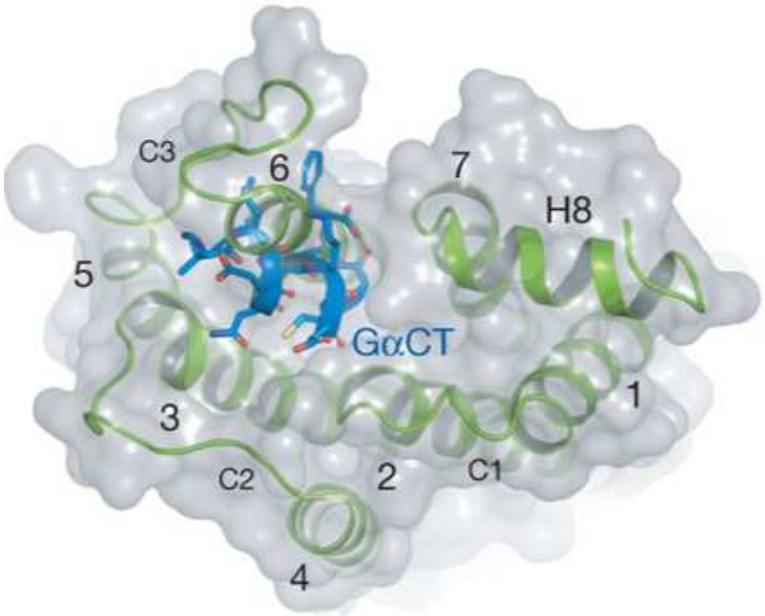

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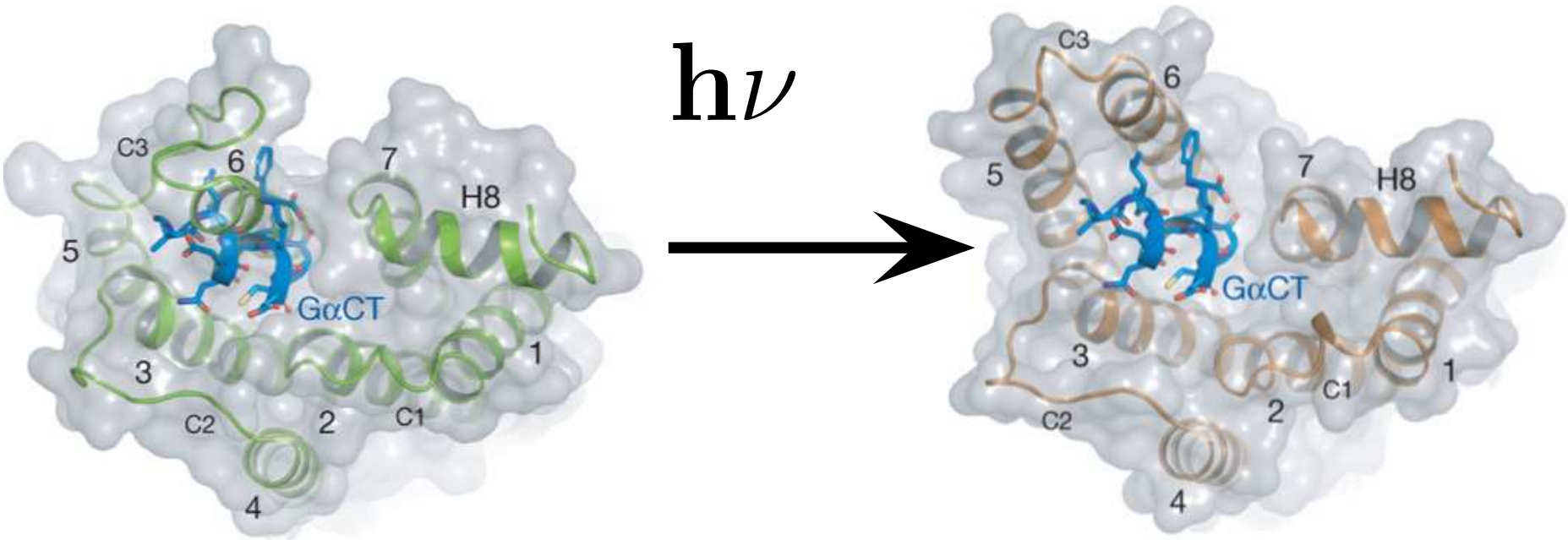
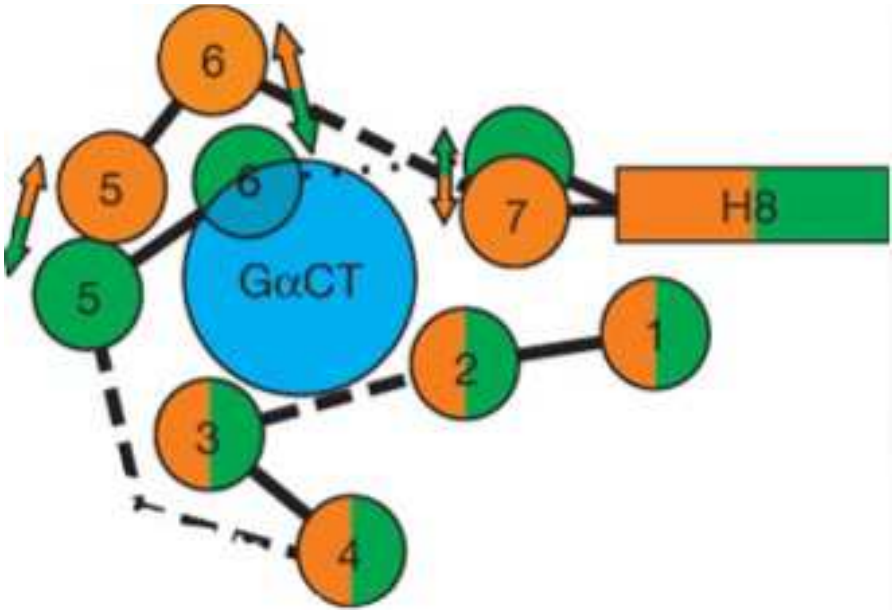
After Photon - Light State





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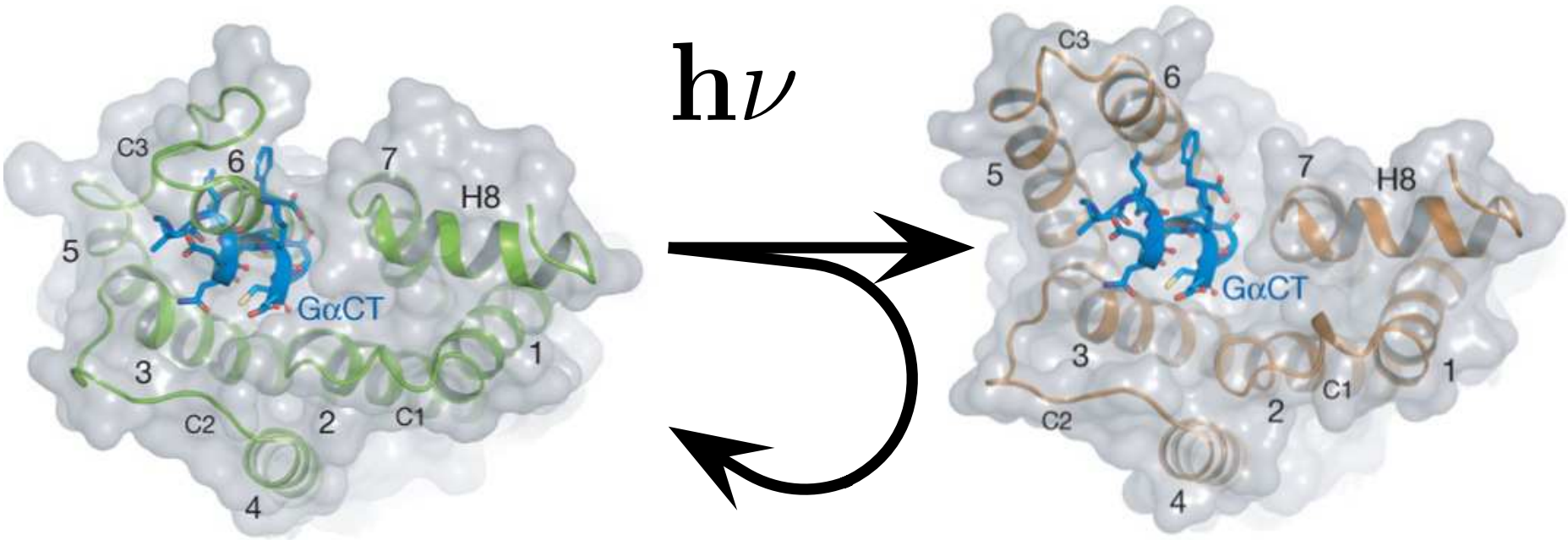

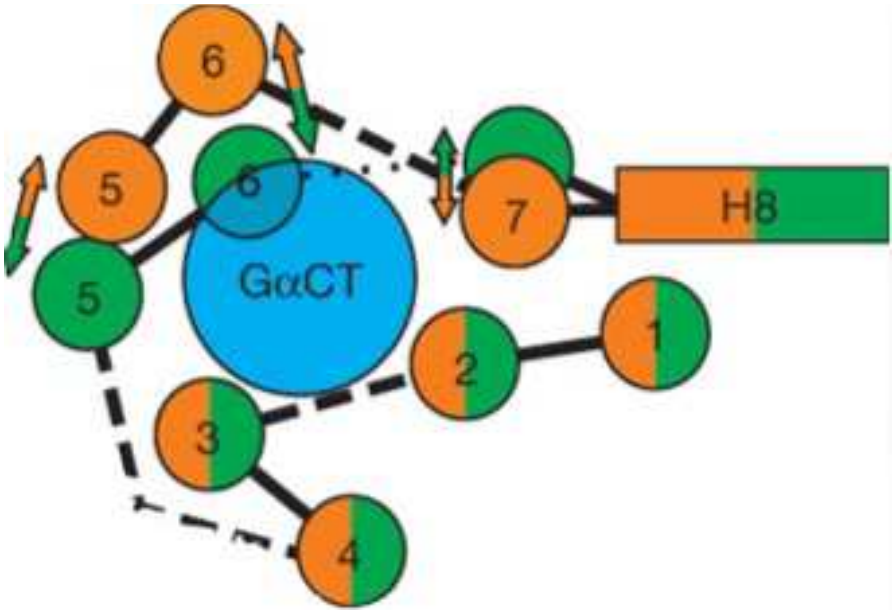

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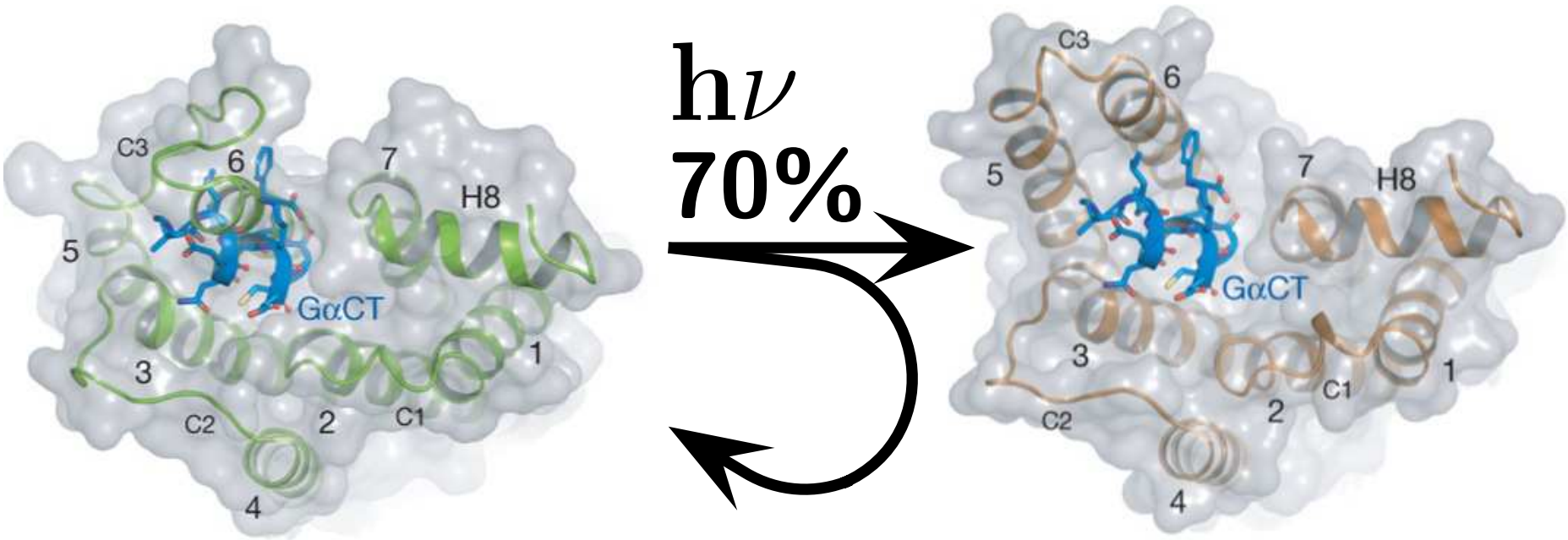

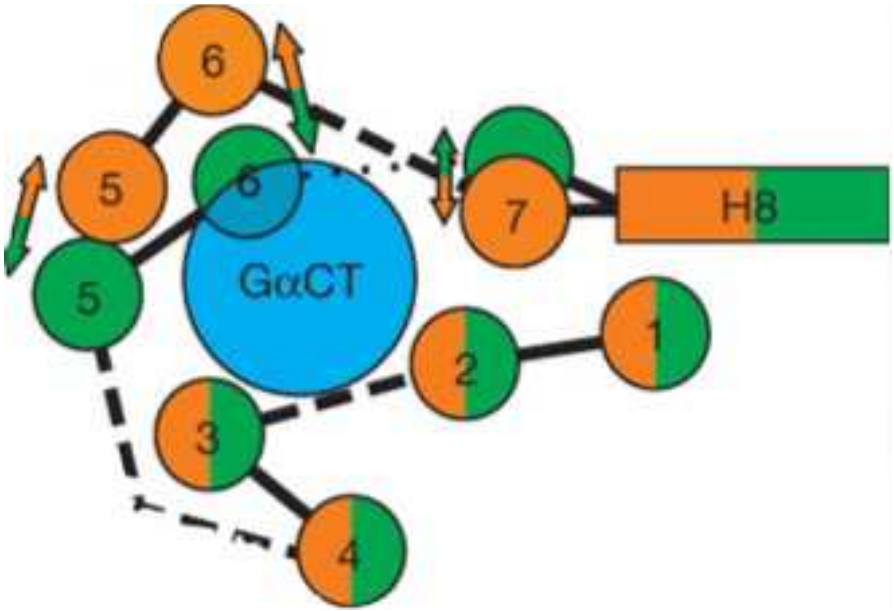

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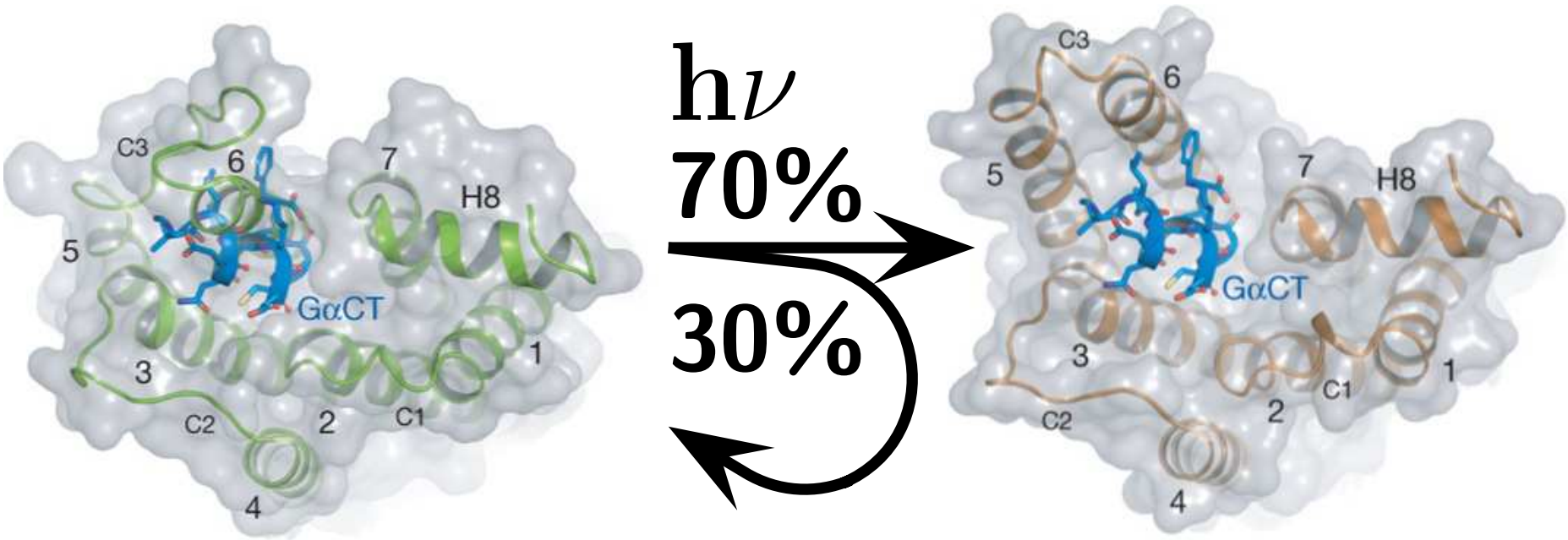

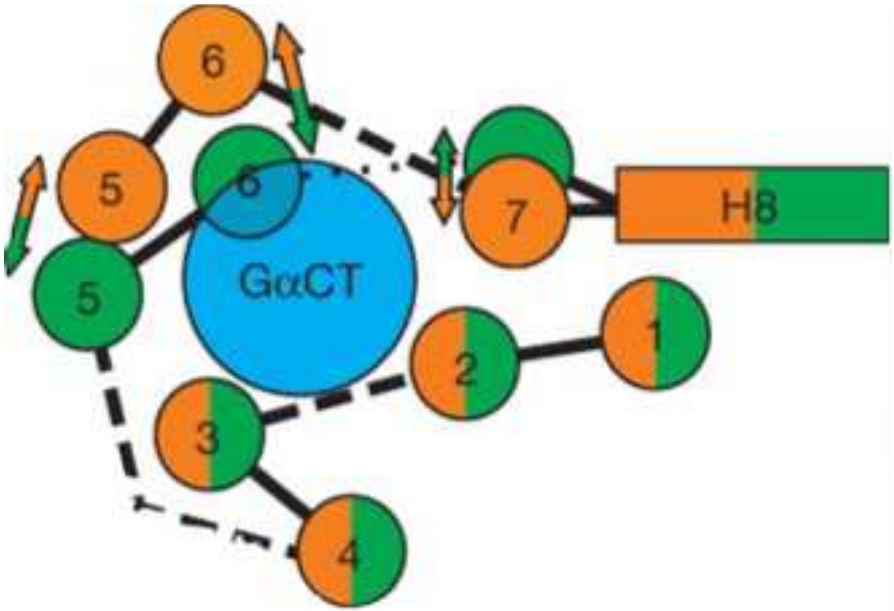

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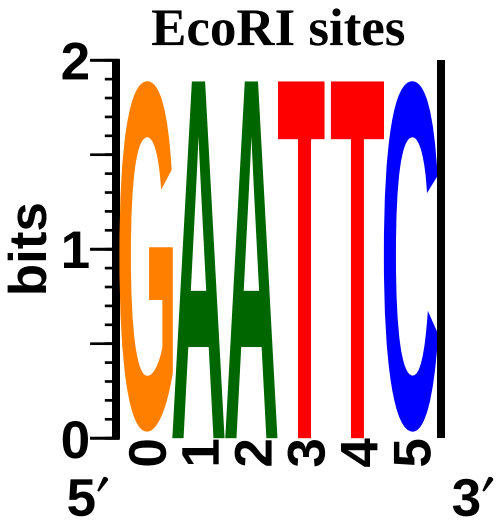
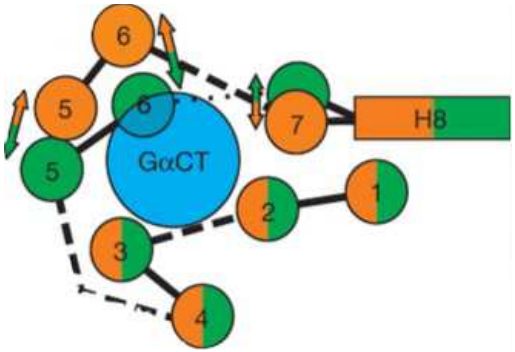
Why are molecular machines 70% efficient?

70% efficiency appears widely in biology:





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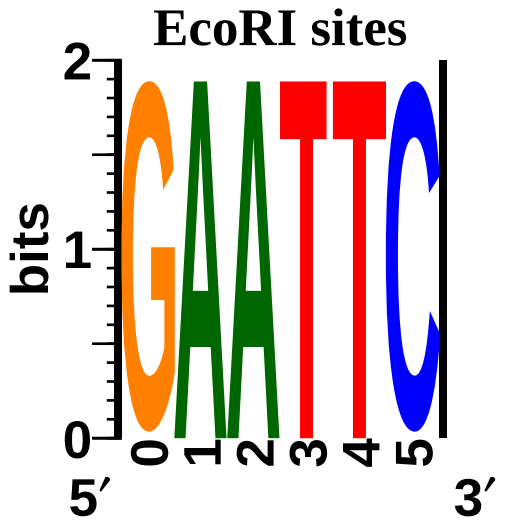
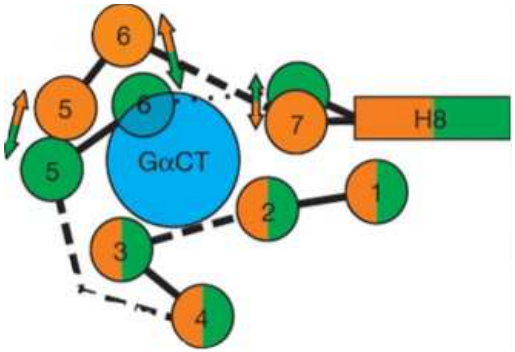
- **DNA - protein binding**





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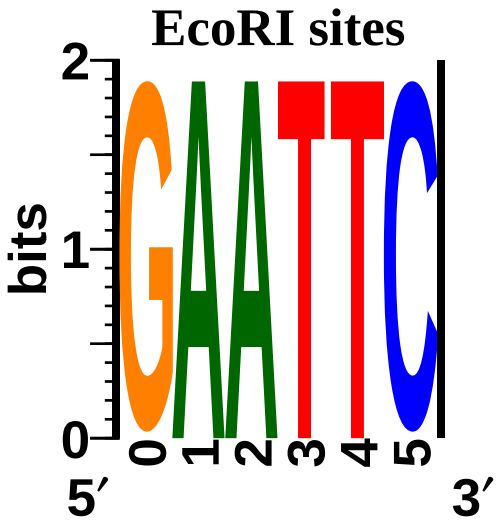

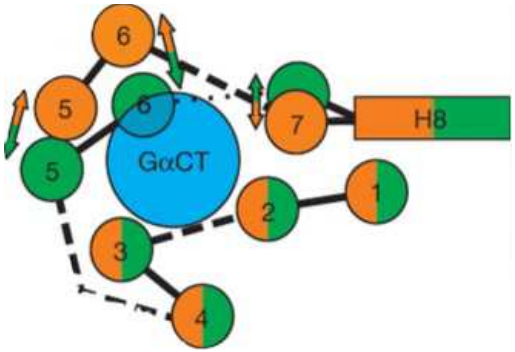

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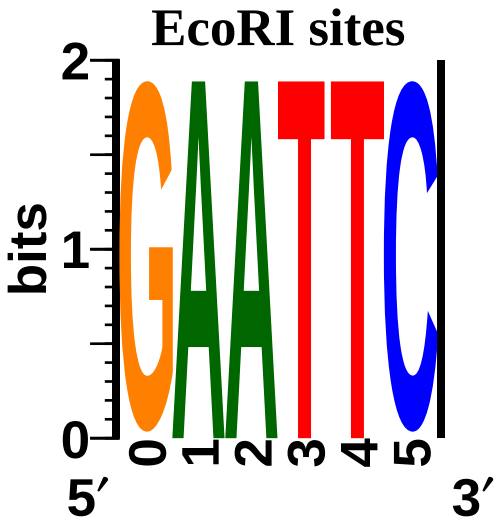

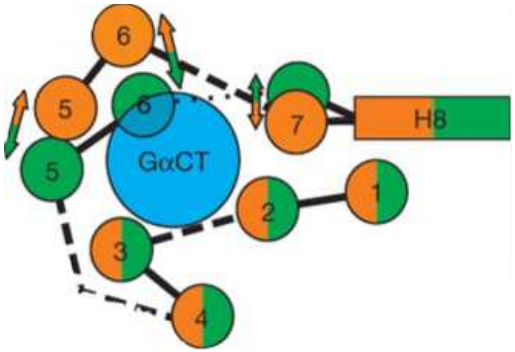

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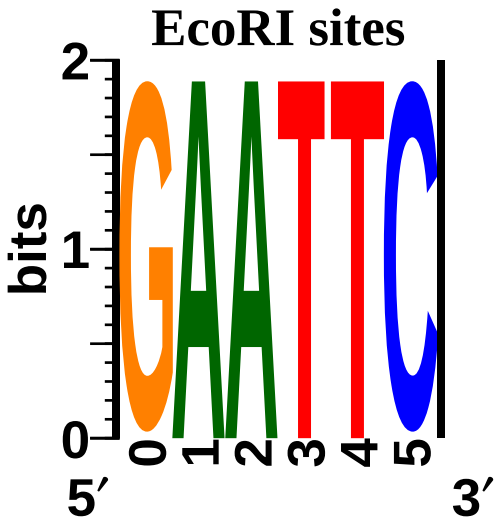

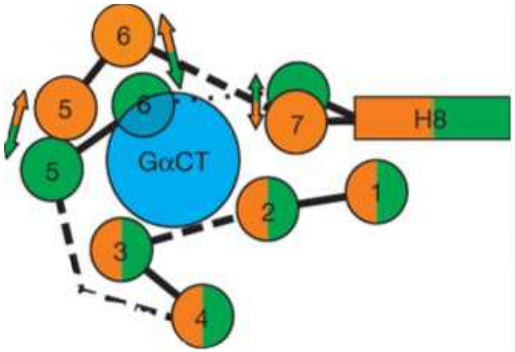

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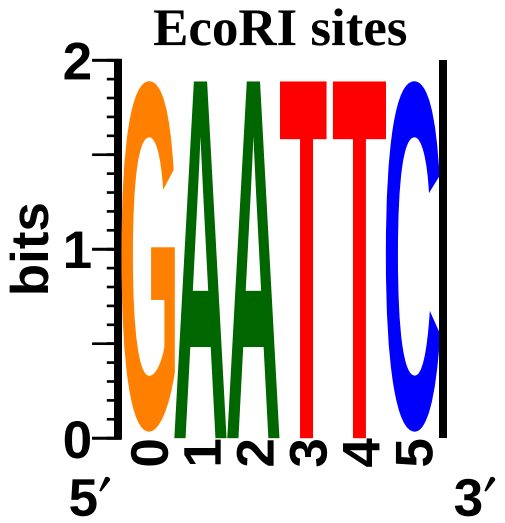
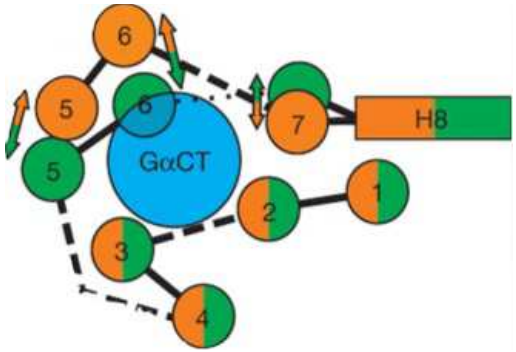
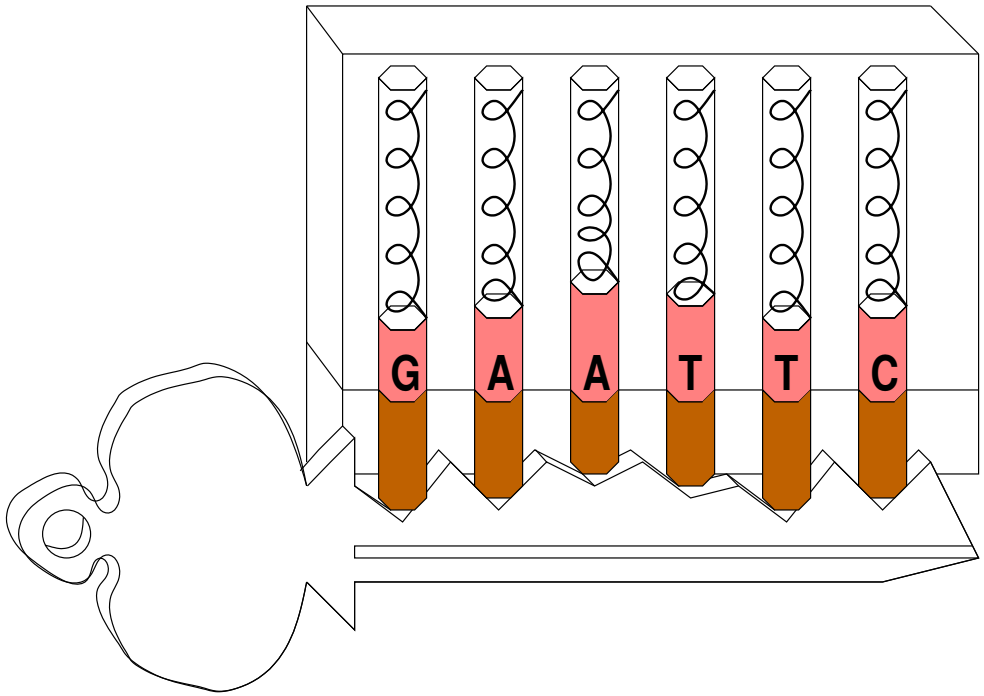


Why 70% efficiency?



Lock and Key

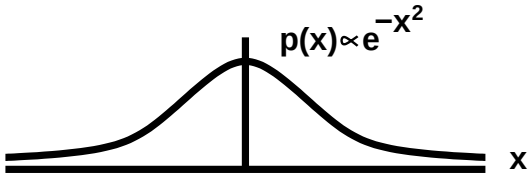


Like a key in a lock
which has many independent pins,
it takes many numbers
to describe the vibrational state
of a molecular machine

Gaussians

- Pin motion x has a Gaussian distribution:

$$p(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$$



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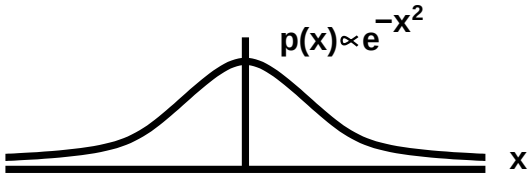

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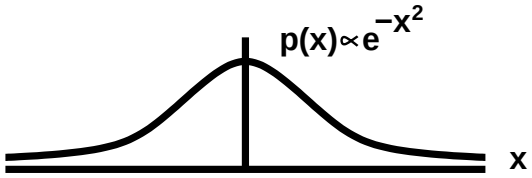
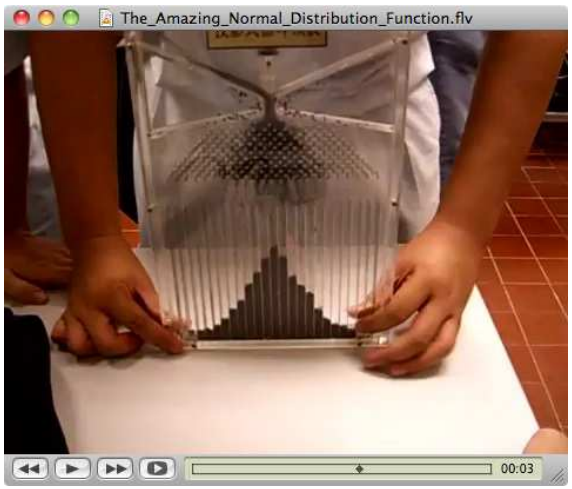
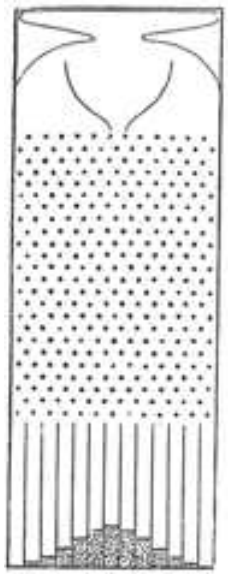


μ = mean, σ = standard deviation

- Gaussian distributions are generated by the sum of many small random variables
- Drunkard's walk: Galton's quincunx device!





http://www.youtube.com/watch?v=xDIyAOBa_yU

Two Gaussians

$$p(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(x-\mu)^2}{2\sigma^2}} \tag{1}$$

$$p(y) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(y-\mu)^2}{2\sigma^2}} \tag{2}$$

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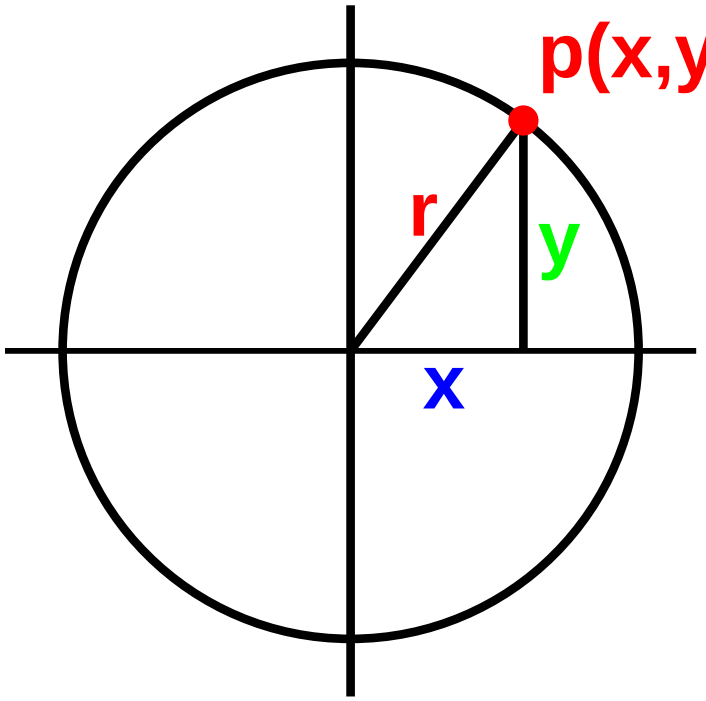

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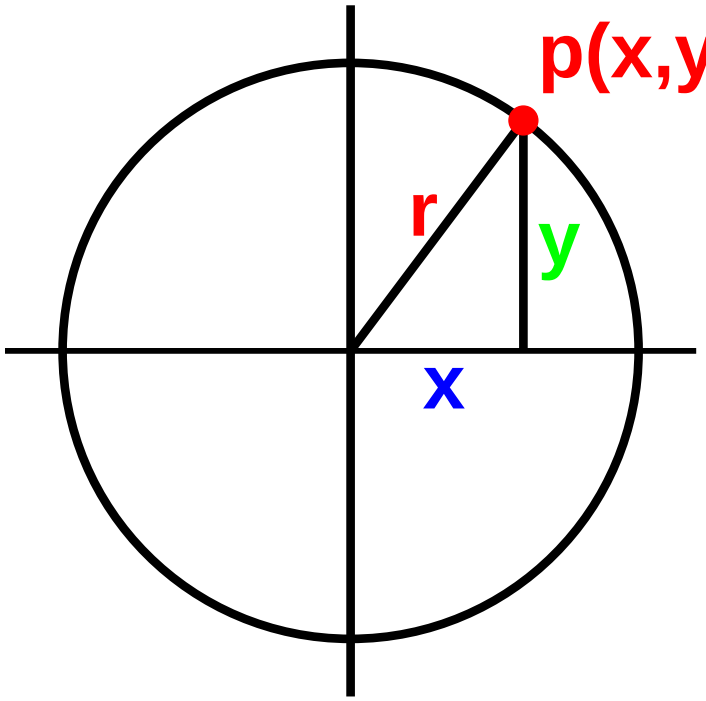

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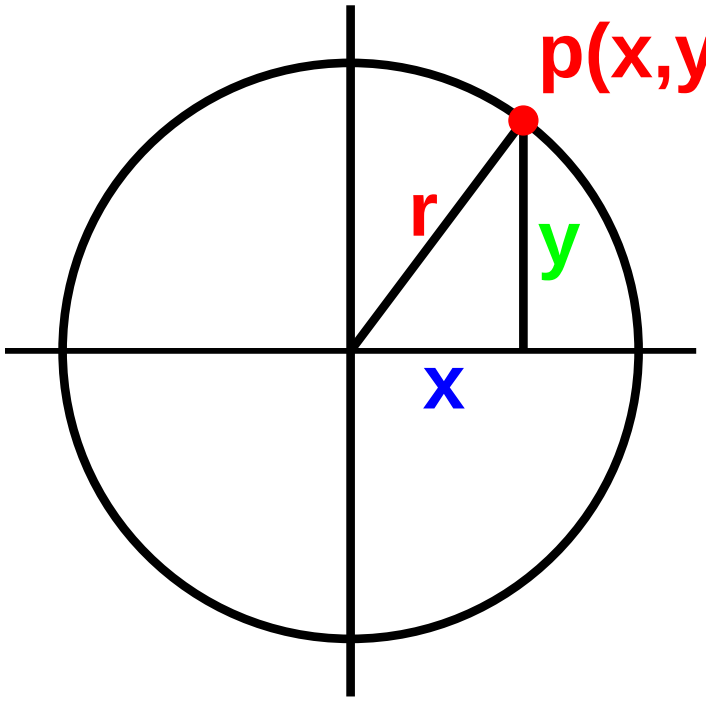

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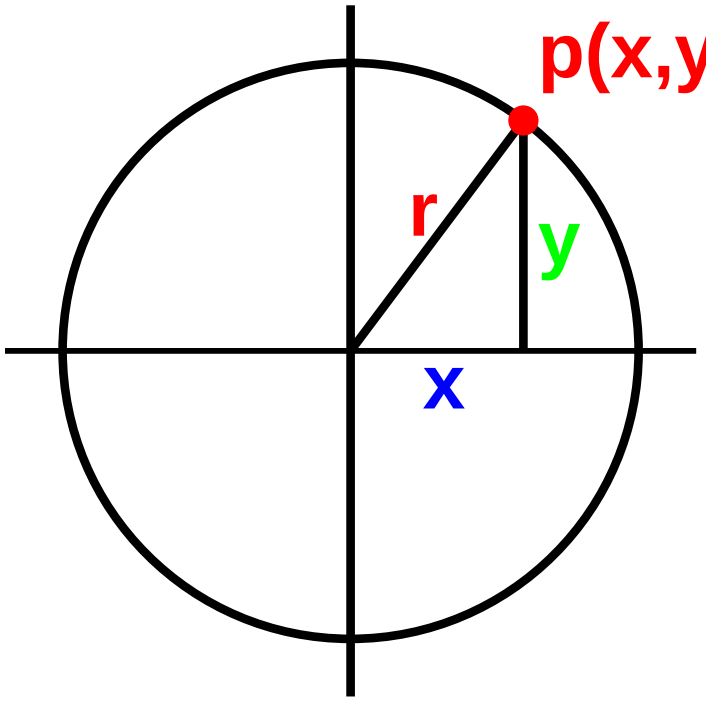

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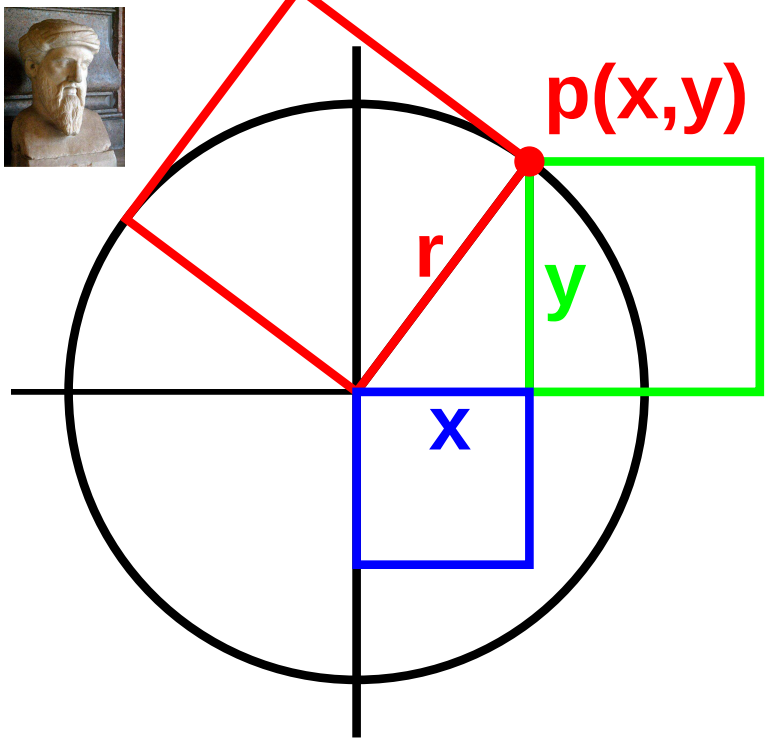

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credit: http://en.wikipedia.org/wiki/Pythagoras

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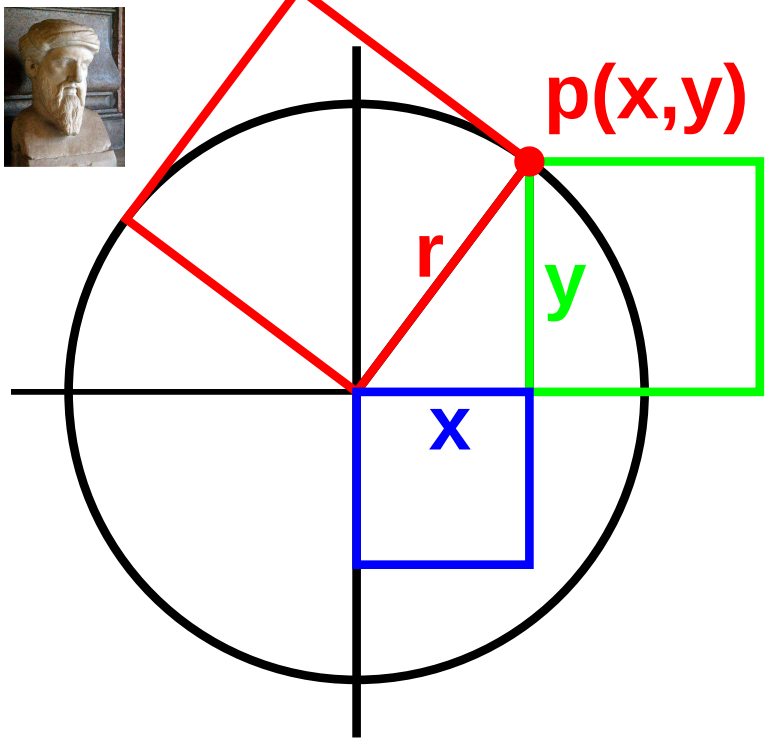

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If $p(x,y)$ is a constant, then r is a constant.

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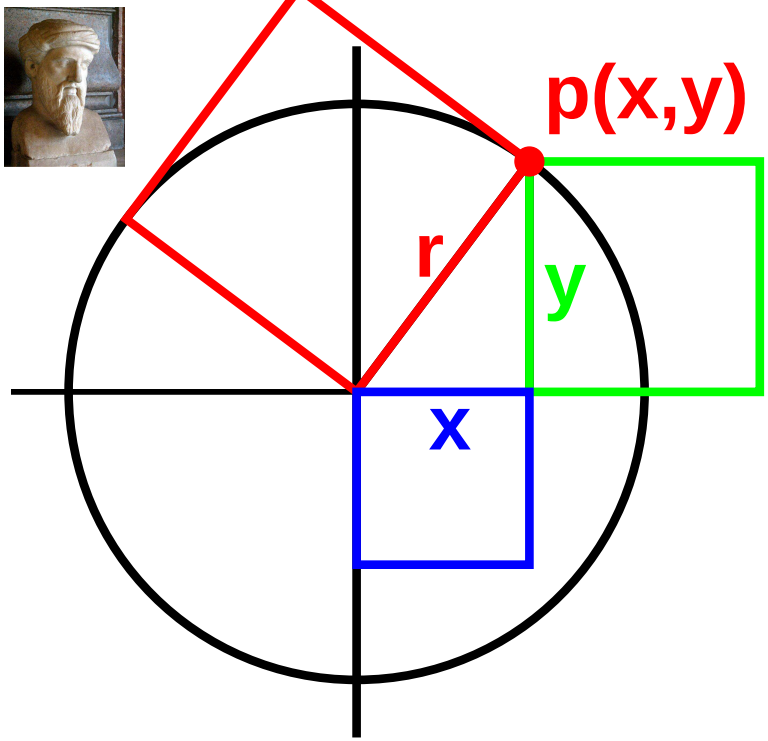

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Circular distribution!

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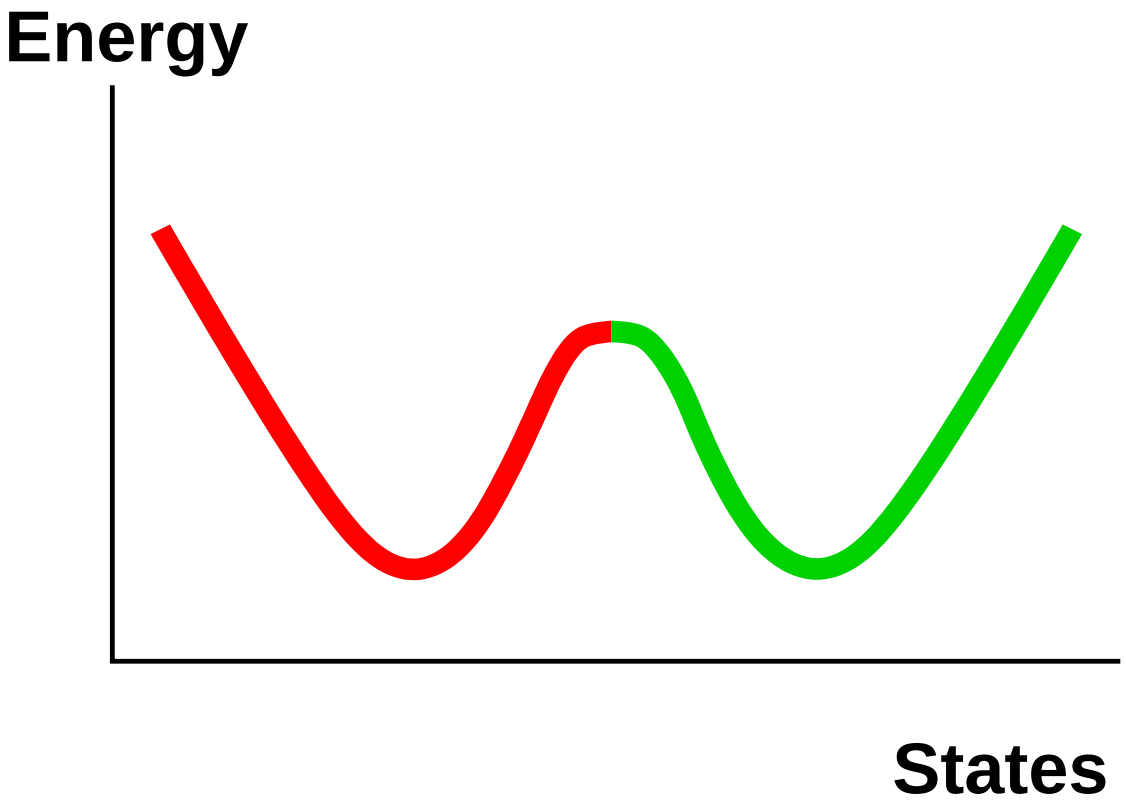
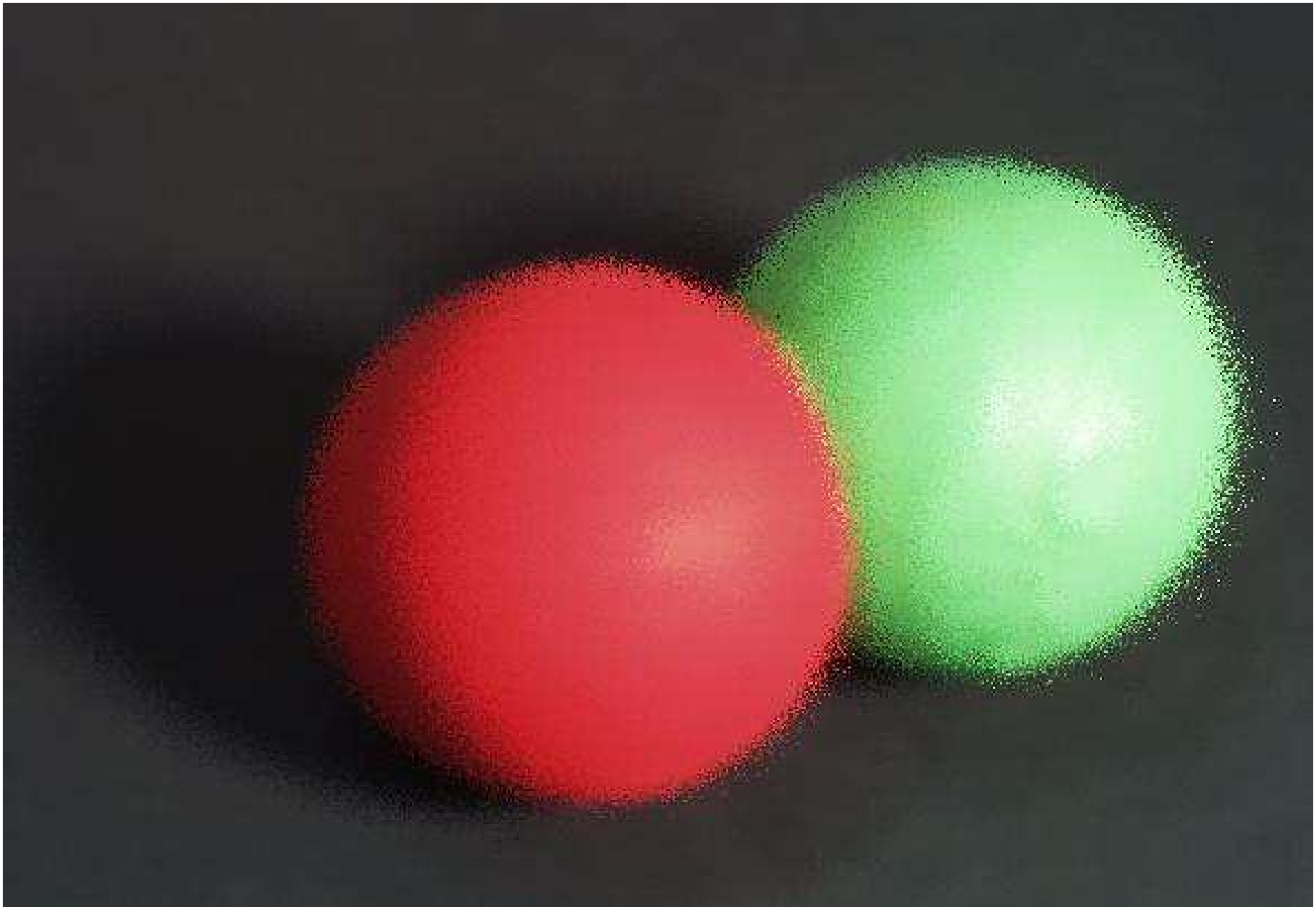
1 Dimension



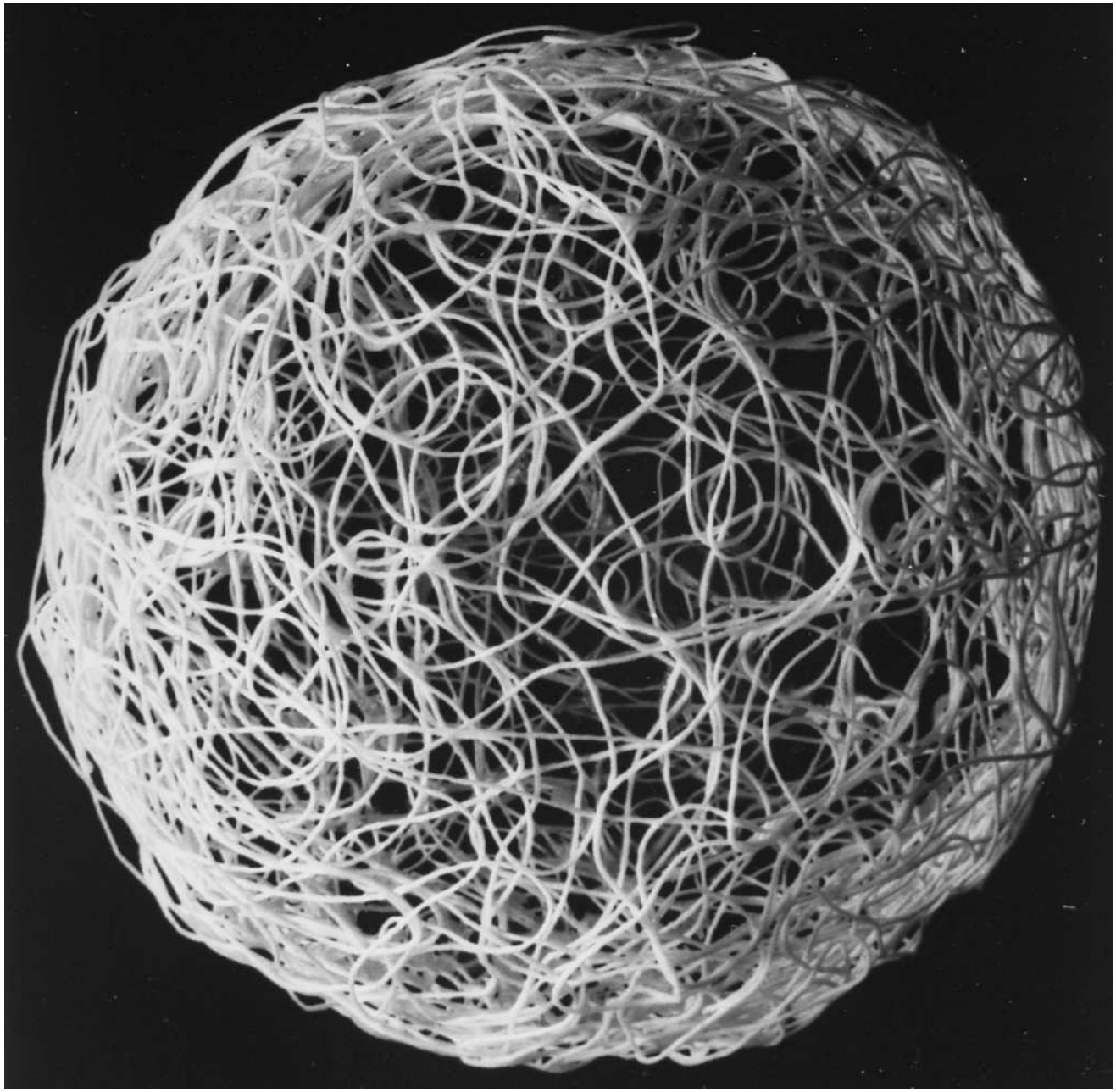
1 dimension is too simple!

Bowles in 2 Dimensions

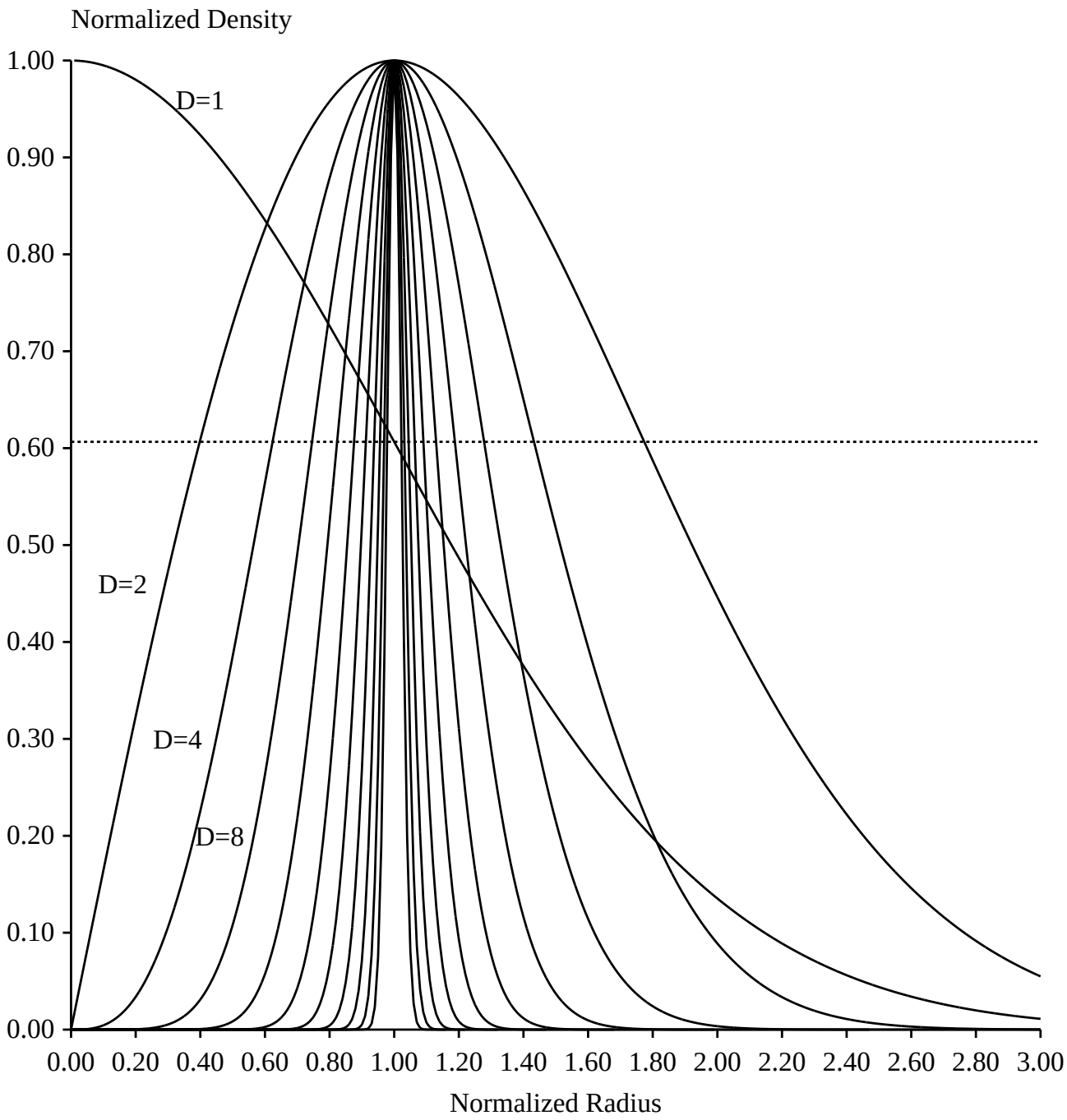
Spheres in 3 Dimensions



N Dimensional Sphere



Spheres tighten in high dimensions

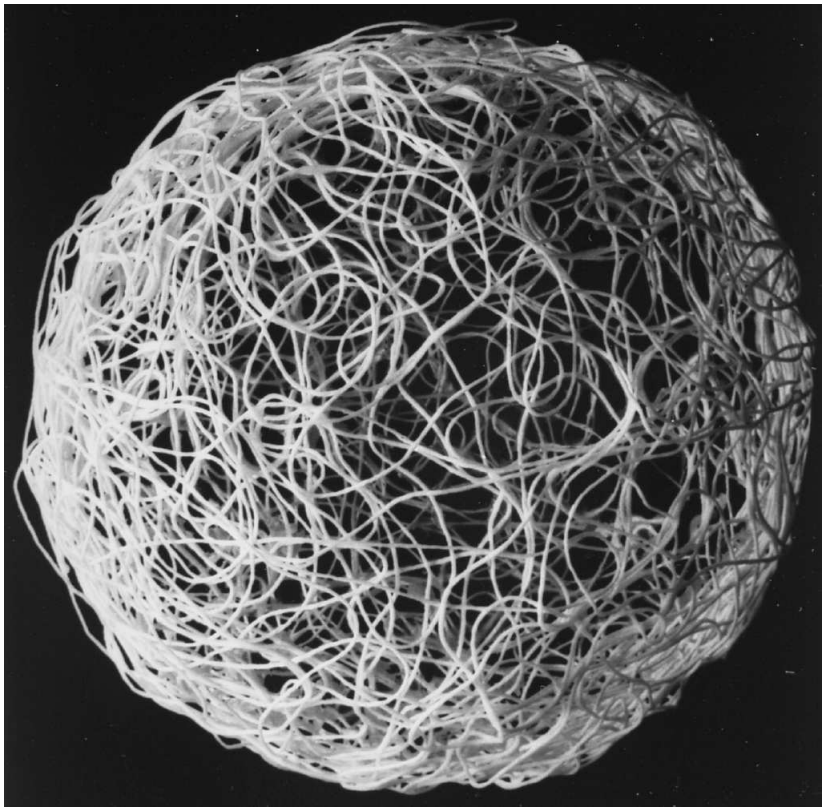


Good Sphere Packing

Good packing of spheres
gives a molecule
the capacity
to make selections efficiently

N Dimensional Sphere Separation

Degenerate Sphere



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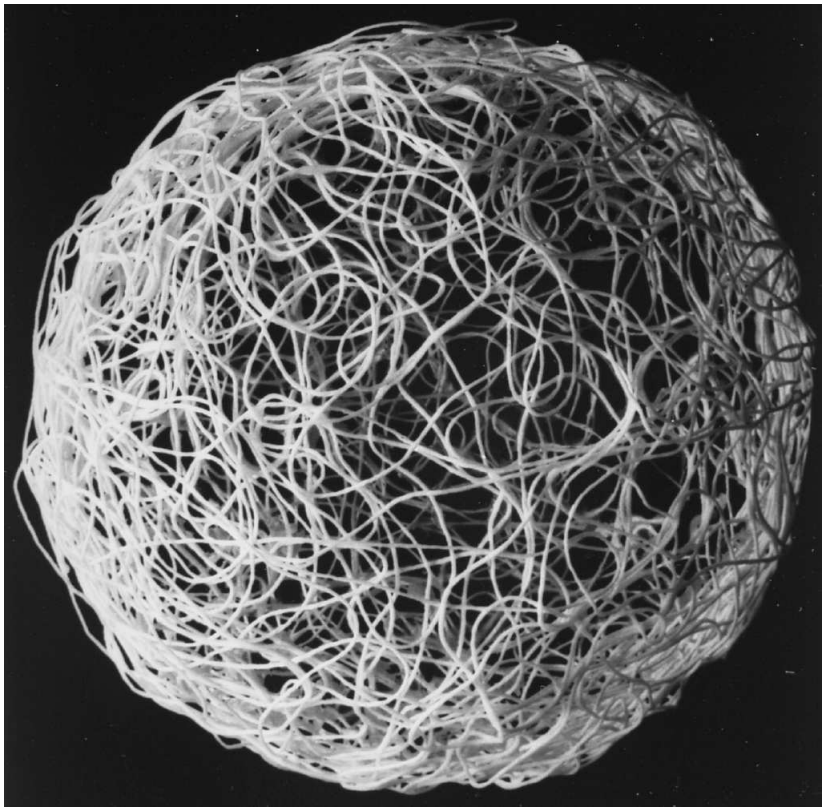
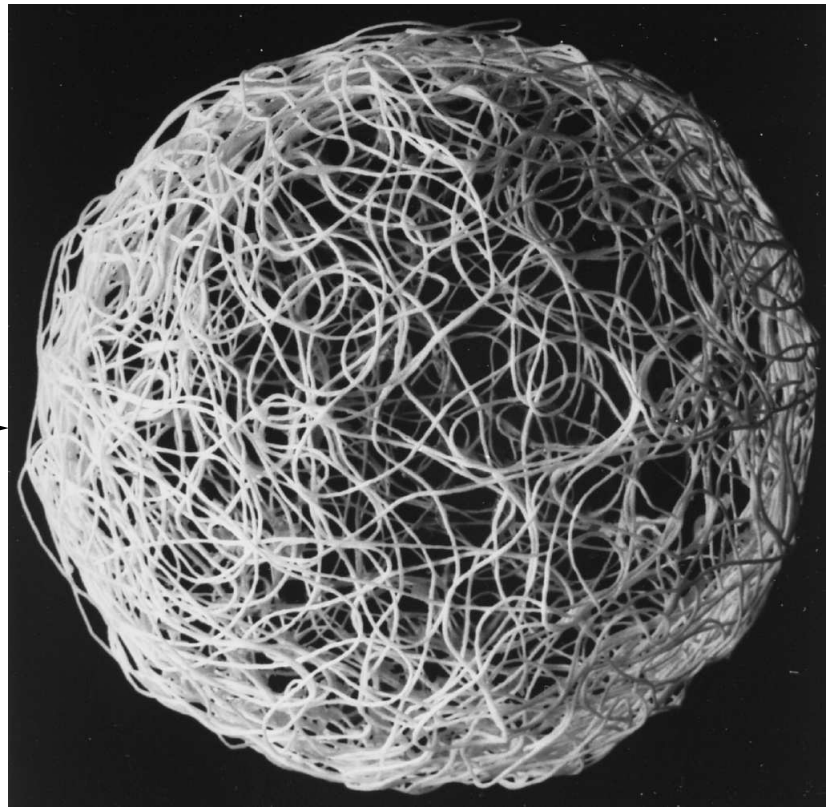
Degenerate Sphere



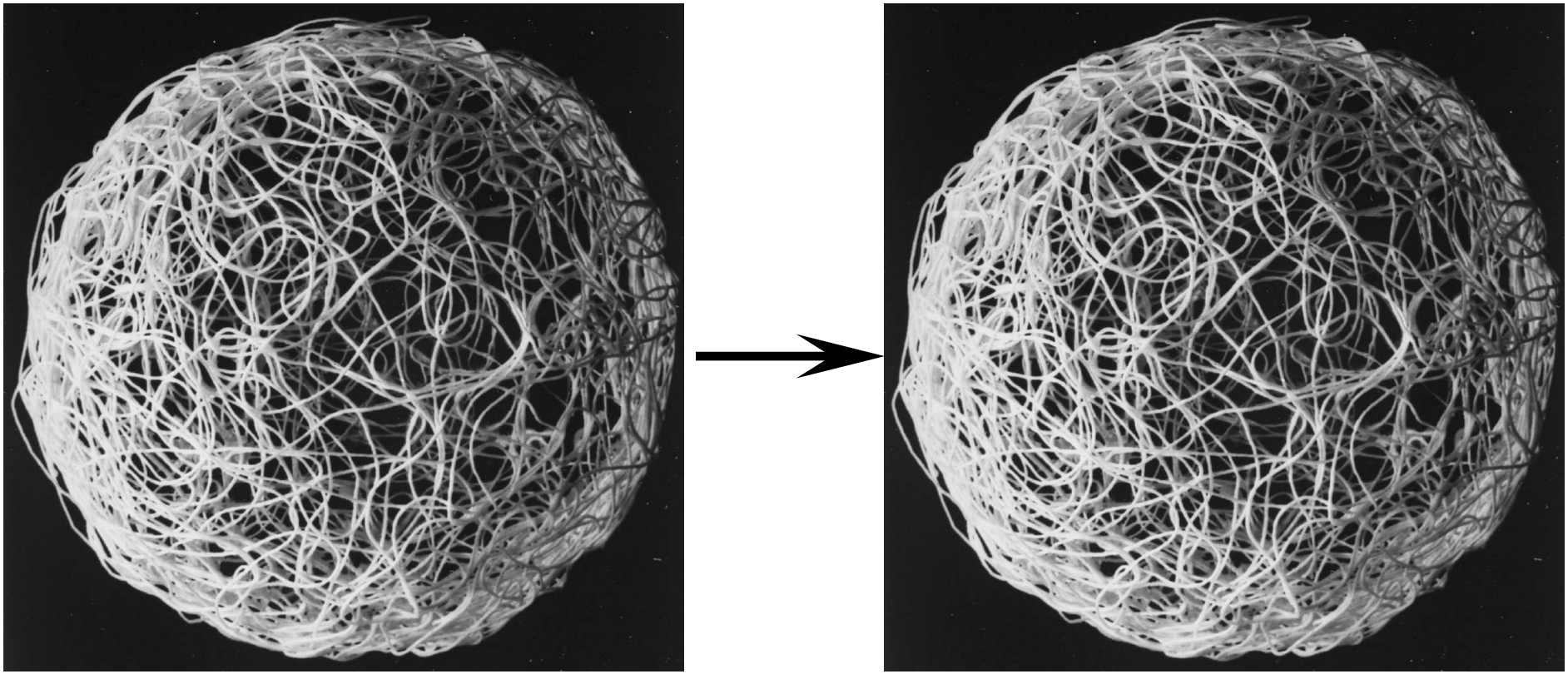
Forward Sphere



N Dimensional Sphere Separation

Degenerate Sphere

Forward Sphere

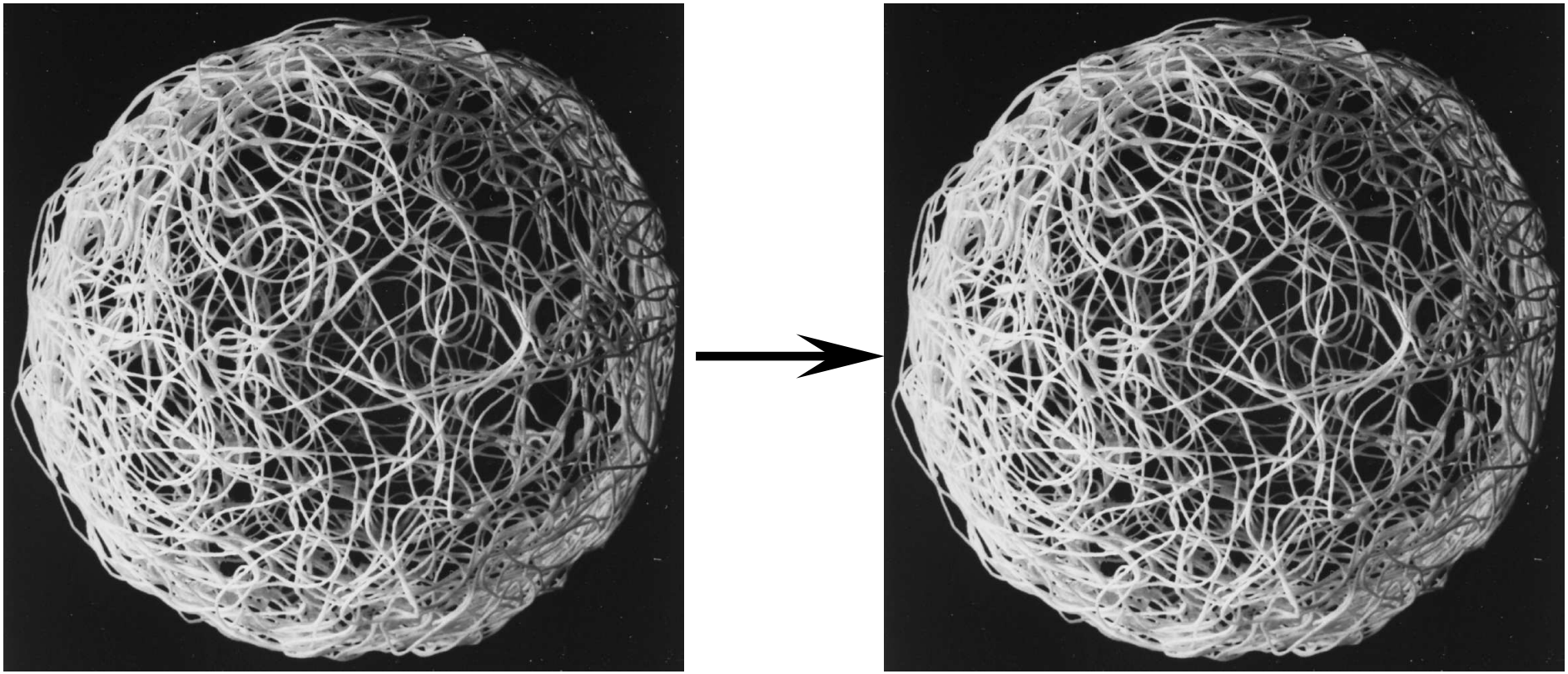


$\sqrt{\text{Noise}}$

N Dimensional Sphere Separation

Degenerate Sphere

Forward Sphere



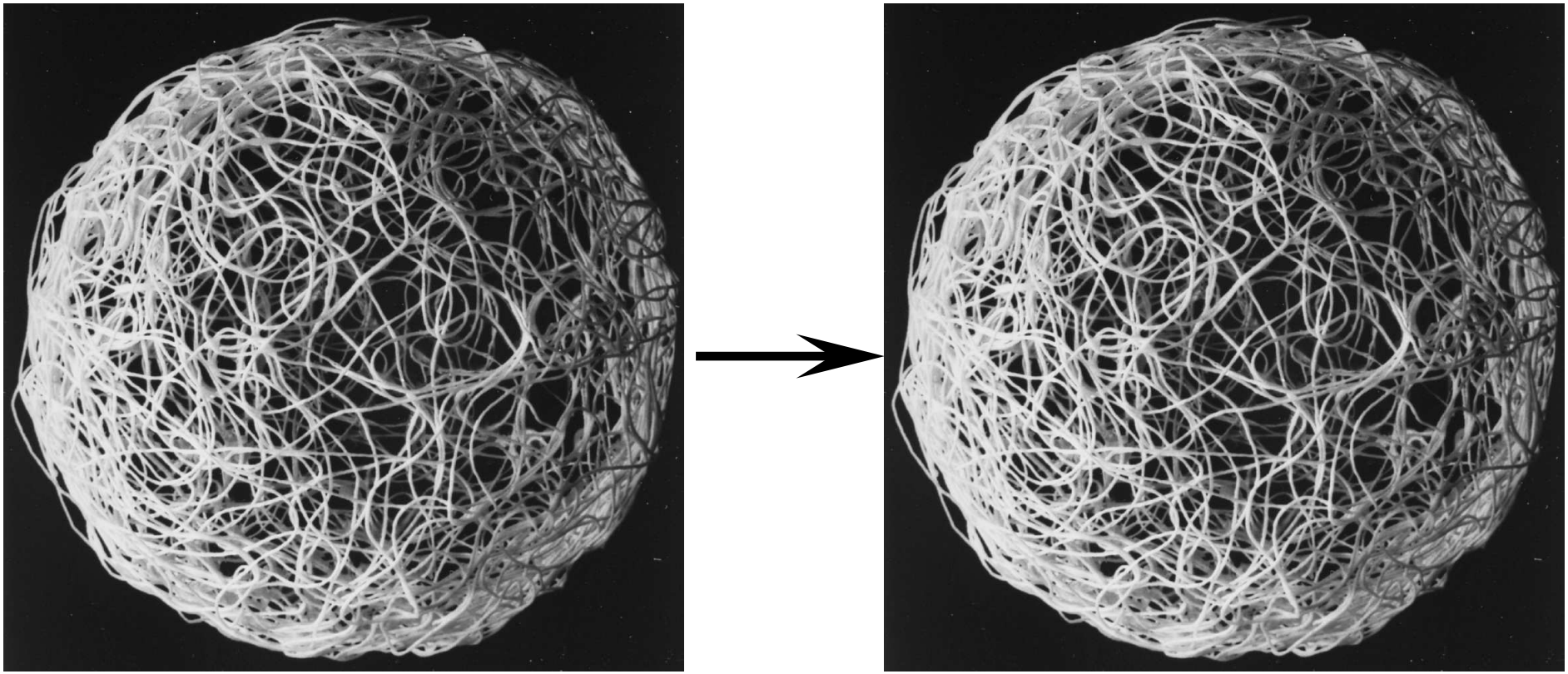
$\sqrt{\text{Noise}}$

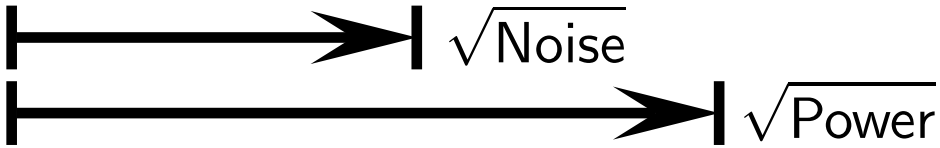
$\sqrt{\text{Power}}$

N Dimensional Sphere Separation

Degenerate Sphere

Forward Sphere

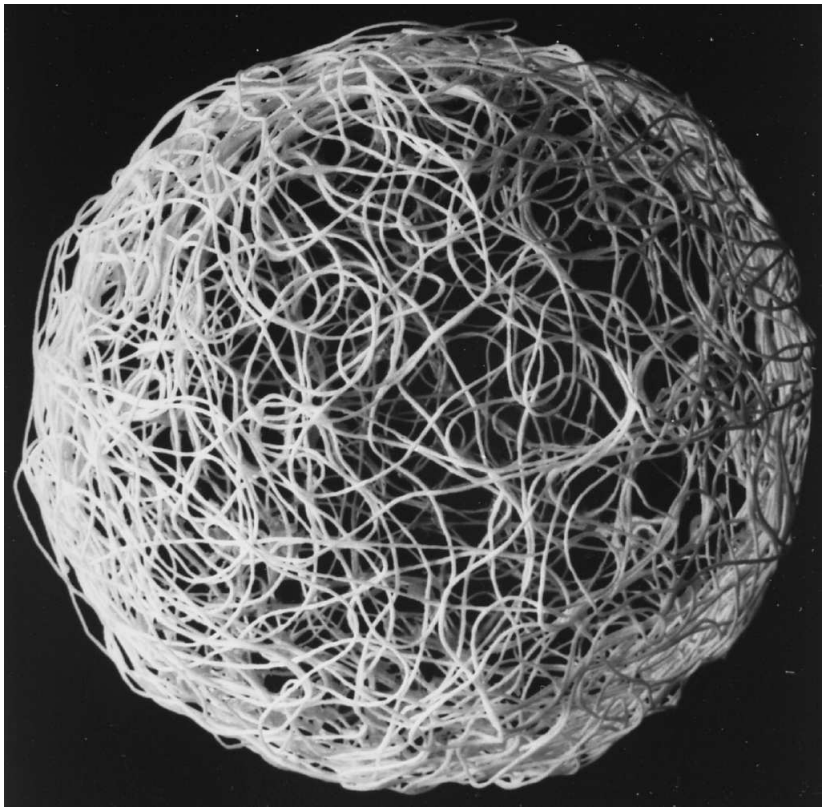




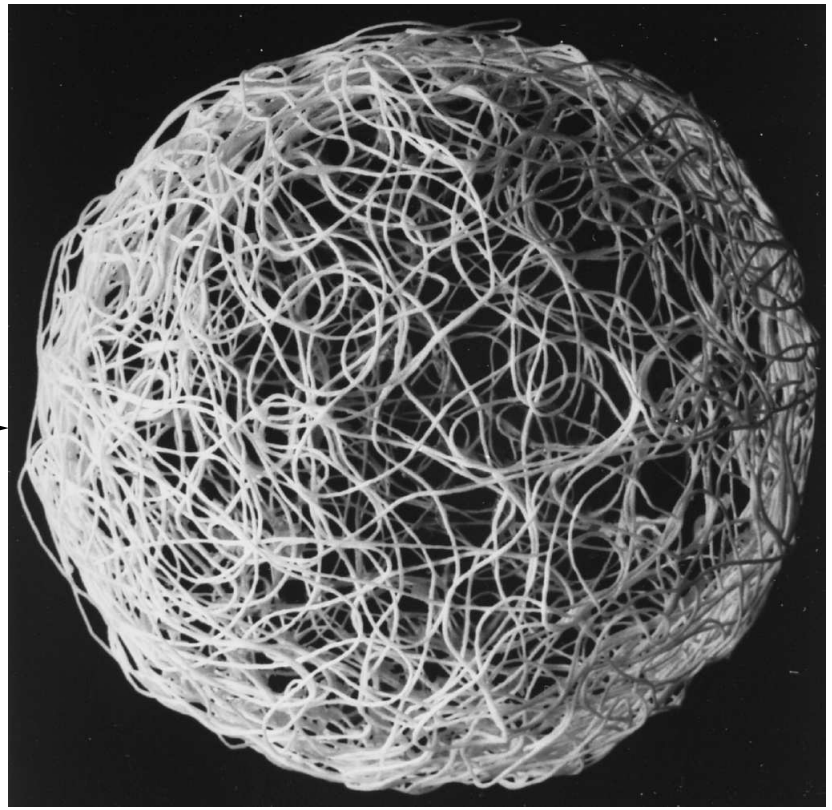
Energy dissipated to escape the Degenerate Sphere must exceed the Noise

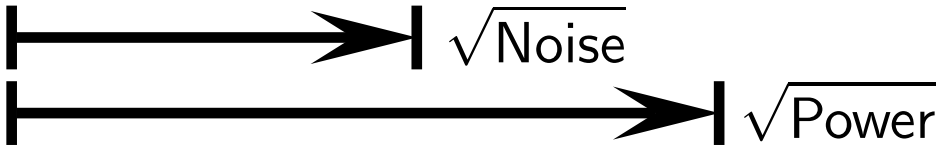
N Dimensional Sphere Separation

Degenerate Sphere



Forward Sphere





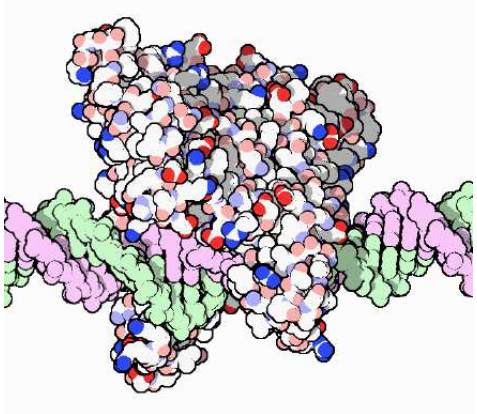
Energy dissipated to escape the Degenerate Sphere must exceed the Noise

$$\sqrt{\text{Power}} > \sqrt{\text{Noise}}$$

Theoretical Isothermal Efficiency

- For molecular states of molecules with d_{space} 'parts' P_y energy is dissipated for noise N_y and

  $C_y = d_{space} \log_2(P_y/N_y + 1) \leftarrow$ machine capacity



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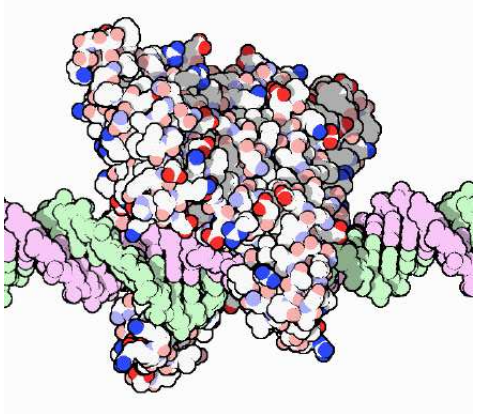
$$\epsilon_t = \frac{\ln\left(\frac{P_y}{N_y}+1\right)}{\frac{P_y}{N_y}} \leftarrow \text{molecular efficiency}$$



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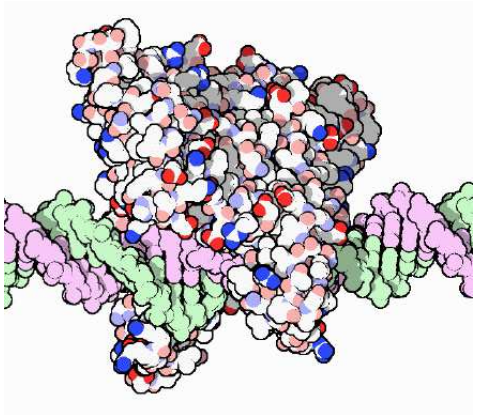
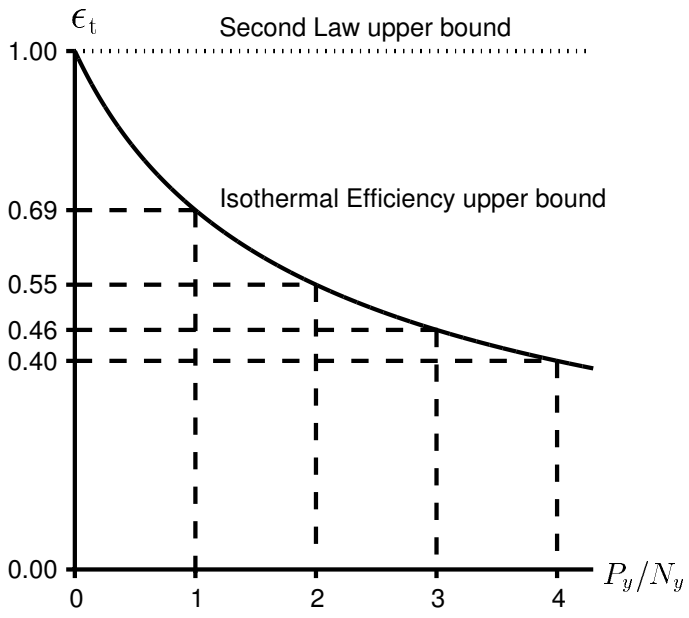
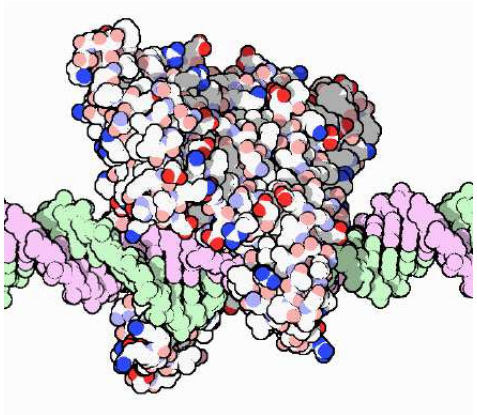




The curve is an upper bound

Theoretical Isothermal Efficiency



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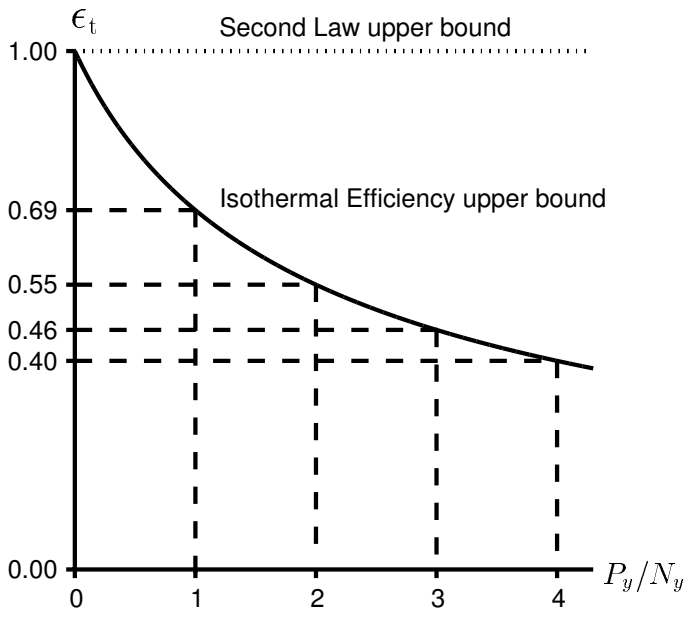
$$C_y = d_{space} \log_2(P_y/N_y + 1) \leftarrow \text{machine capacity}$$

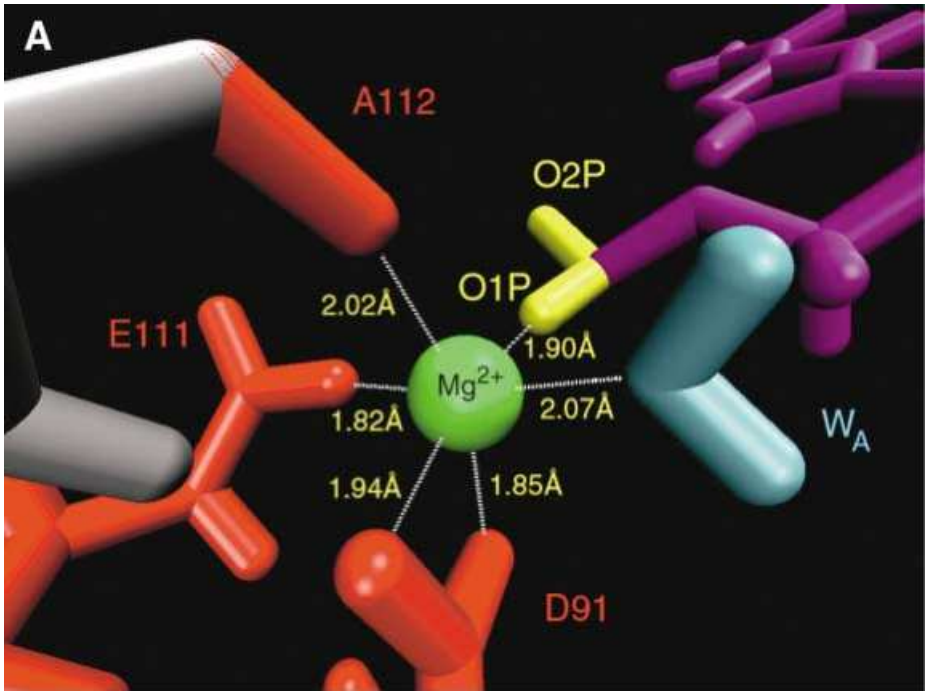
$$\epsilon_t = \frac{\ln\left(\frac{P_y}{N_y}+1\right)}{\frac{P_y}{N_y}} \leftarrow \text{molecular efficiency}$$



The curve is an upper bound

- If $P_y/N_y = 1$ the efficiency is 70%!

Magnesium bound by EcoRI



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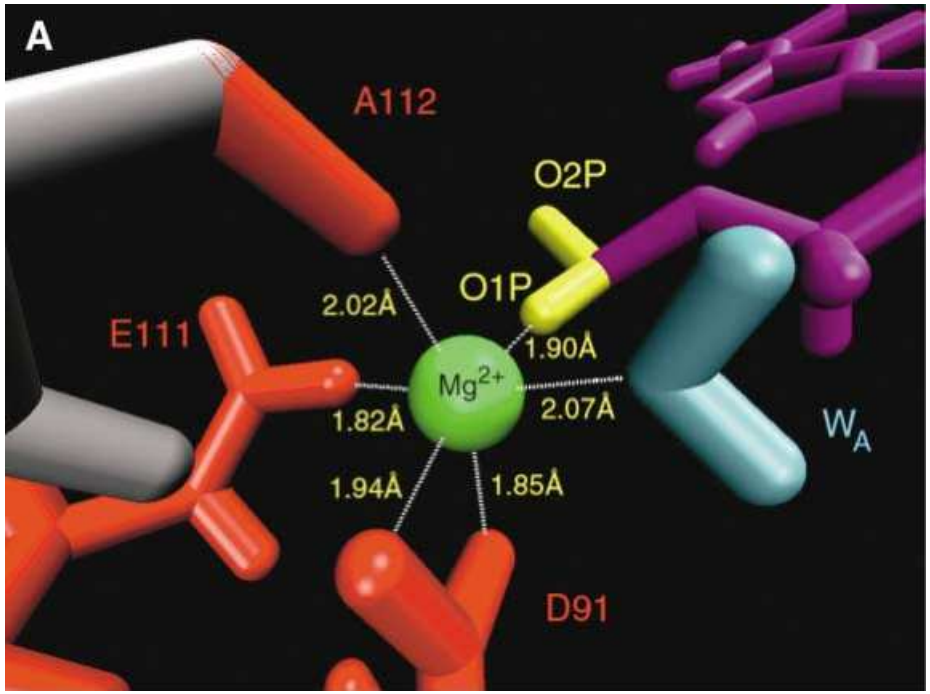

- Mg^{2+} bound to EcoRI has 6 coordination bonds

Kurpiewski *et. al* Structure 12: 1775-1788, 2004

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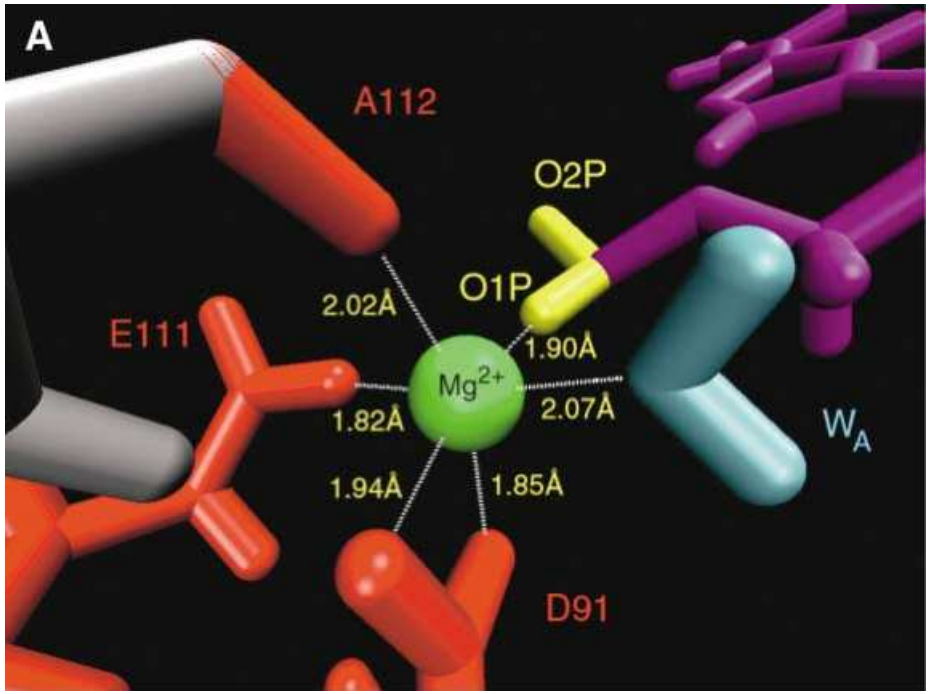

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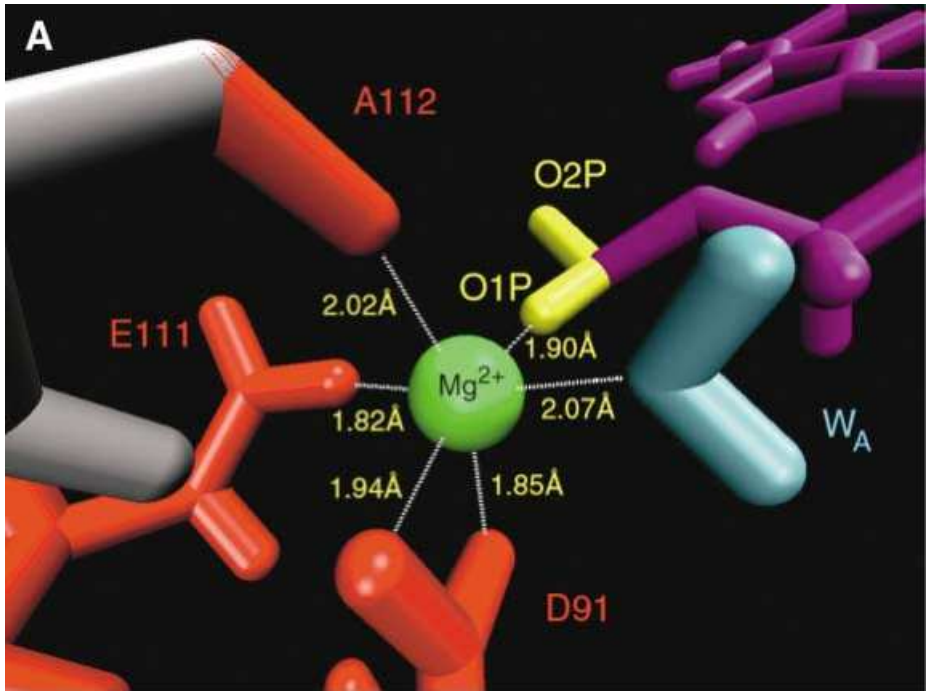

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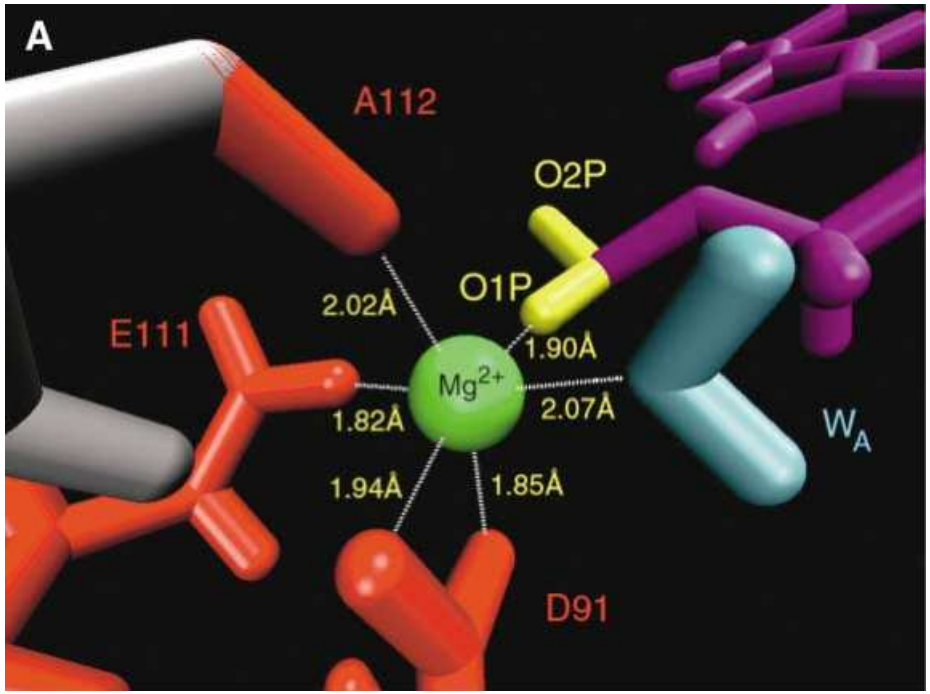

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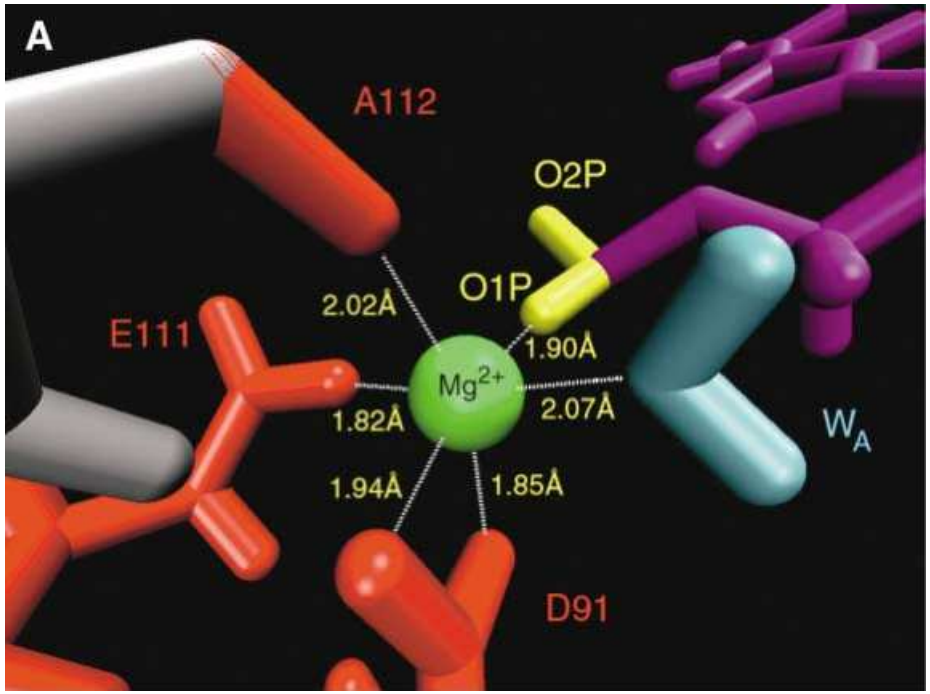

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Kurpiewski *et. al* Structure 12: 1775-1788, 2004
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Ecosystem Evenness

- Even ecosystem:
  all species equally represented

  $\boxed{\text{evenness} \approx 100\%}$

http://en.wikipedia.org/wiki/Noah%27s_Ark, http://en.wikipedia.org/wiki/Maize

Ecosystem Evenness

- Even ecosystem:
  all species equally represented
  $\boxed{\text{evenness} \approx 100\%}$

- Uneven ecosystem:
  one species dominates
  $\boxed{\text{evenness} \approx 0\%}$

http://en.wikipedia.org/wiki/Noah%27s_Ark, http://en.wikipedia.org/wiki/Maize

Ecological Efficiency = 'Evenness'

Family

Images: http://en.wikipedia.org/wiki, Flea, Nuclear_family, Goldfish, Cat, Dog

Ecological Efficiency = ‘Evenness’

Family

4 humans

Ecological Efficiency = 'Evenness'

Family

4 humans

1 dog

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Ecological Efficiency = 'Evenness'

Family

4 humans

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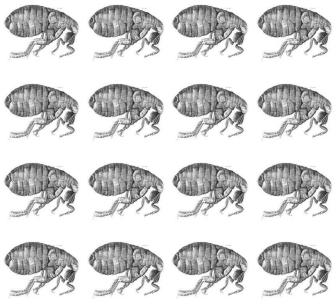
16 fleas



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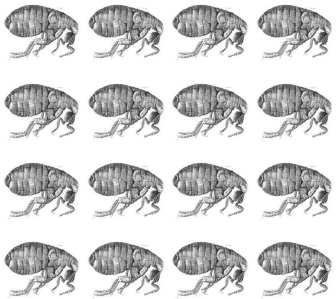

Shannon Diversity (= uncertainty) for $M = 5$ species with probabilities p_i:

$$H = -\sum_{i=1}^{M} p_i \log_2 p_i = 1.72 \quad \text{bits per species}$$

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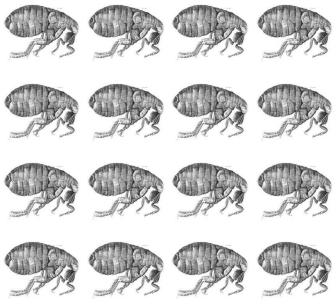

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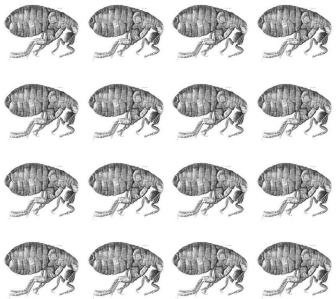

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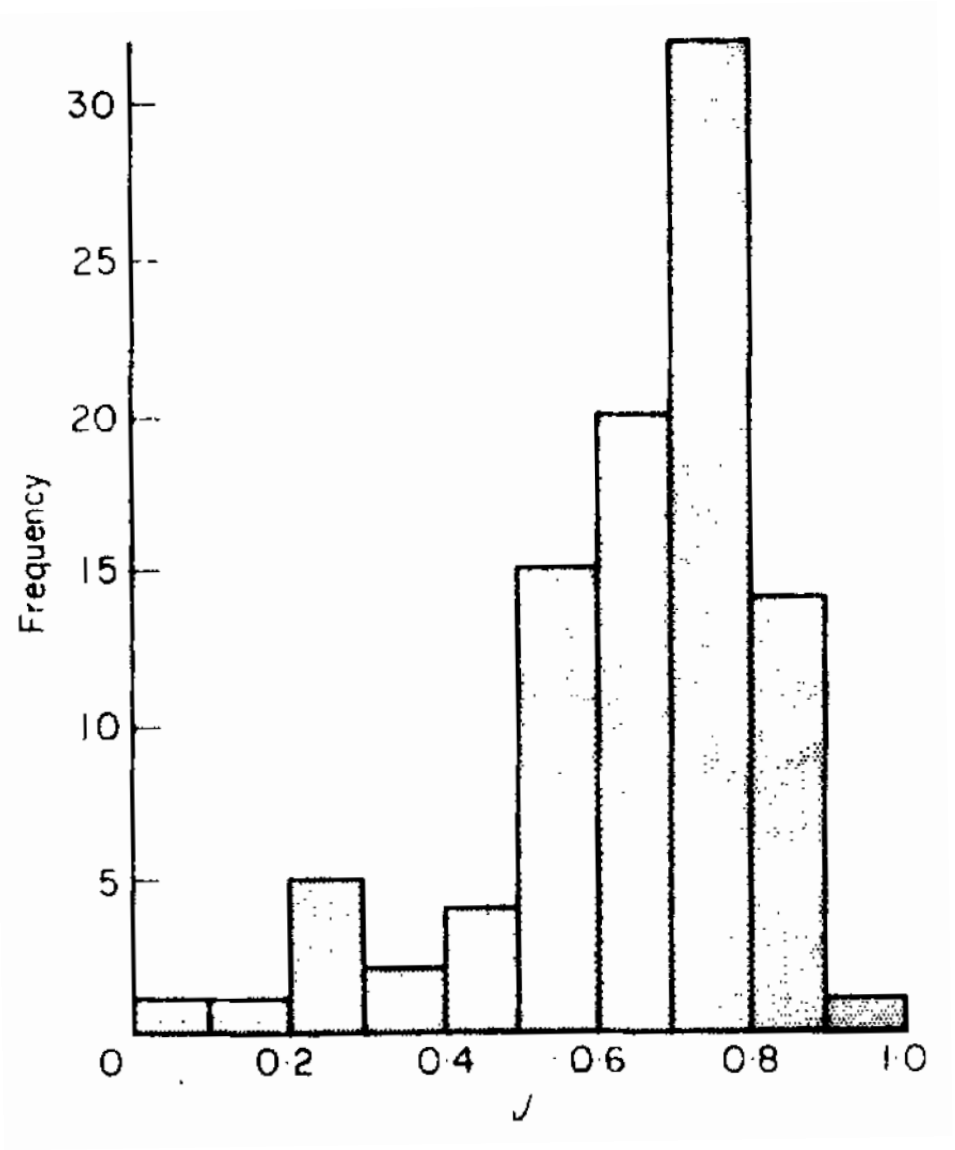
Normalized Shannon Diversity = "evenness":

$$J = H/Hmax = 0.69$$

Images: http://en.wikipedia.org/wiki, Flea, Nuclear_family, Goldfish, Cat, Dog

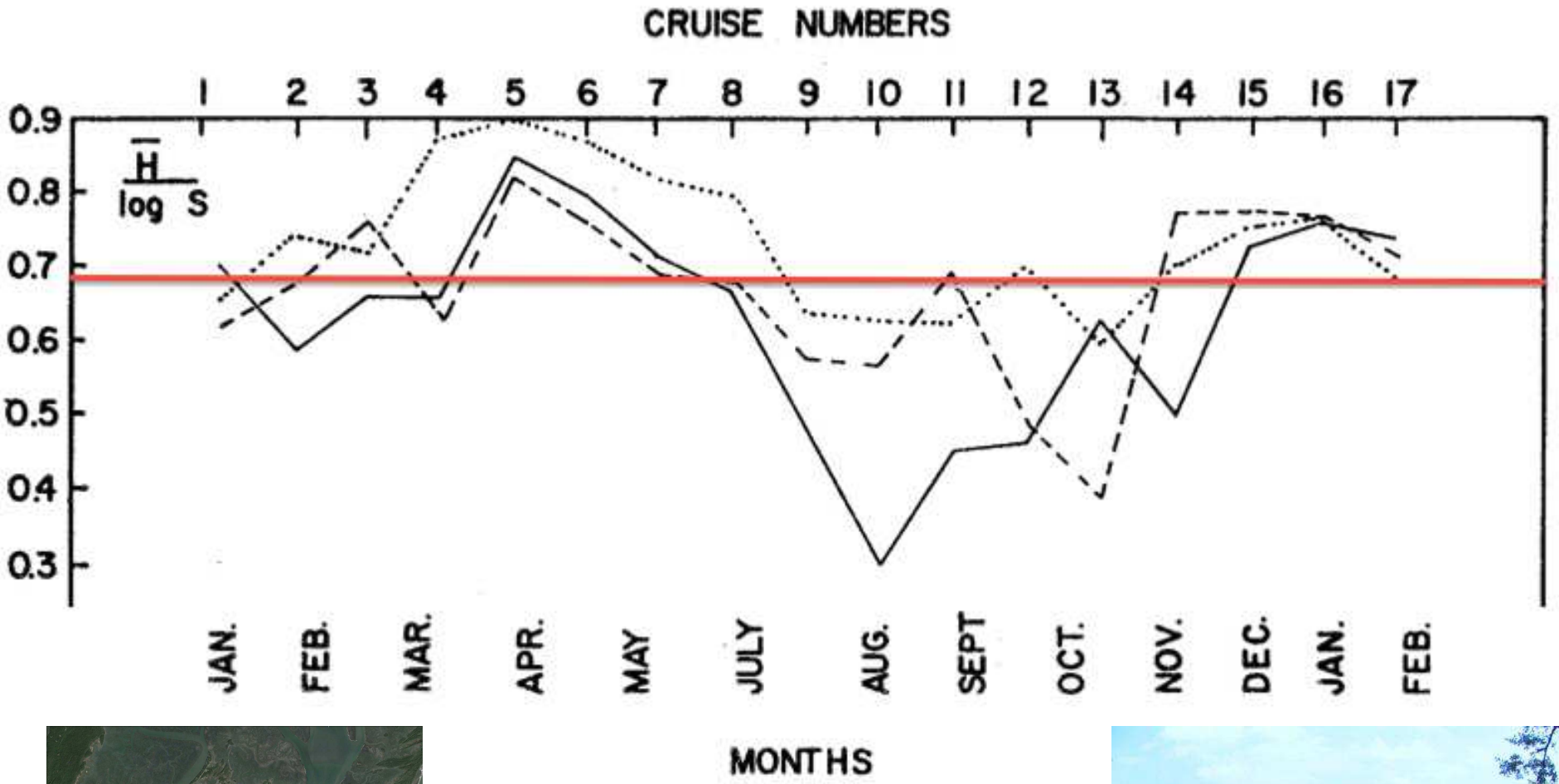
Evelyn Pielou's First Evenness Measure was ~ 0.7!



Normalized Shannon Diversity distribution of ground vegetation from Pielou 1966

Pielou1966 Theoret. Biol. (1966) 13, 131-144

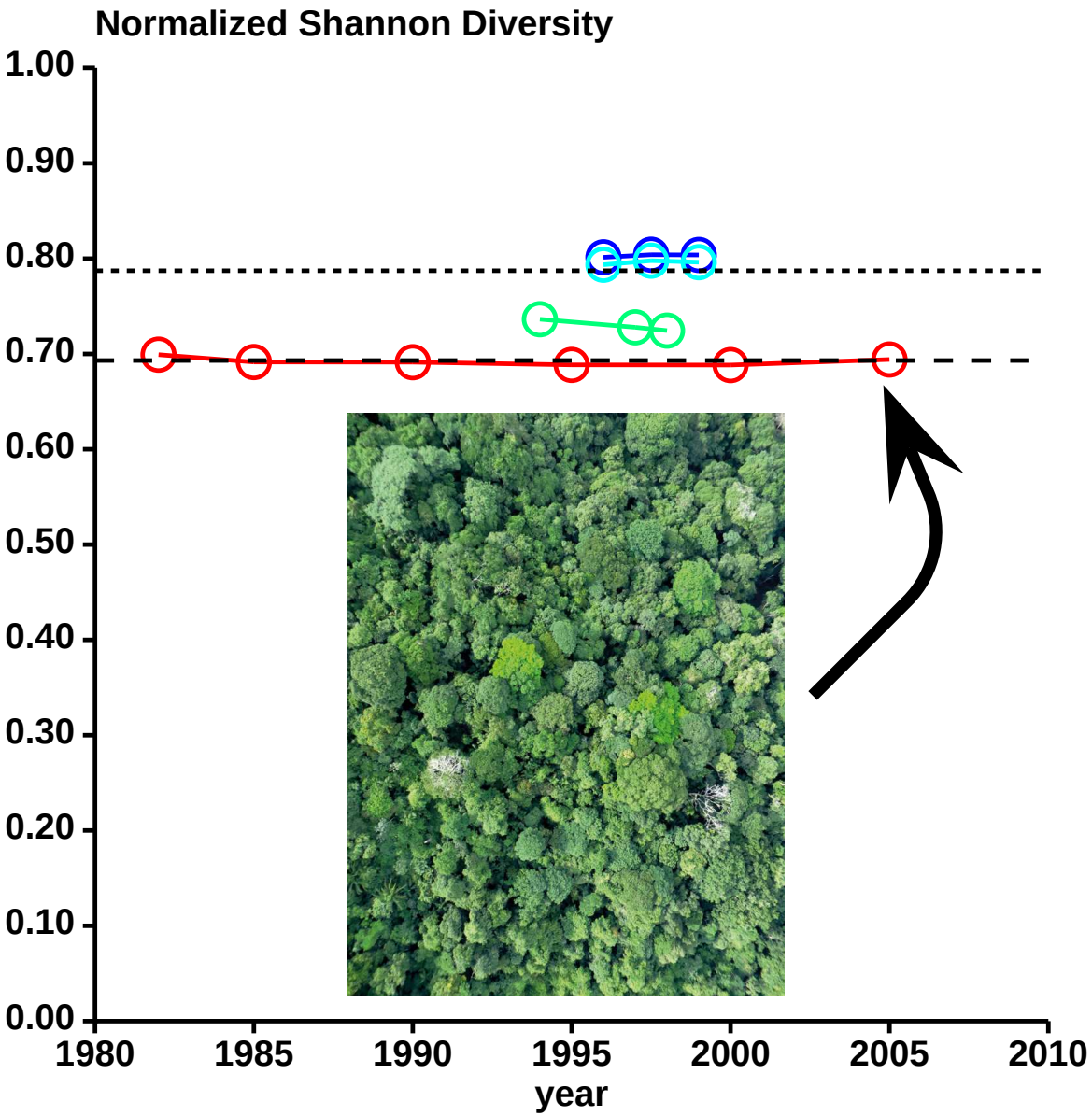
Normalized Shannon diversity of Estuarine fish



70 fish species from a Georgia salt marsh estuary, Sapelo Sound, Georgia.

Dahlberg.Odum1970 Am. Midland Nat., 83:382-392, 1970.

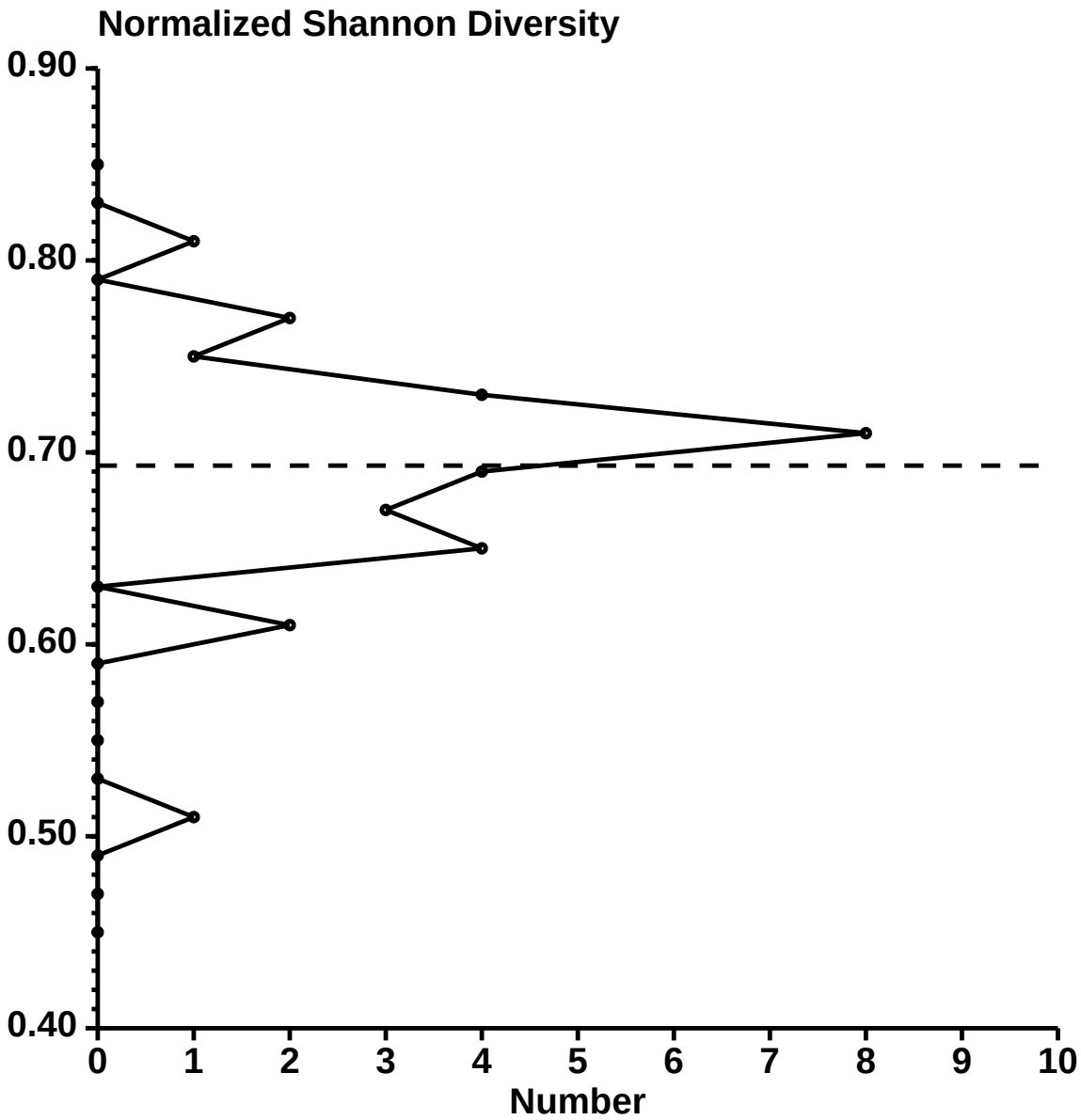
Tropical forest trees



Barro Colorado Island data have $\sim 10\times$
more counts than the other data sets: 0.692 ± 0.004

Condit.Yamakura2000 Science, 288:1414-1418, 2000

Sponge microbiota



The mean and standard deviation are 0.69 ± 0.06.
Dashed line is at $\ln 2 = 0.69$.

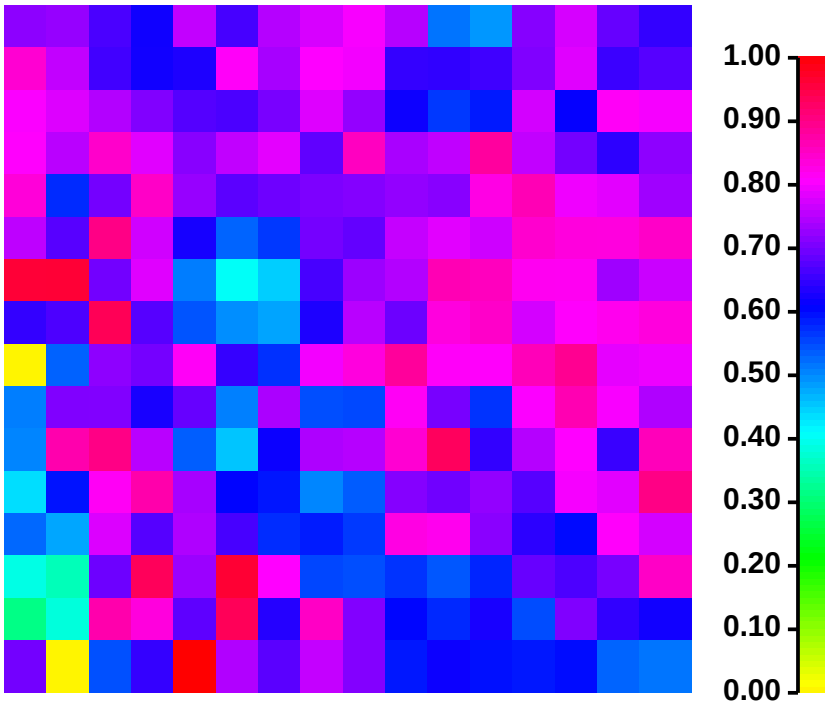
Schmitt.Taylor2012 ISME J, 6:564-576, 2012

Serpentine Grassland

- Jessica Green recorded the number of all plant species in 256 subdivisions of an 8m $\times$ 8m plot in Yolo county, CA.

Green.Ostling2003 Ecology Letters, 6:919-928, 2003

Serpentine Grassland

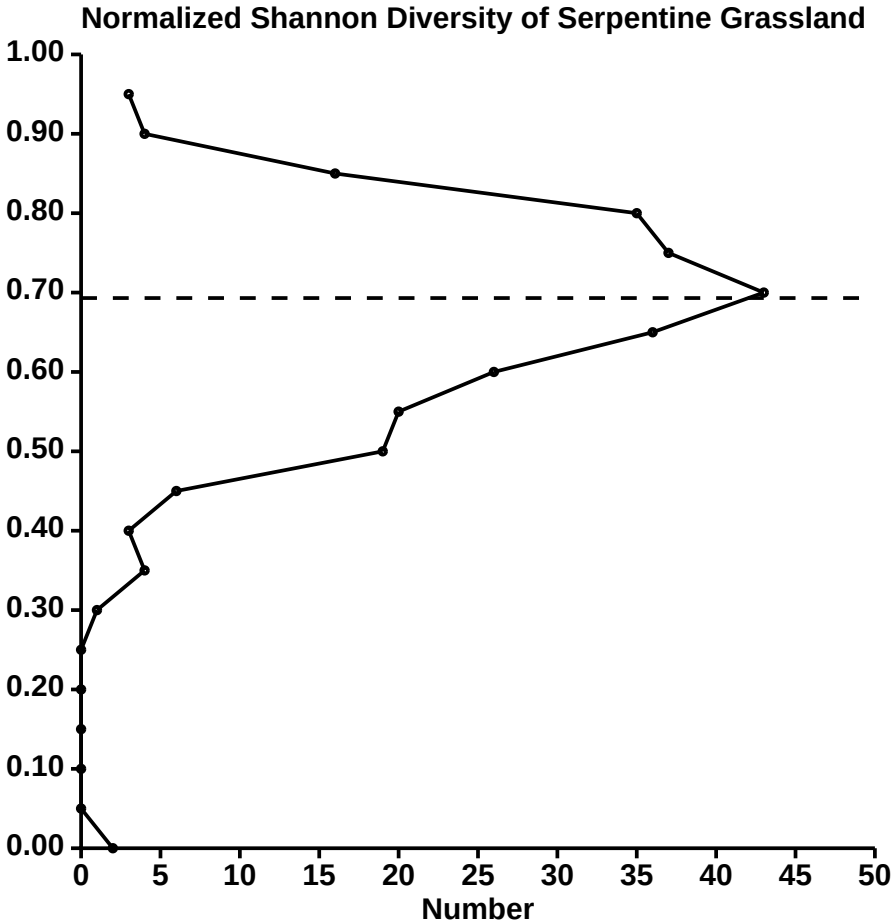


Normalized Shannon Diversity in serpentine grassland

- Jessica Green recorded the number of all plant species in 256 subdivisions of an 8m $\times$ 8m plot in Yolo county, CA.
- Compute the evenness for each subdivision

Green.Ostling2003 Ecology Letters, 6:919-928, 2003

Serpentine Grassland



- Plot the histogram of the 256 subdivisions.

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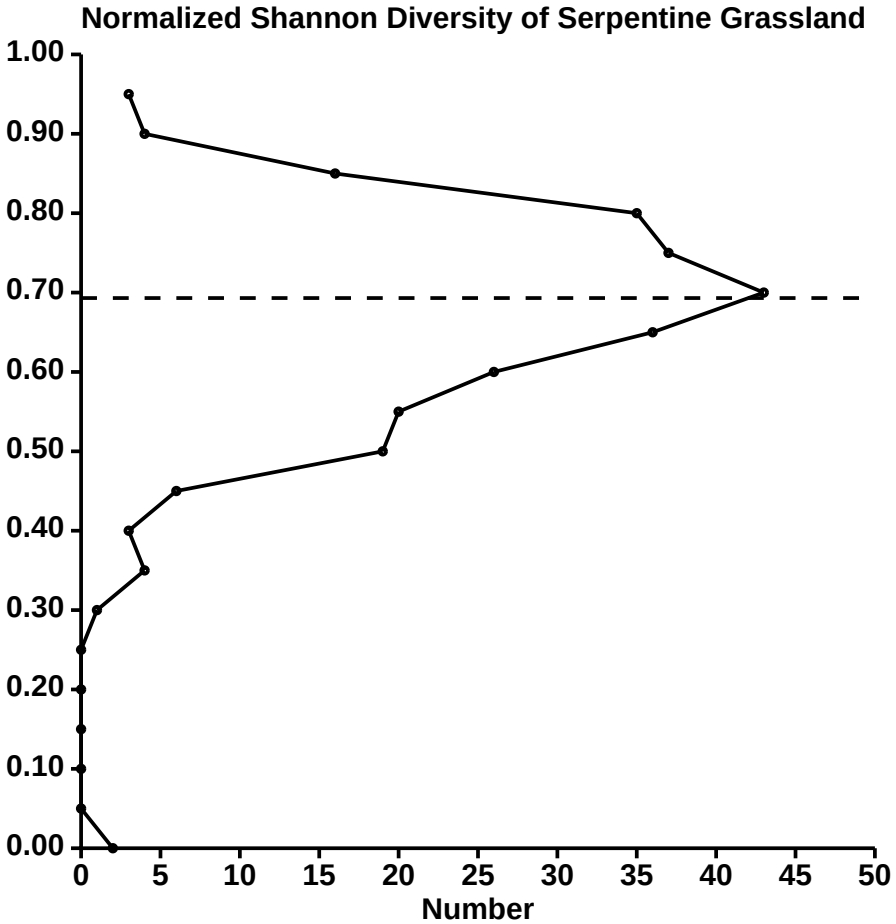
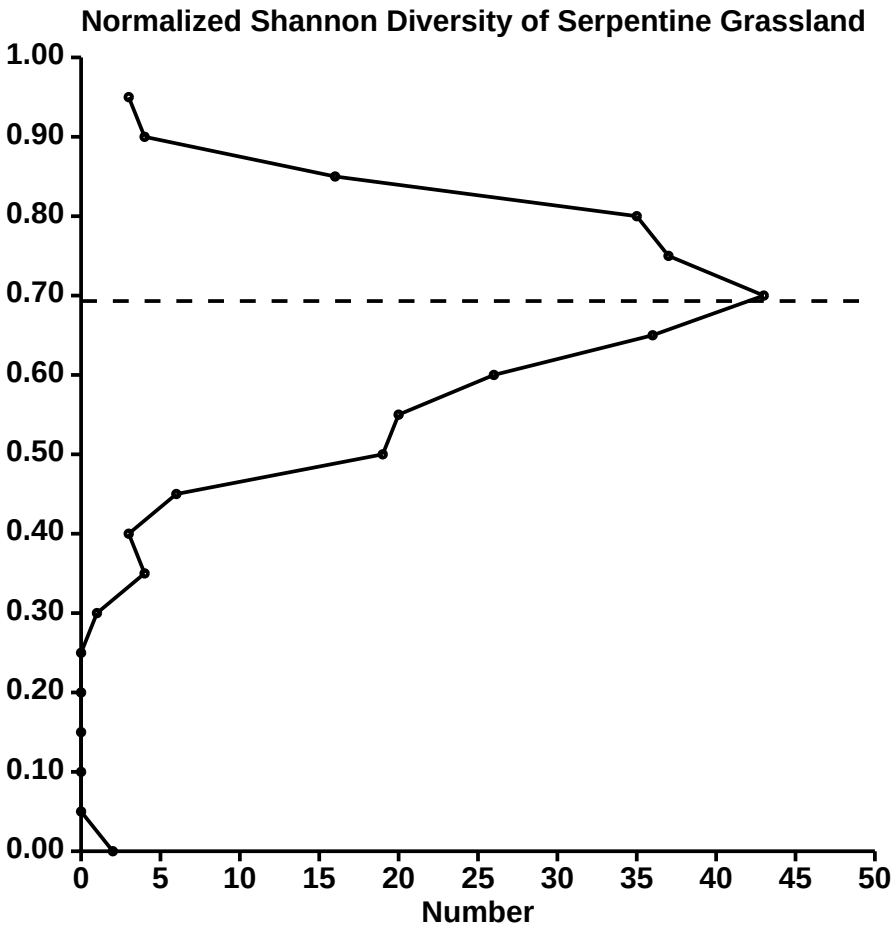
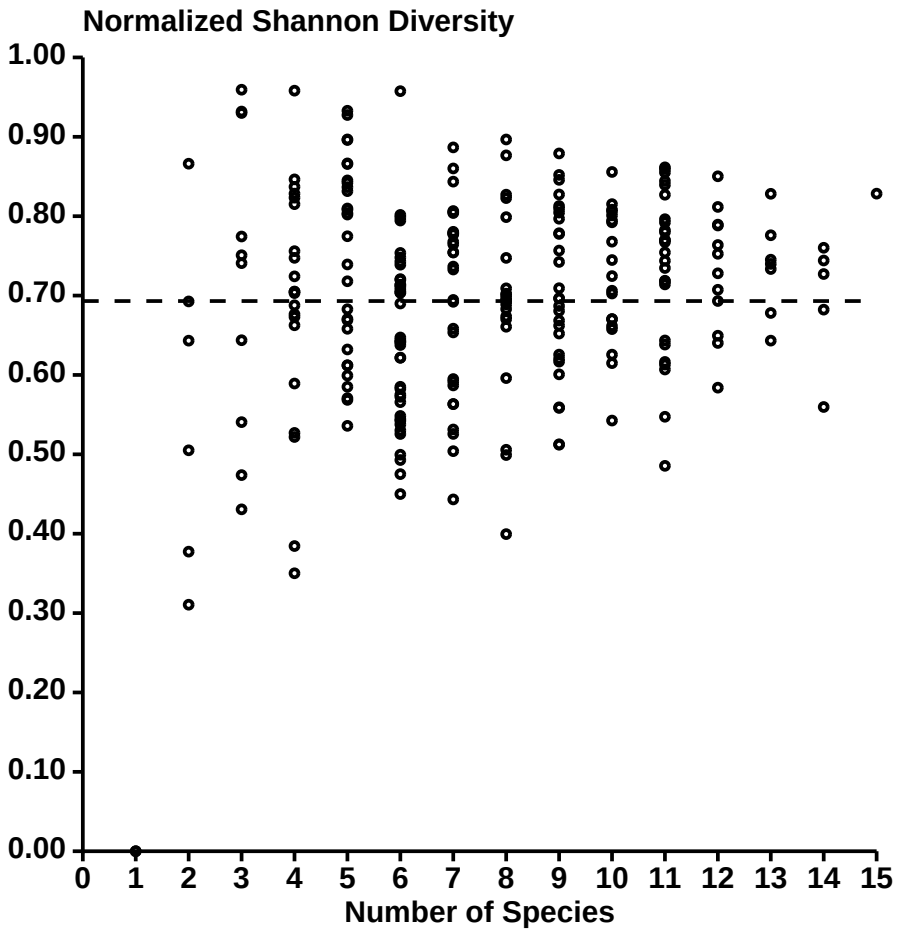


- Plot the histogram of the 256 subdivisions.
- The evenness for the 256 subdivisions is 0.697 ± 0.137
  standard error of the mean: 0.009
  Dashed line is at $\ln 2 = 0.693$.

Serpentine Grassland





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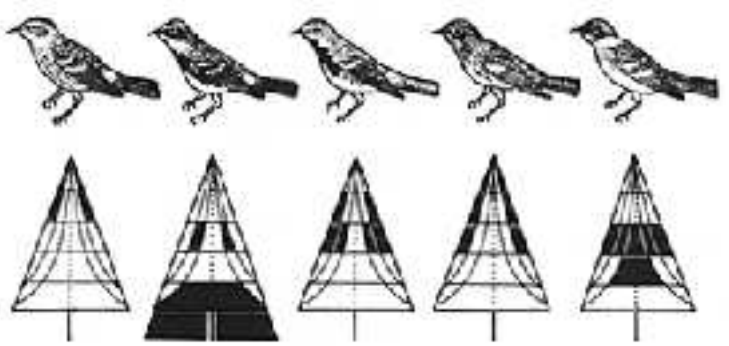
- The measured normalized Shannon diversity converges to near 0.7 as the number of species increases per subdivision.

Green.Ostling2003 Ecology Letters, 6:919-928, 2003

Why 70% Evenness Appears in Ecology? It's the Same Math!

- McArthur's famous Cape May Warblers:
  5 species sharing conifer trees -
  Why don't they conflict?



MacArthur1958 Ecology, 39:599-619, 1958, Gause1934 The Struggle for Existence

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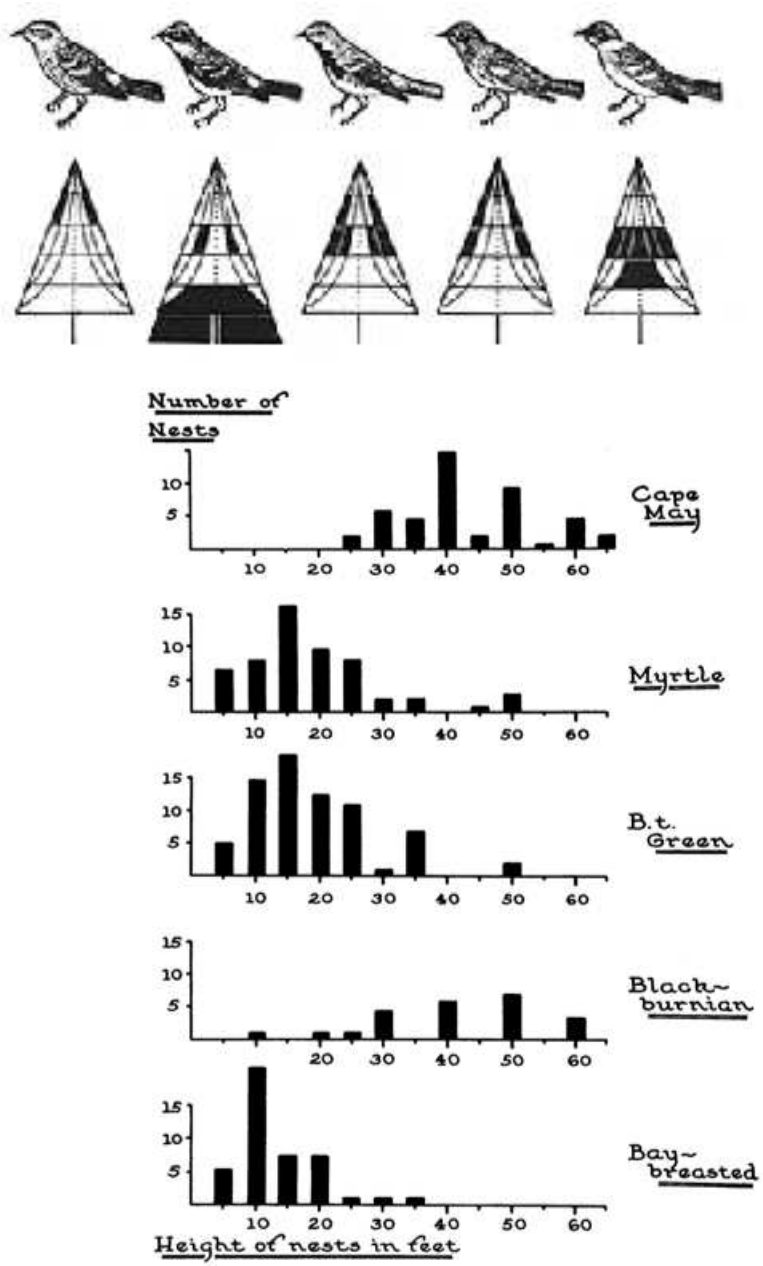

Fig. 8. Nesting heights of warblers.

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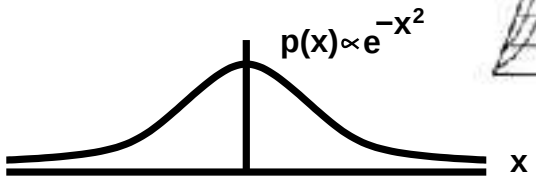

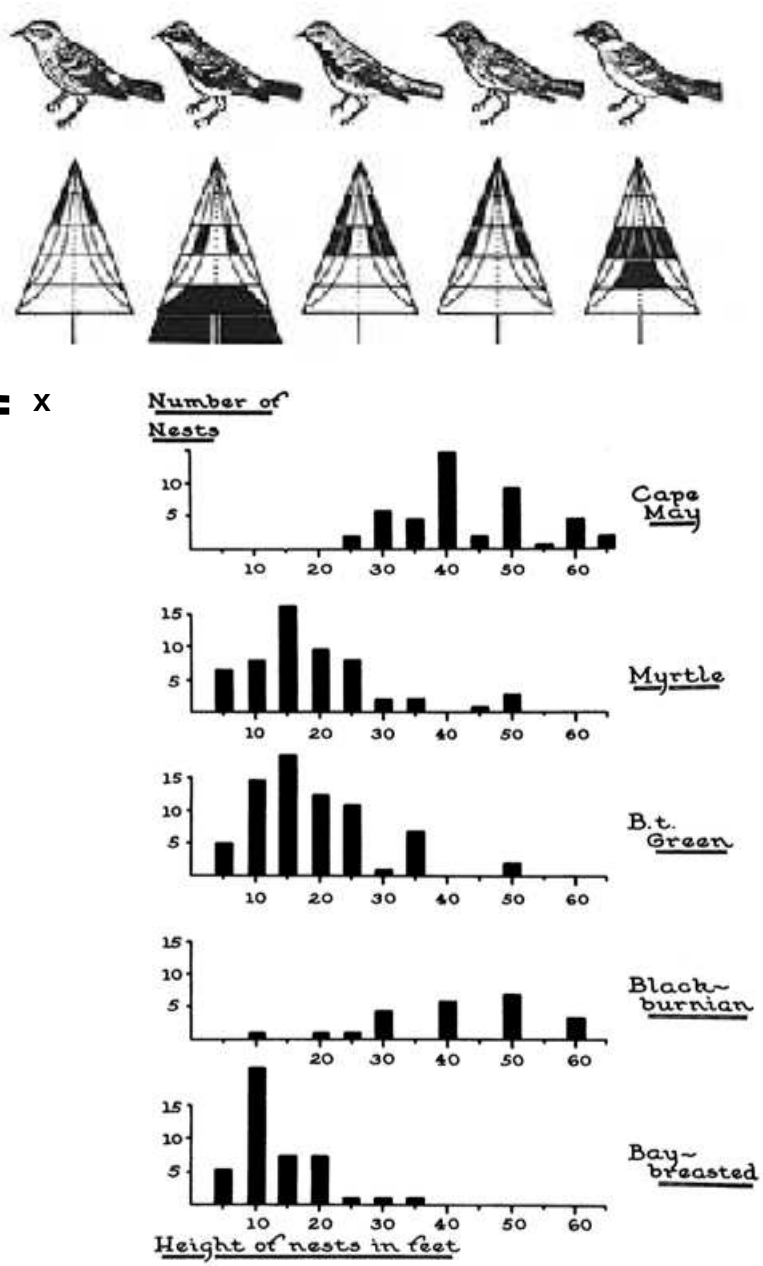

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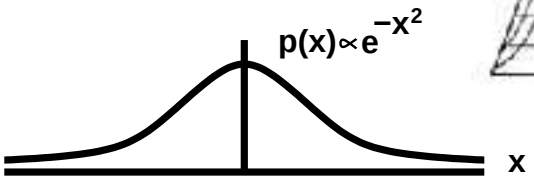

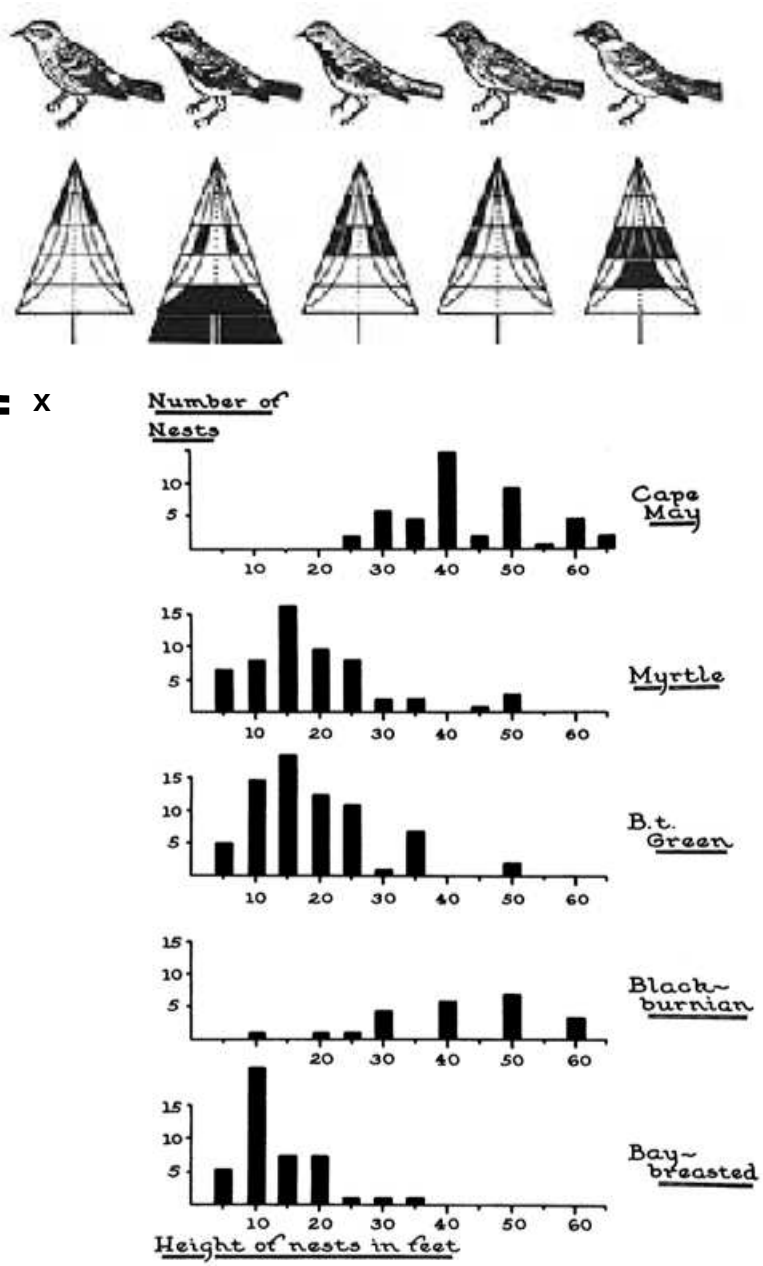

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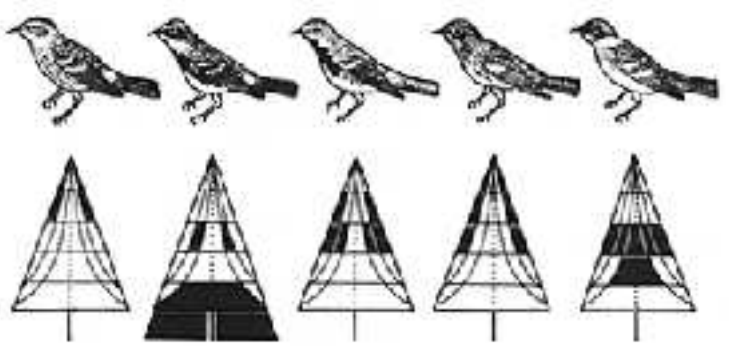

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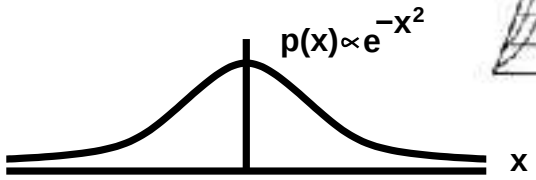

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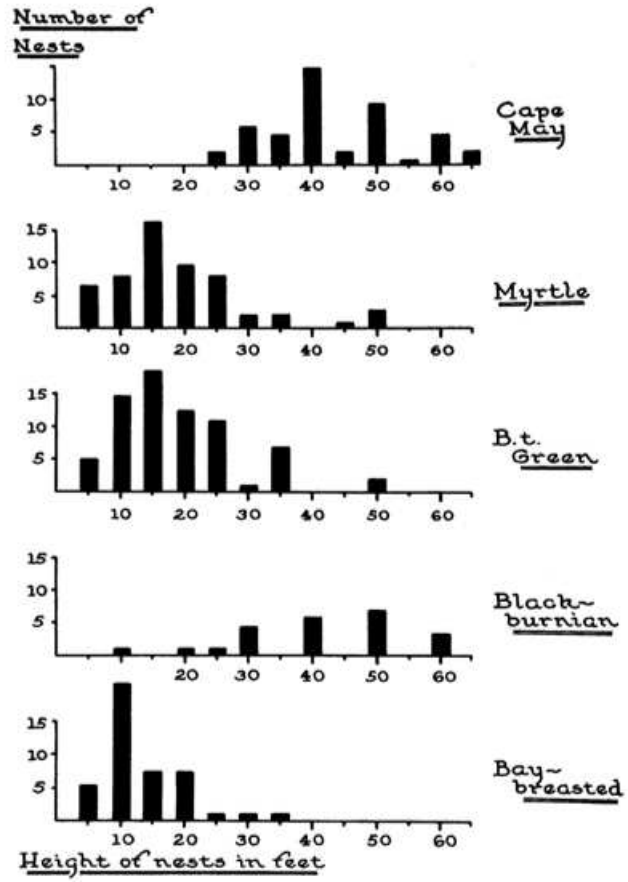

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- Nesting height in tree, nesting date, temperature, kinds of insects *etc*
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- That's high dimensionality just like
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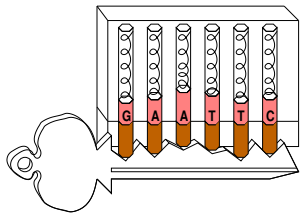

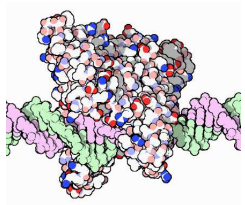

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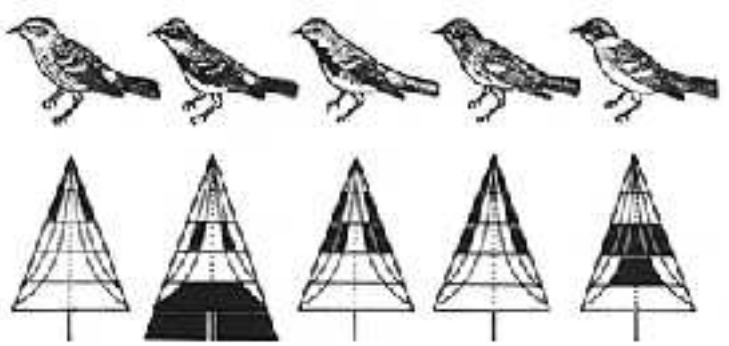

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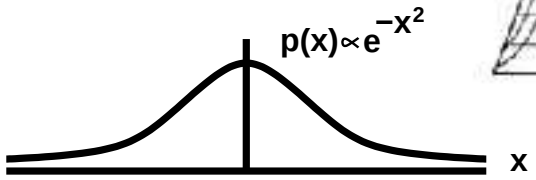

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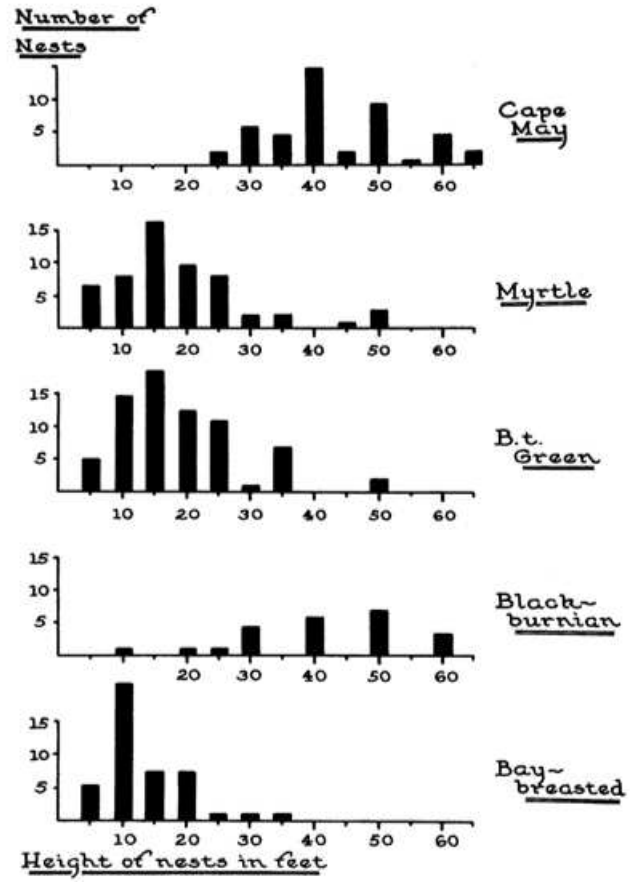

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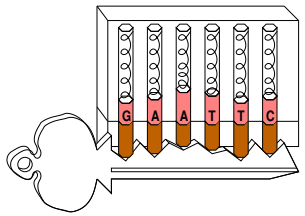

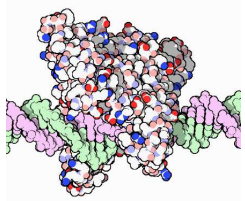

- Gause's 1934 Principle = niches are unique
  . . . That's separation of states!

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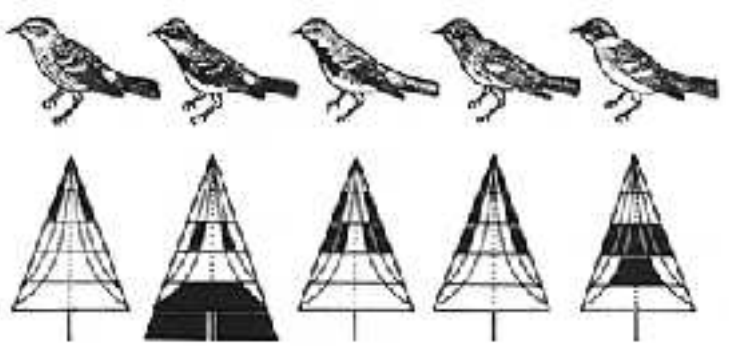

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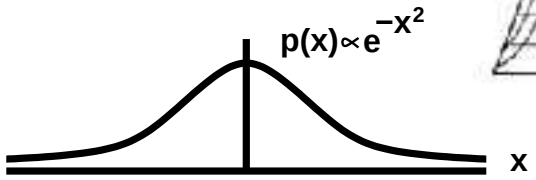

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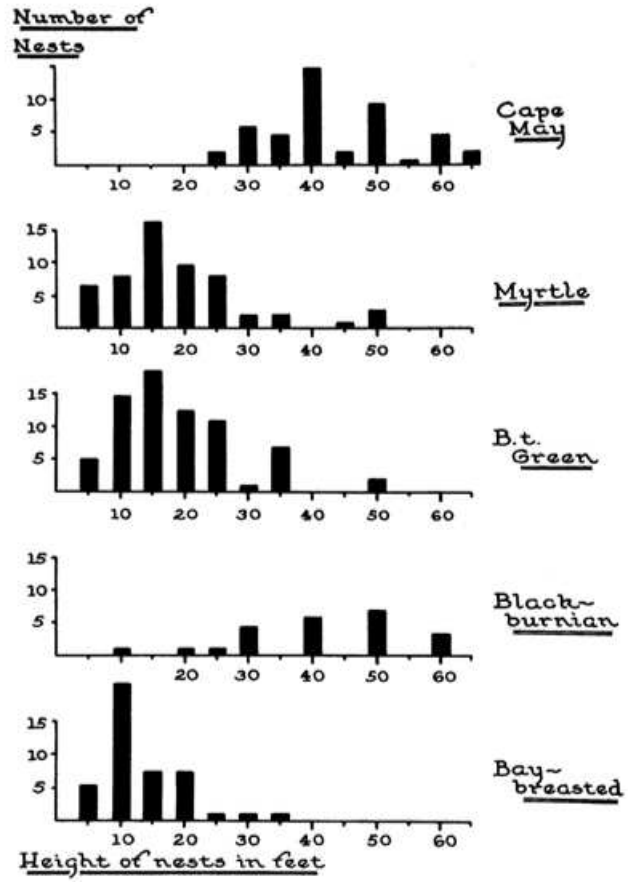

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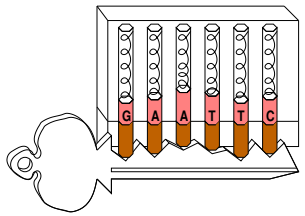
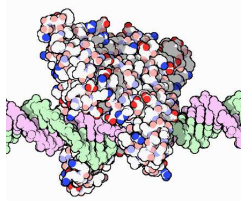


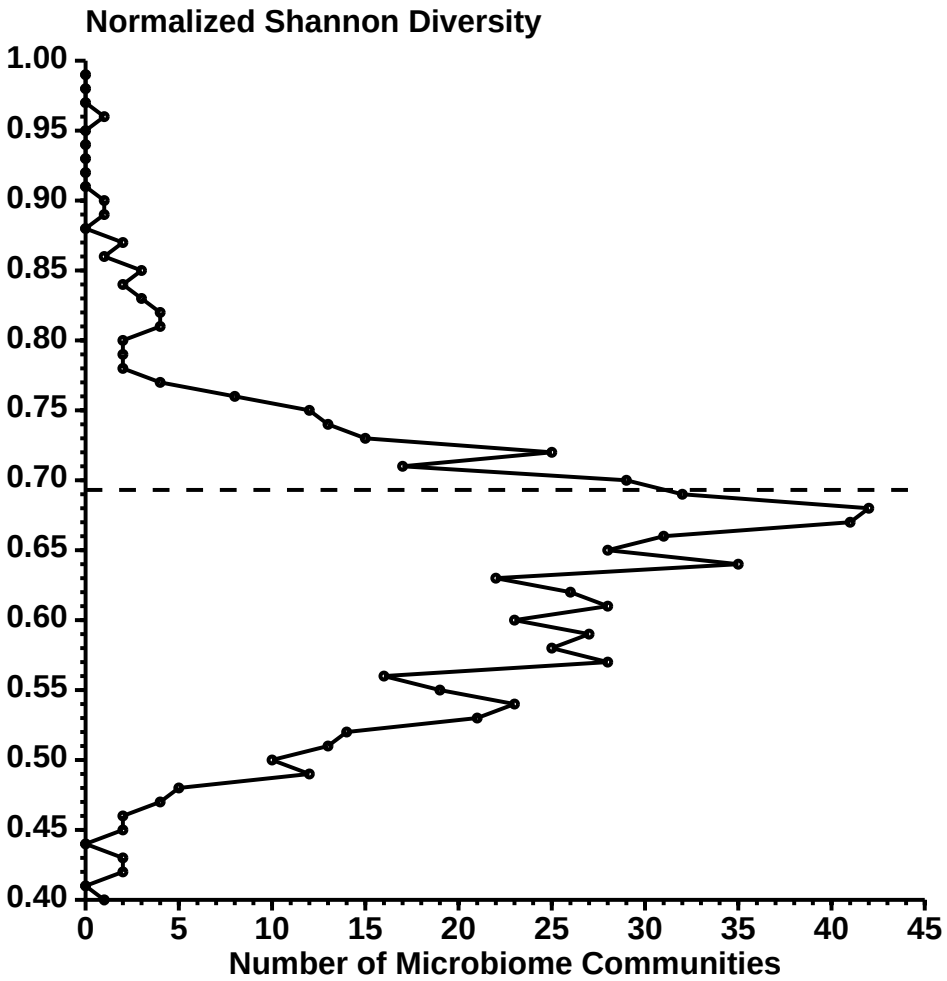


- Gause's 1934 Principle = niches are unique
  ... That's separation of states!

- RESULT: Packing spheres
  in a high dimensional space!
  $\Rightarrow$ the efficiency equation and 70%!

MacArthur1958 Ecology, 39:599-619, 1958, Gause1934 The Struggle for Existence

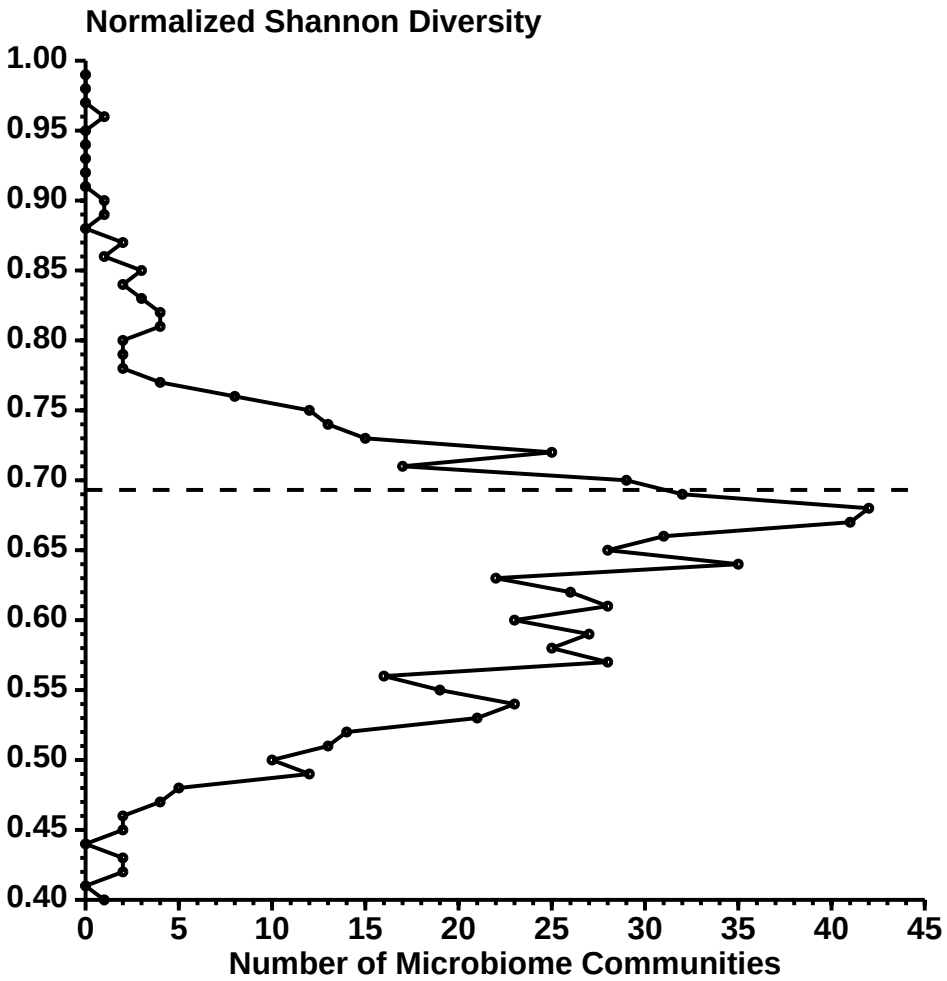
Healthy Human Microbiota



- Species abundencies of 690 microbiome samples from the human body

Huttenhower.White2012 Nature, 486:207-214, 2012

Healthy Human Microbiota



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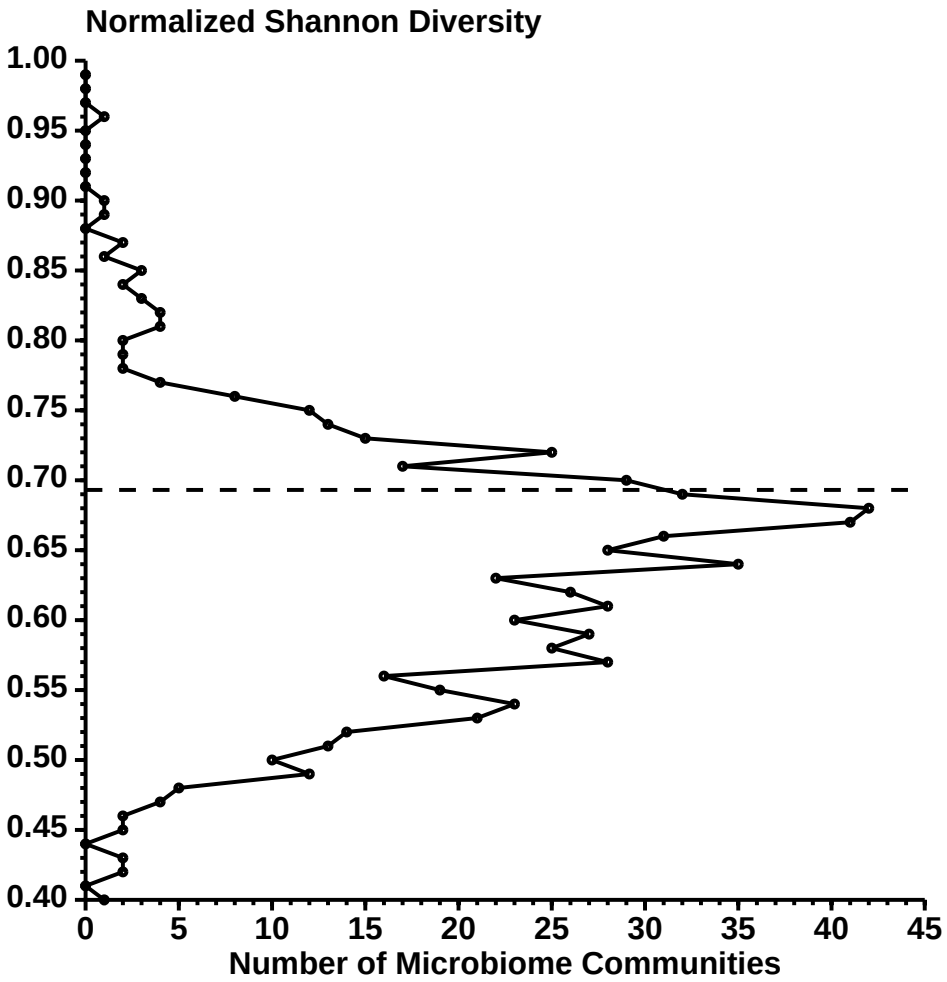
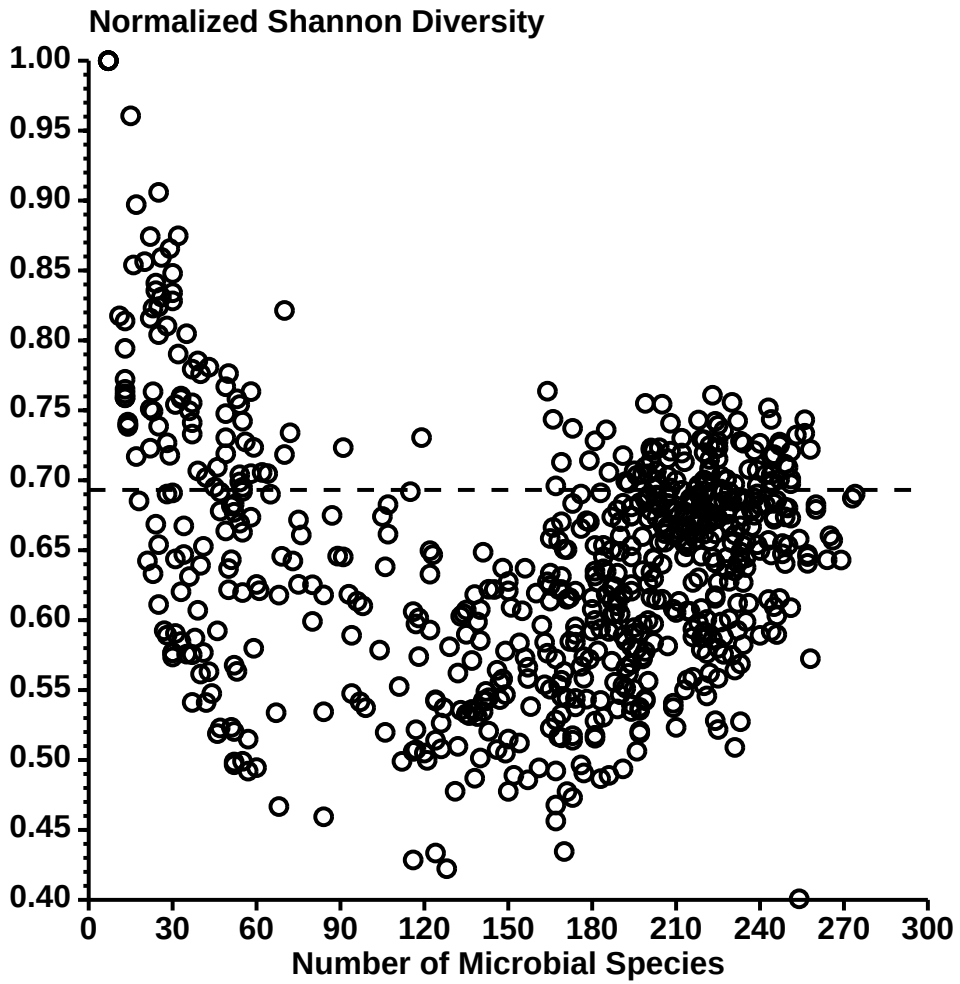
Healthy Human Microbiota

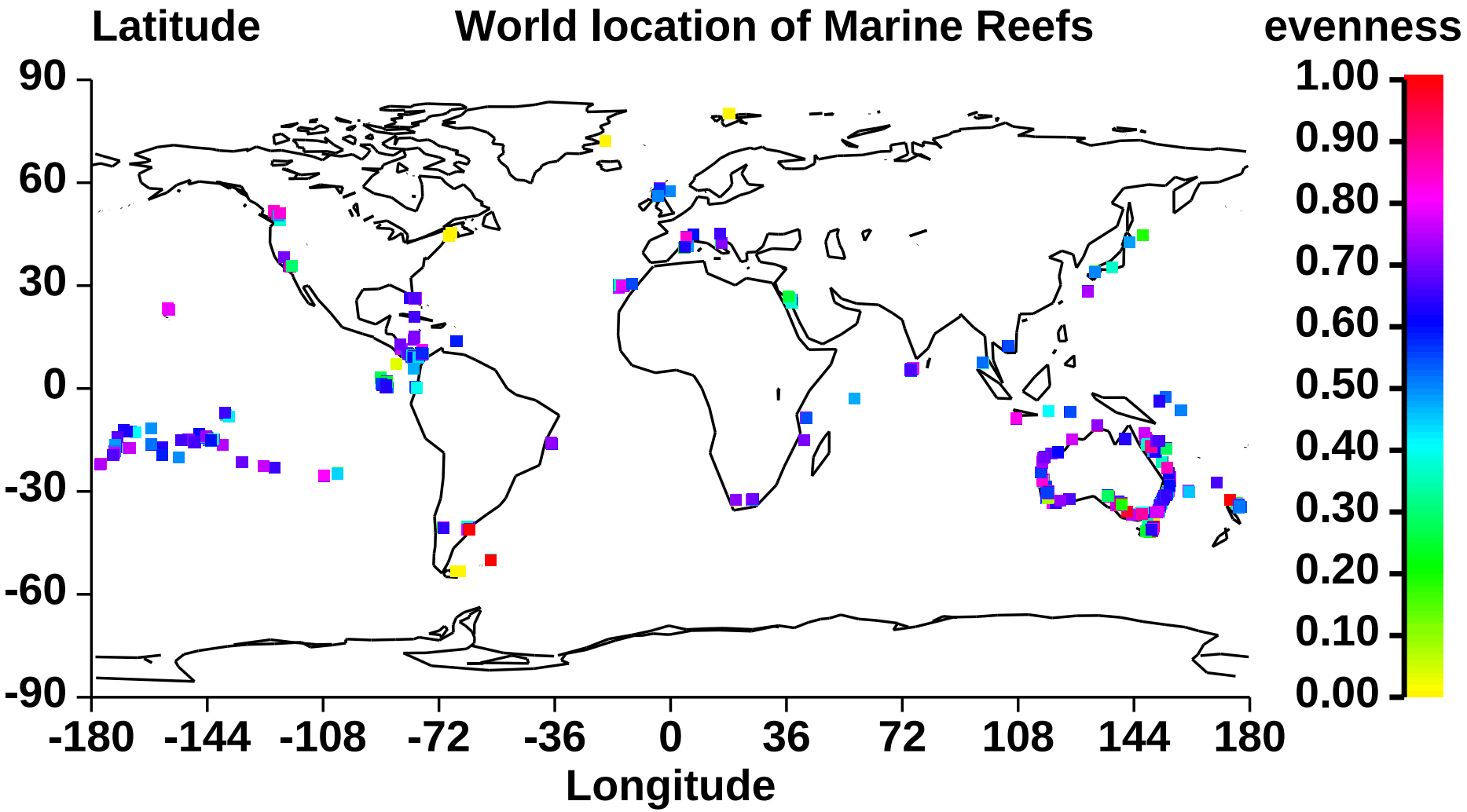




- Species abundencies of 690 microbiome samples from the human body
- Peak near 69% but big tail downwards. **PUZZLE!**
- Spread by species - comma shape is unexplained!! **PUZZLE!**

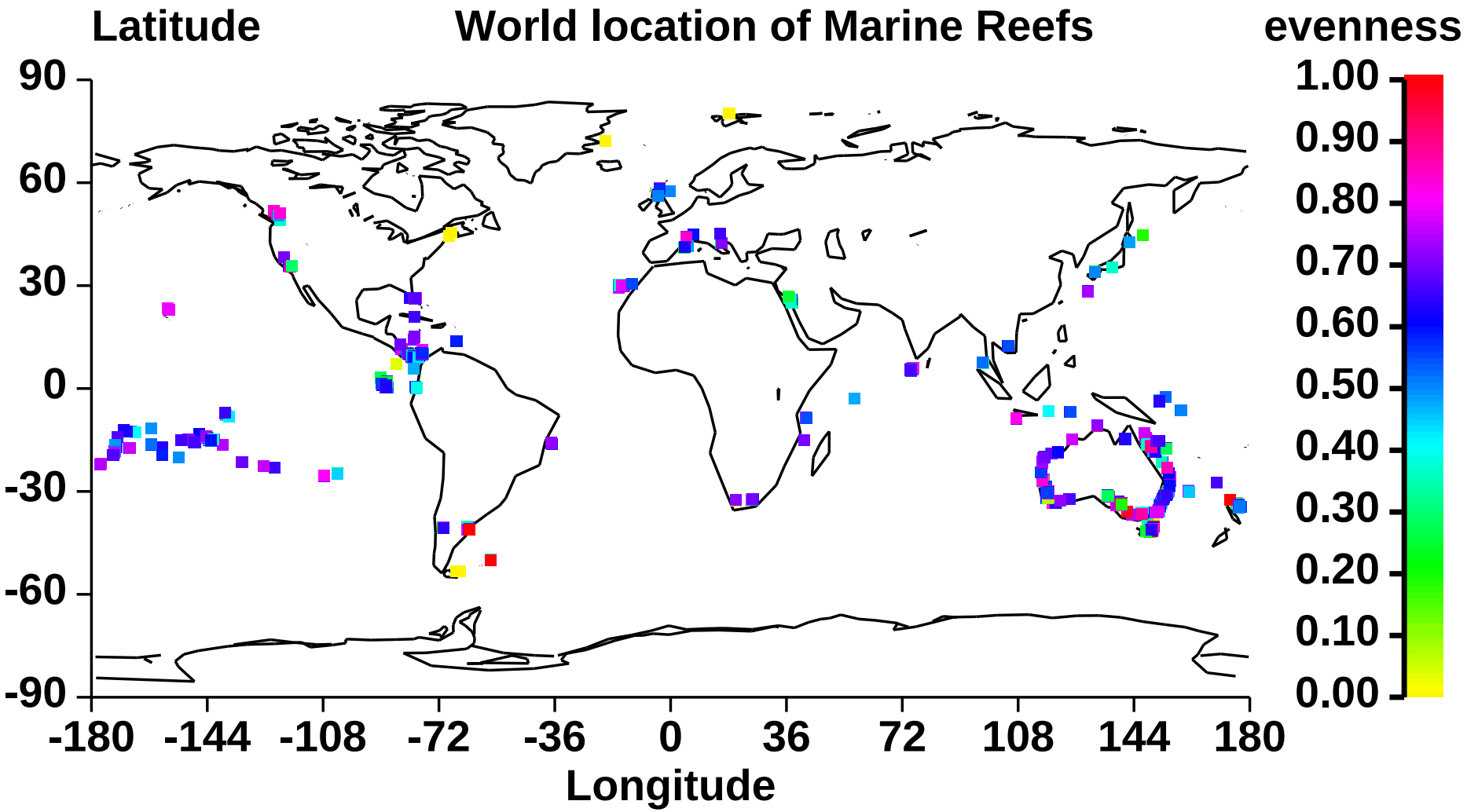
Huttenhower.White2012 Nature, 486:207-214, 2012

Marine Reef Fish



- World map of 1,844 sites with the normalized Shannon diversity at each site ('evenness') shown in color.

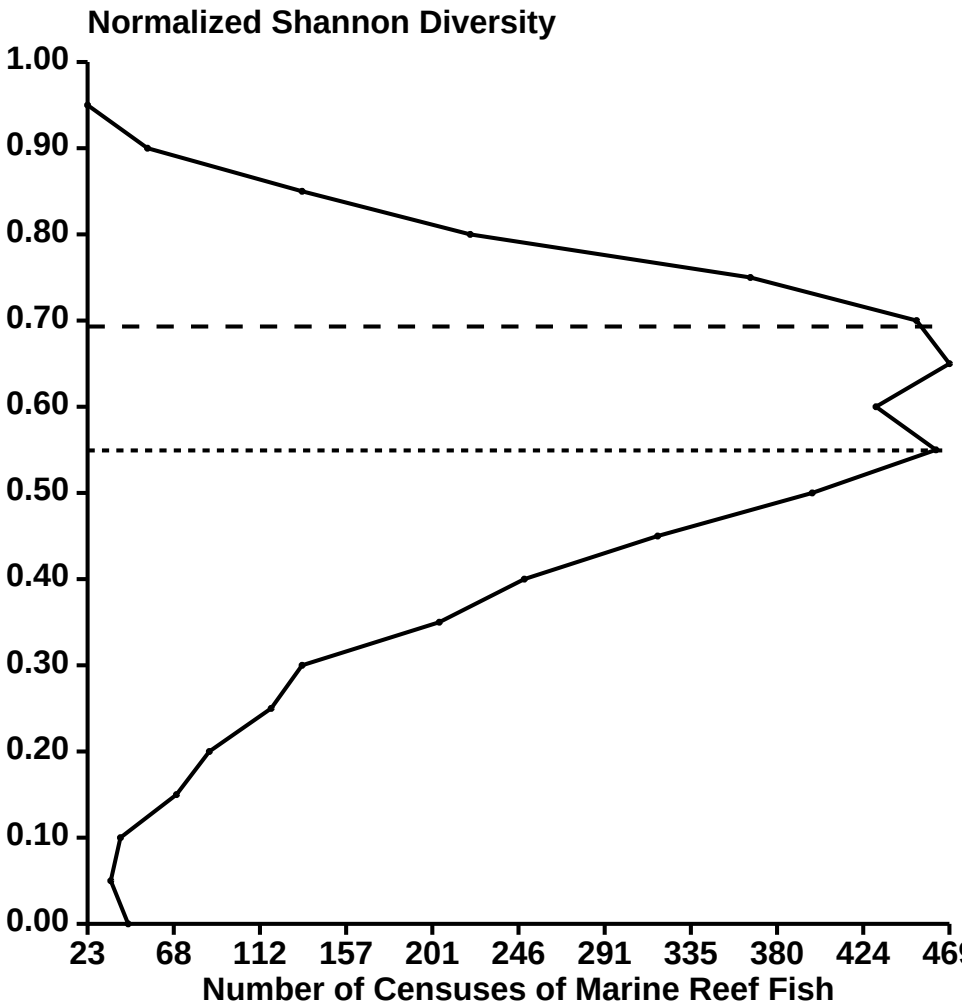
Marine Reef Fish

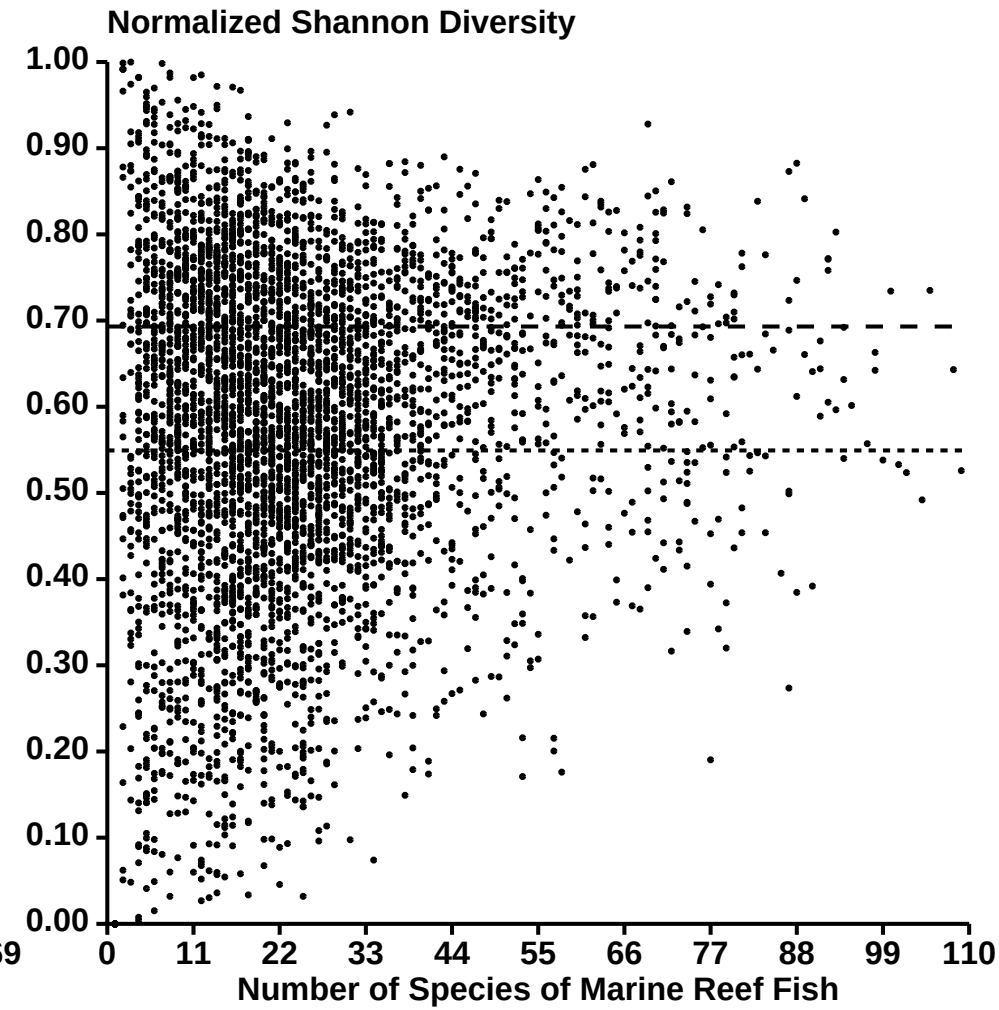


- World map of 1,844 sites with the normalized Shannon diversity at each site ('evenness') shown in color.
- Except for low evenness in extreme latitudes, there is little correlation of world location with evenness.

Stuart-Smith.Edgar2013 Nature, 501:539-542, 2013

Marine Reef Fish





- The measured normalized Shannon diversity converges to near 0.7 as the number of species increases but the data suggest two populations.

Stuart-Smith.Edgar2013 Nature, 501:539-542, 2013

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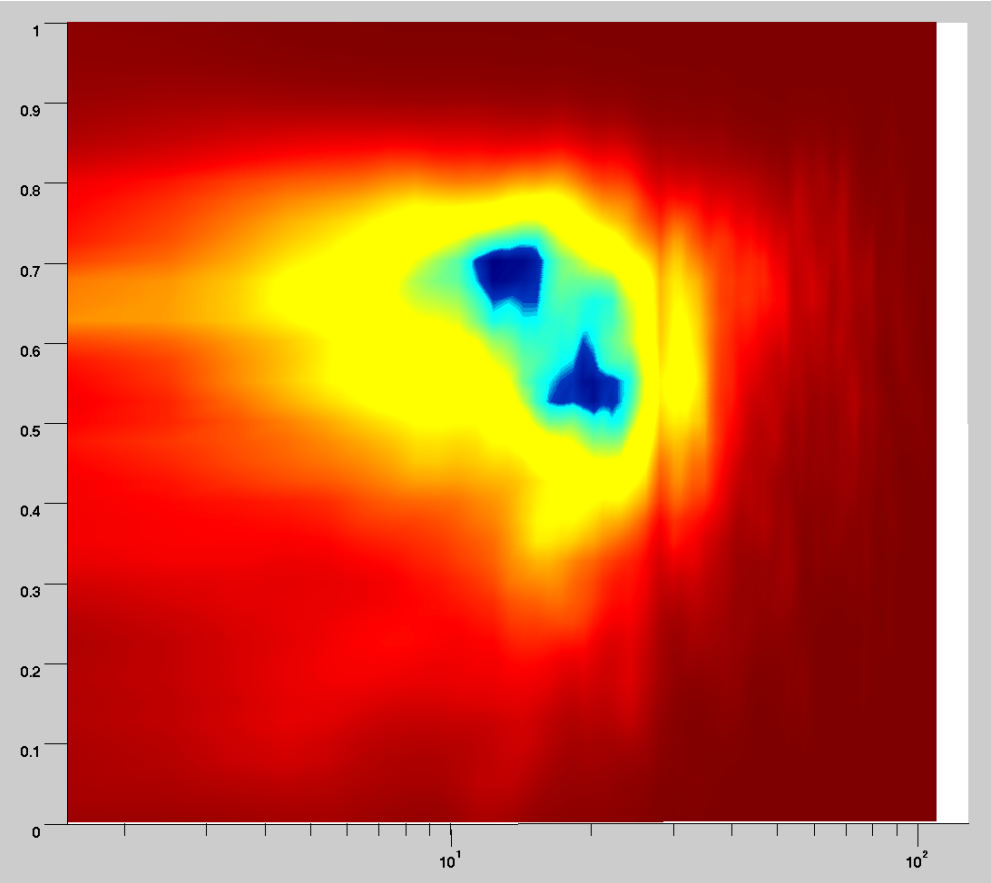

- Smoothing using Matlab reveals two peaks.
  The x axis (species counts) is on a log scale.
  The colors were selected to show the two peaks, which appear around 0.70 and 0.55.

Stuart-Smith.Edgar2013 Nature, 501:539-542, 2013

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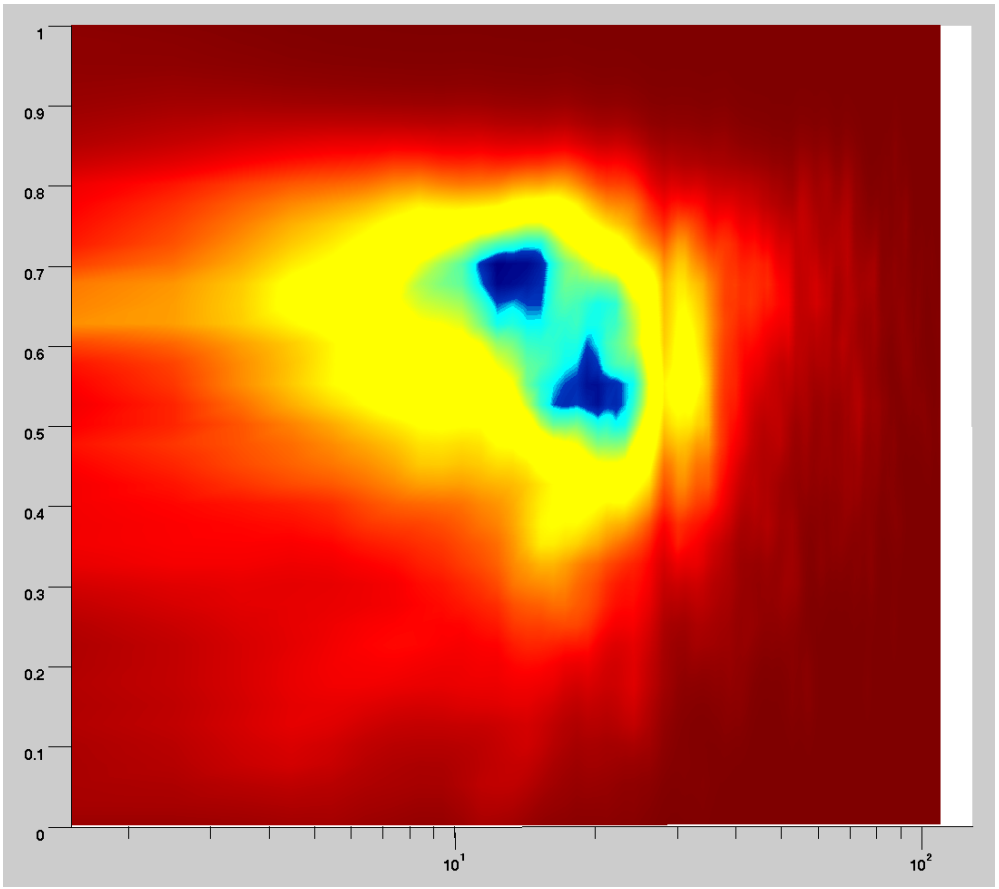

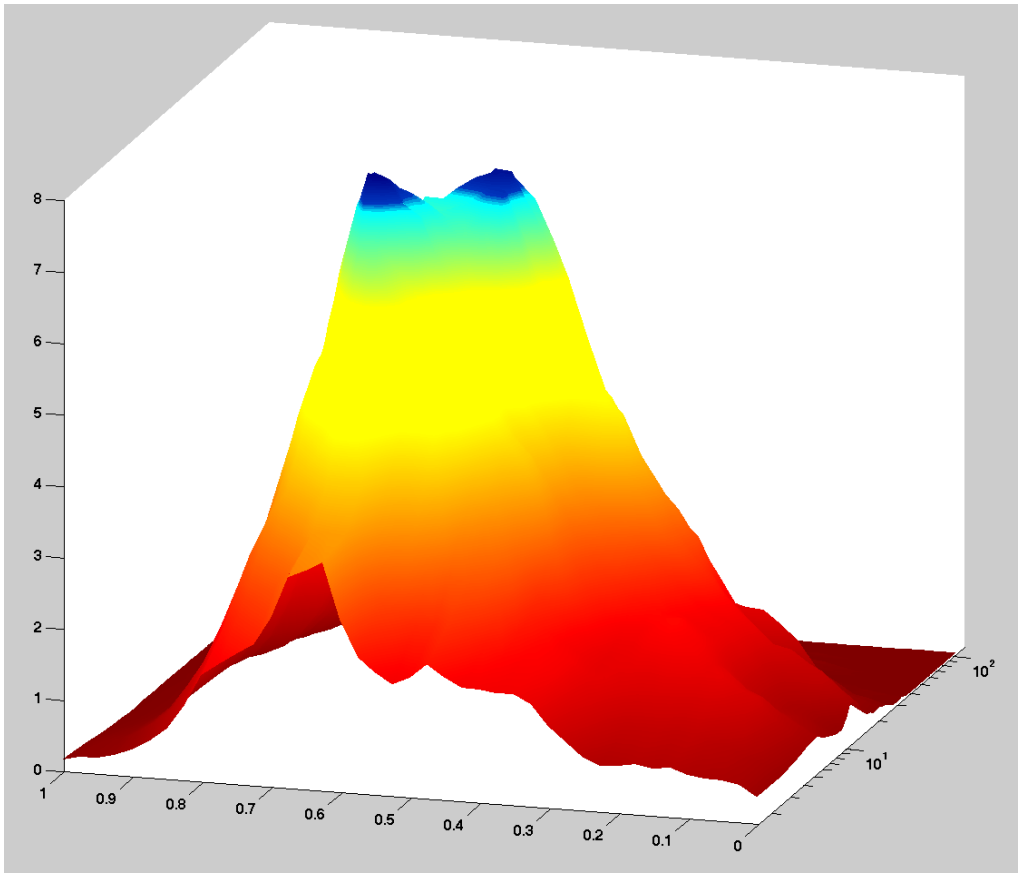

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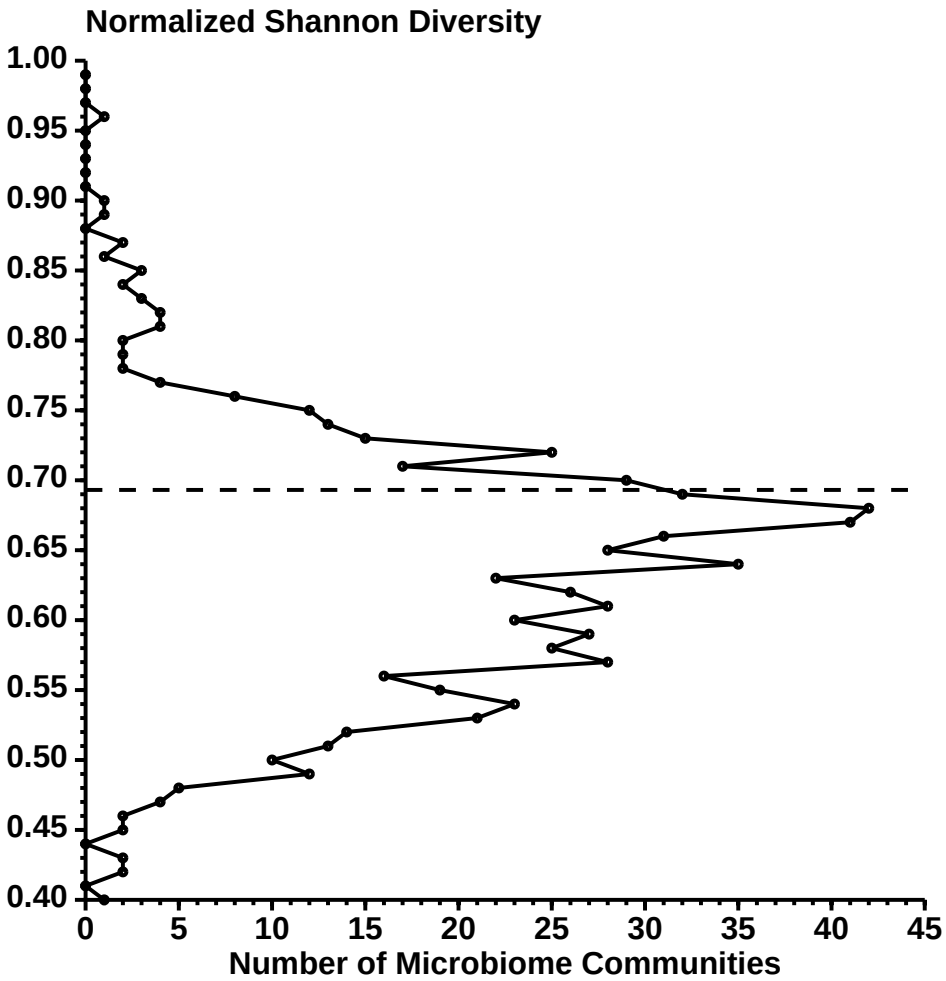
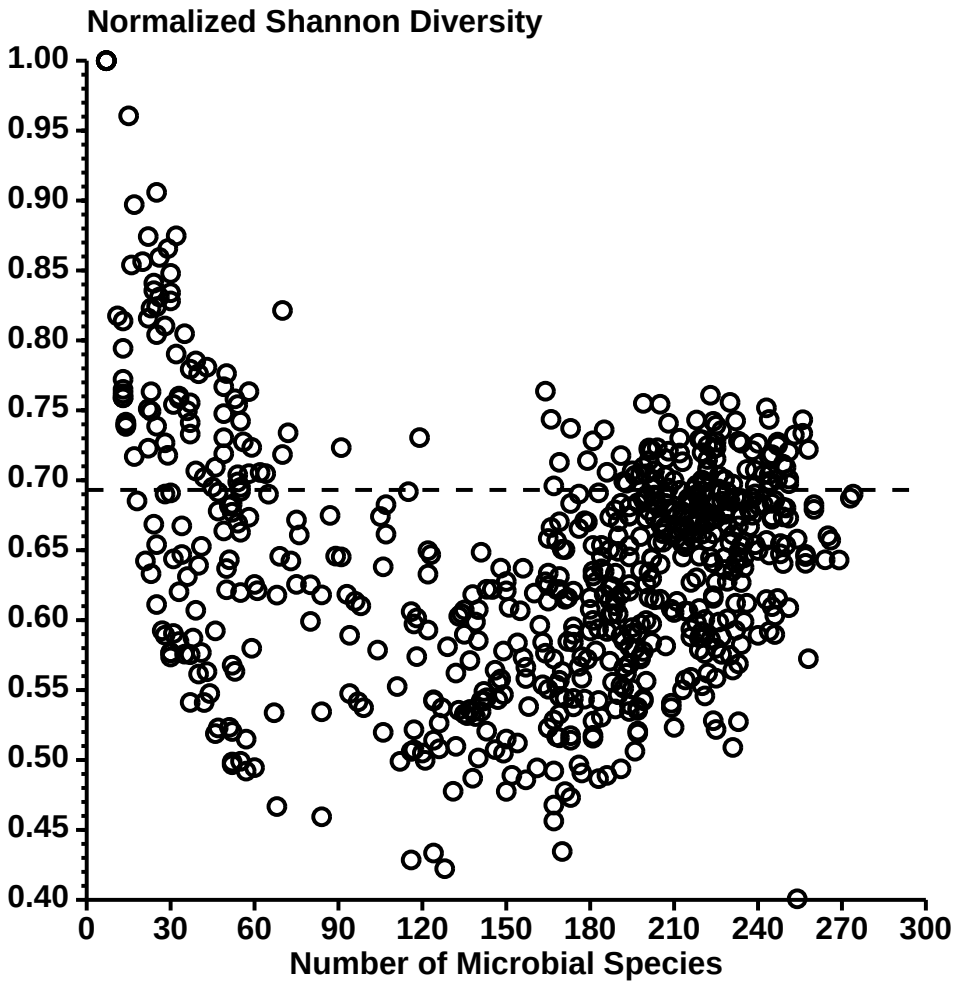
- Perspective view

Stuart-Smith.Edgar2013 Nature, 501:539-542, 2013

Healthy Human Microbiota PART 2





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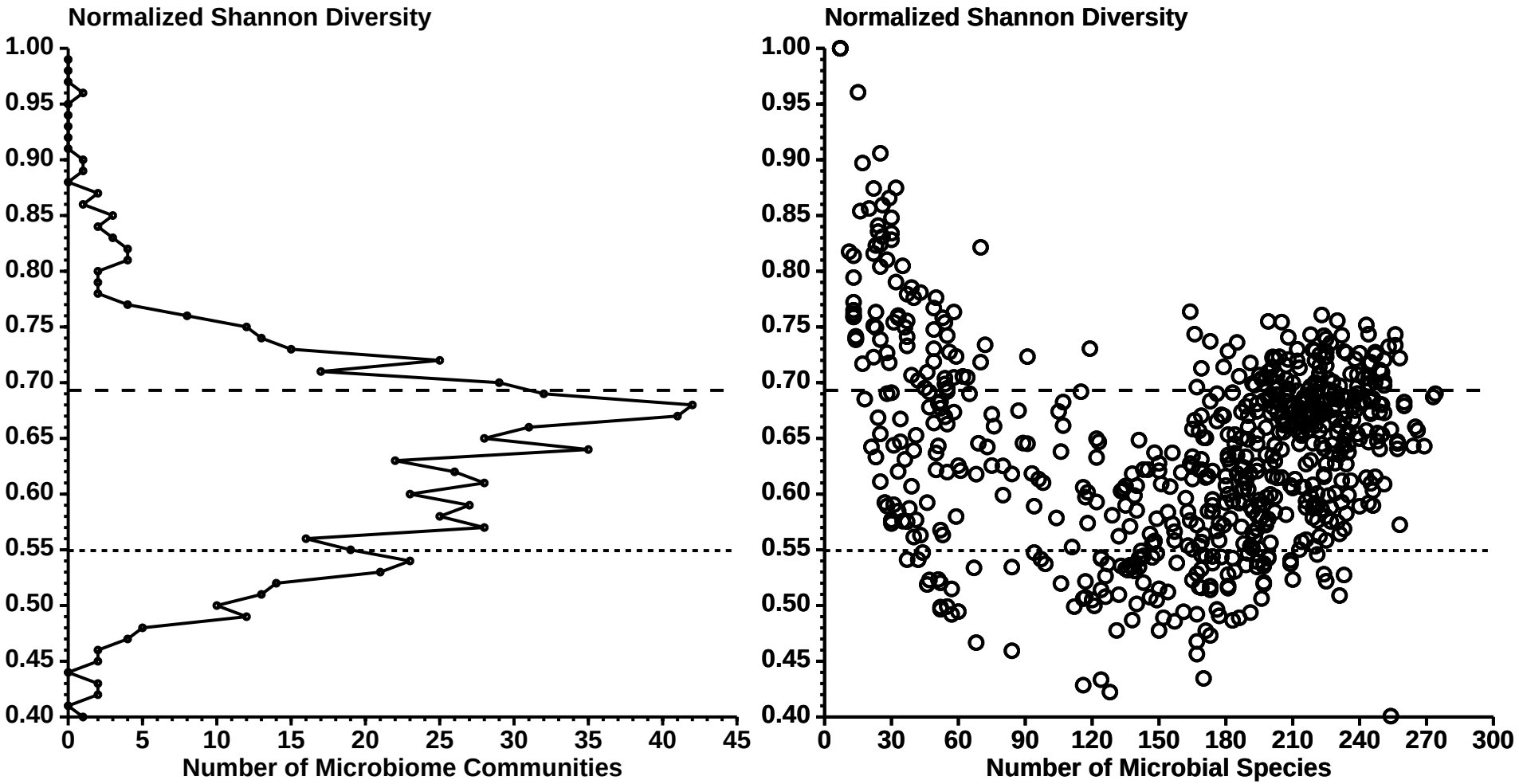

- Species abundencies of 690 microbiome samples from the human body
- Maybe there is a peak at 55%?

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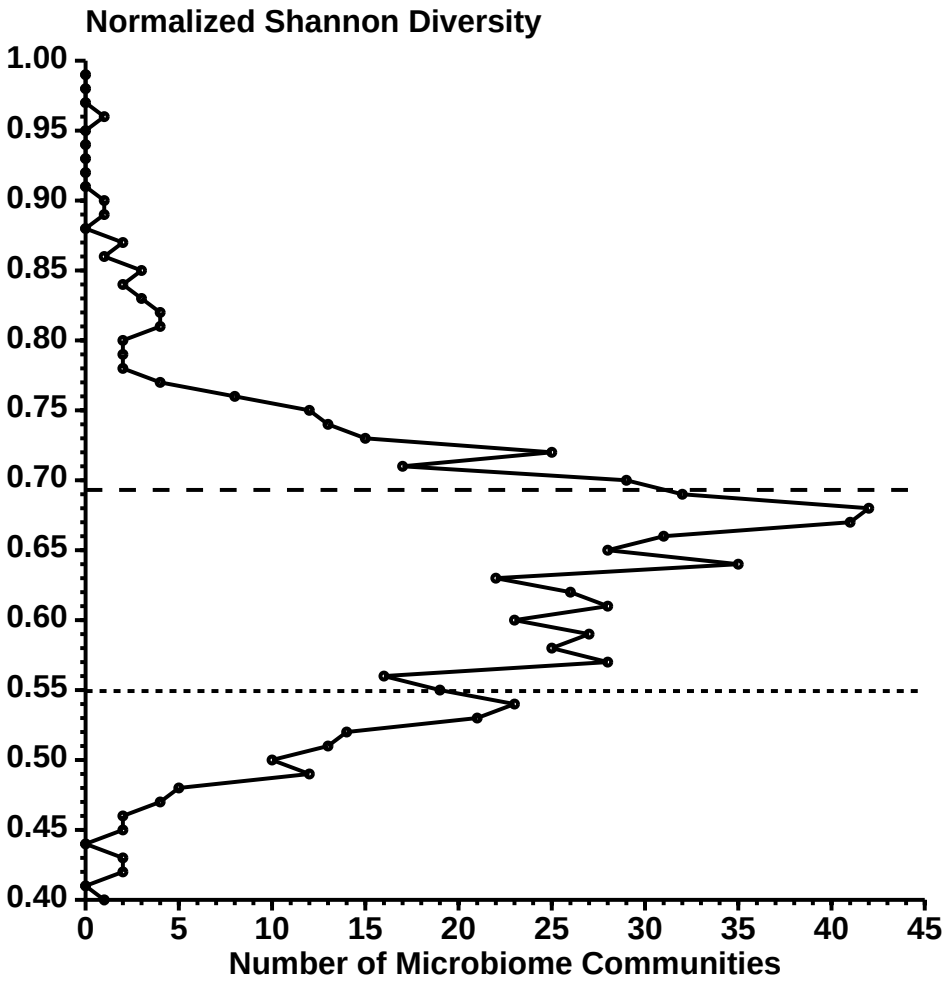

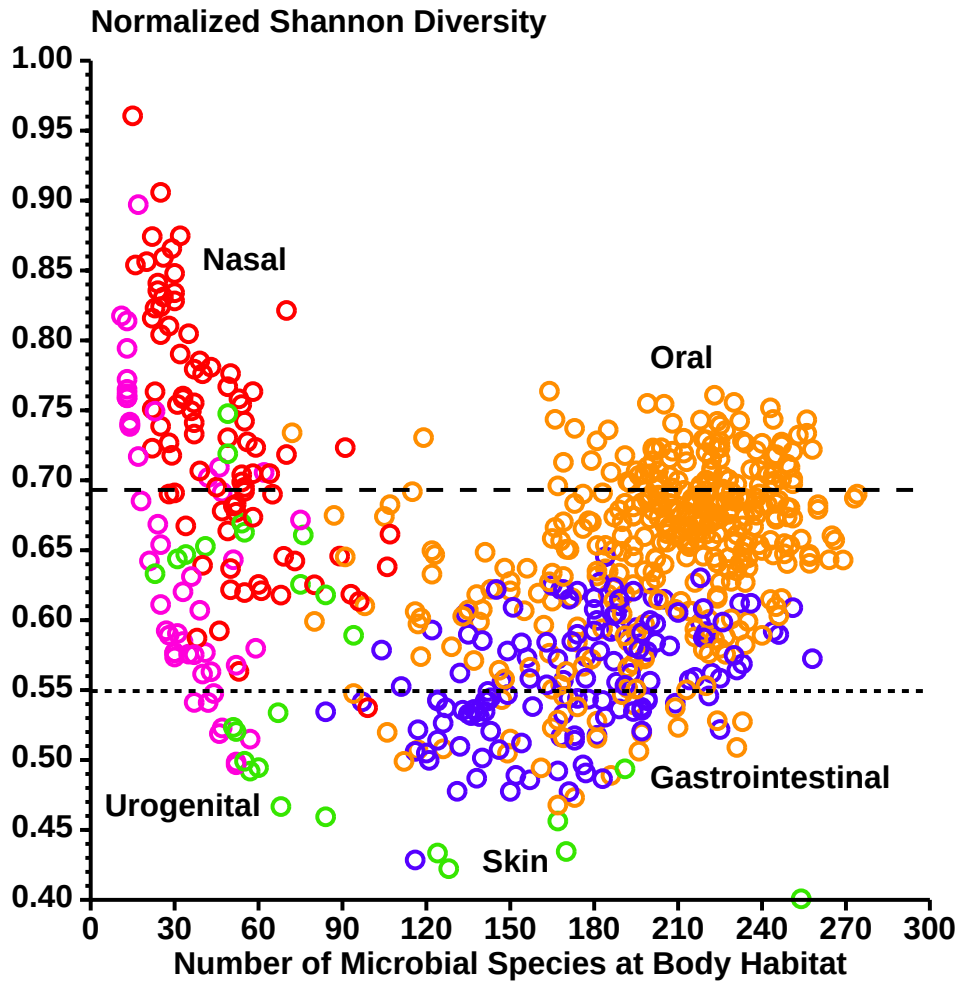

- Species abundencies of 690 microbiome samples from the human body
- Maybe there is a peak at 55%?
- Color the Body Habitats - the comma shape is resolved!!

Huttenhower.White2012 Nature, 486:207-214, 2012

Healthy Human Microbiota PART 3

Body Habitat	color key	n	Evennes
Nasal	red	87	0.73 ± 0.09
Urogenital	purple	56	0.68 ± 0.14
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Oral	orange	382	0.65 ± 0.06
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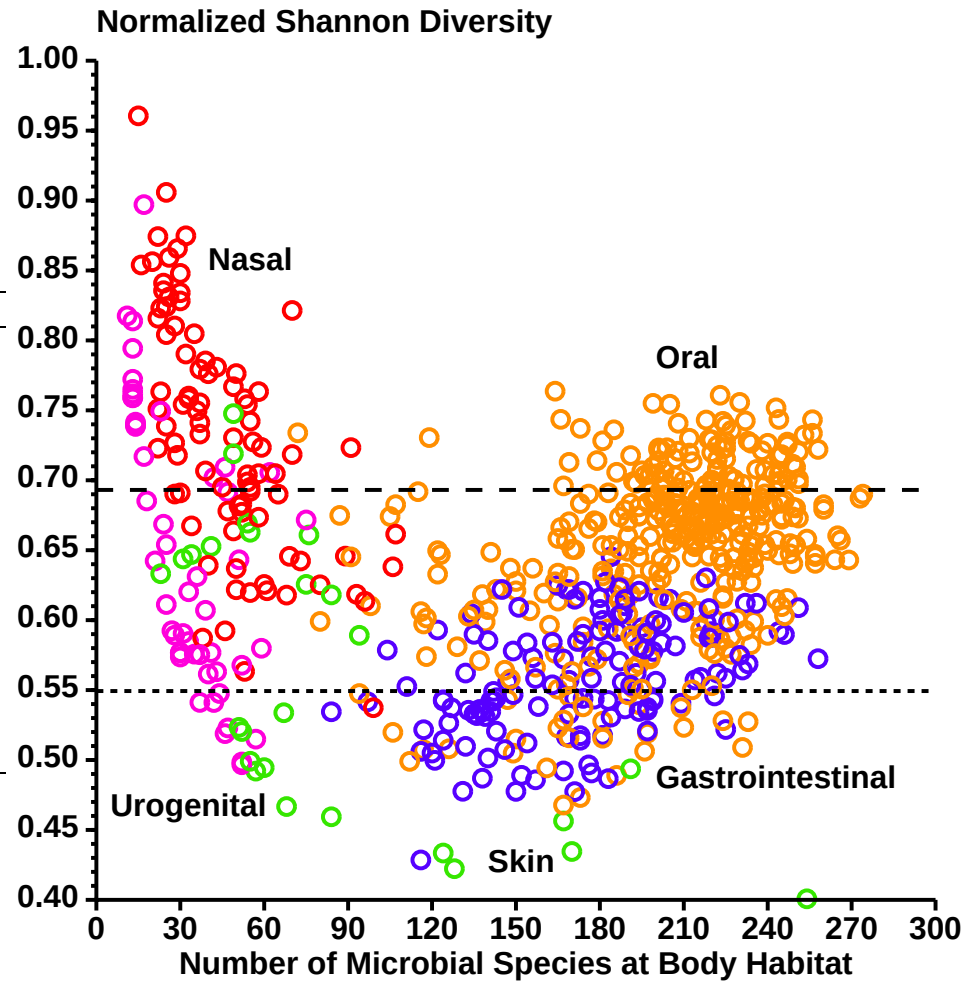

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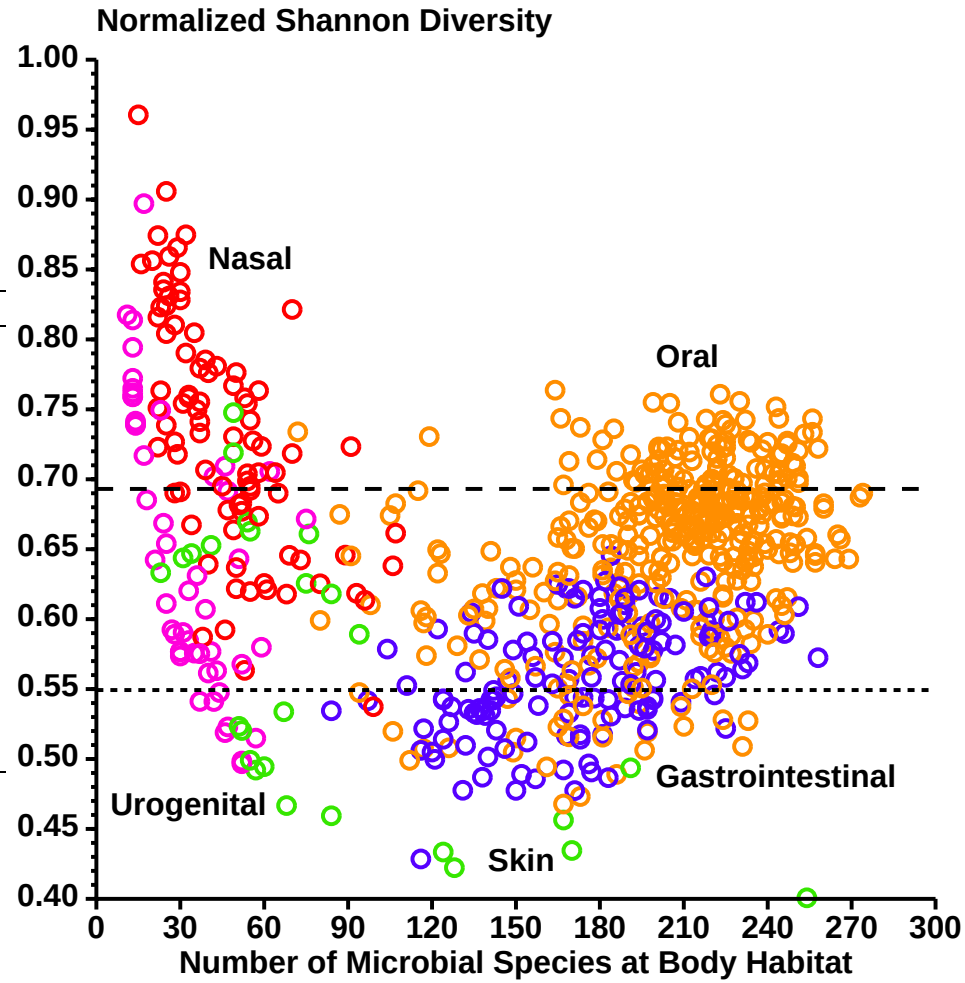

- The body habitats fall into two classes: 70% and 55%

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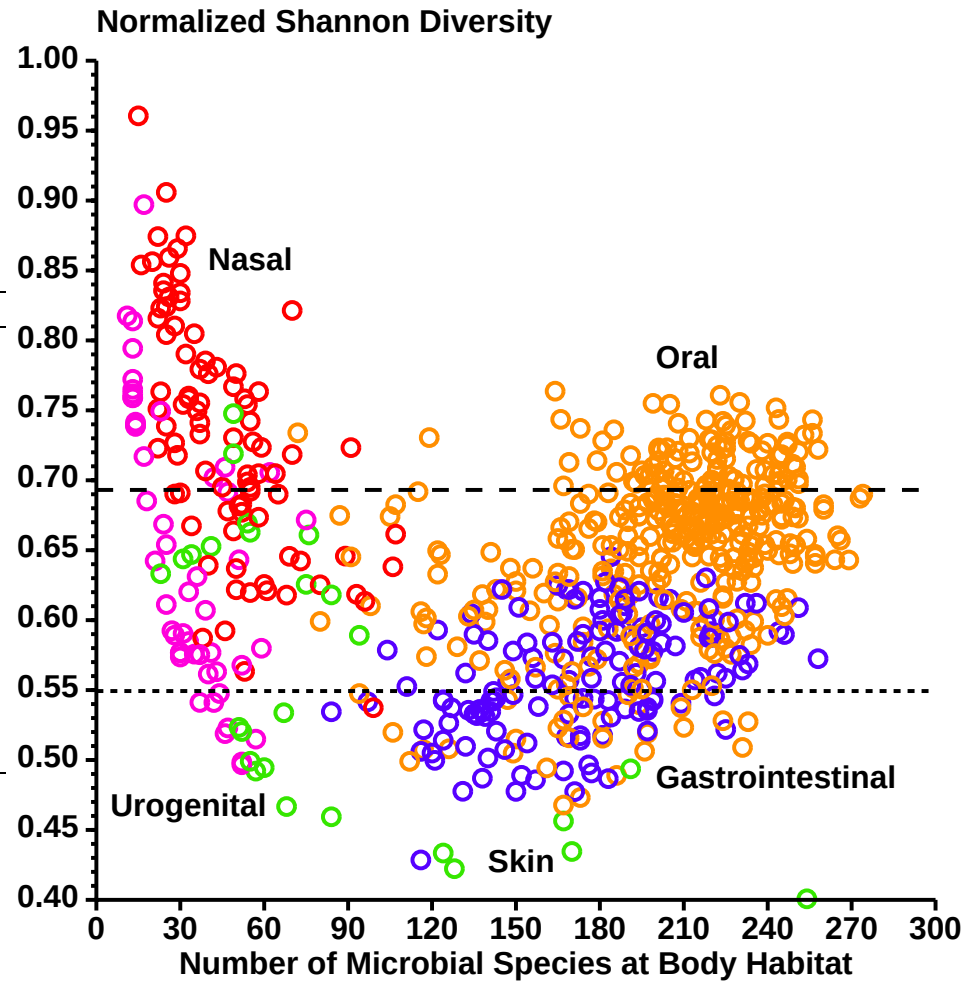


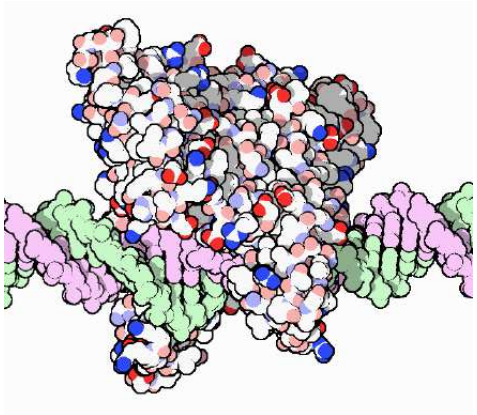
- The body habitats fall into two classes: 70% and 55%
- Two possible exceptions are

Oral-attached keratinized gingiva	0.57 ± 0.04	gums attached to teeth
Oral-buccal mucosa	0.60 ± 0.06	cheeks

Huttenhower.White2012 Nature, 486:207-214, 2012

The Discovery of Class 2 Biological Systems!

- $\epsilon_t = \frac{\ln\left(\frac{P_y}{N_y}+1\right)}{\frac{P_y}{N_y}}$ $\leftarrow$ molecular efficiency



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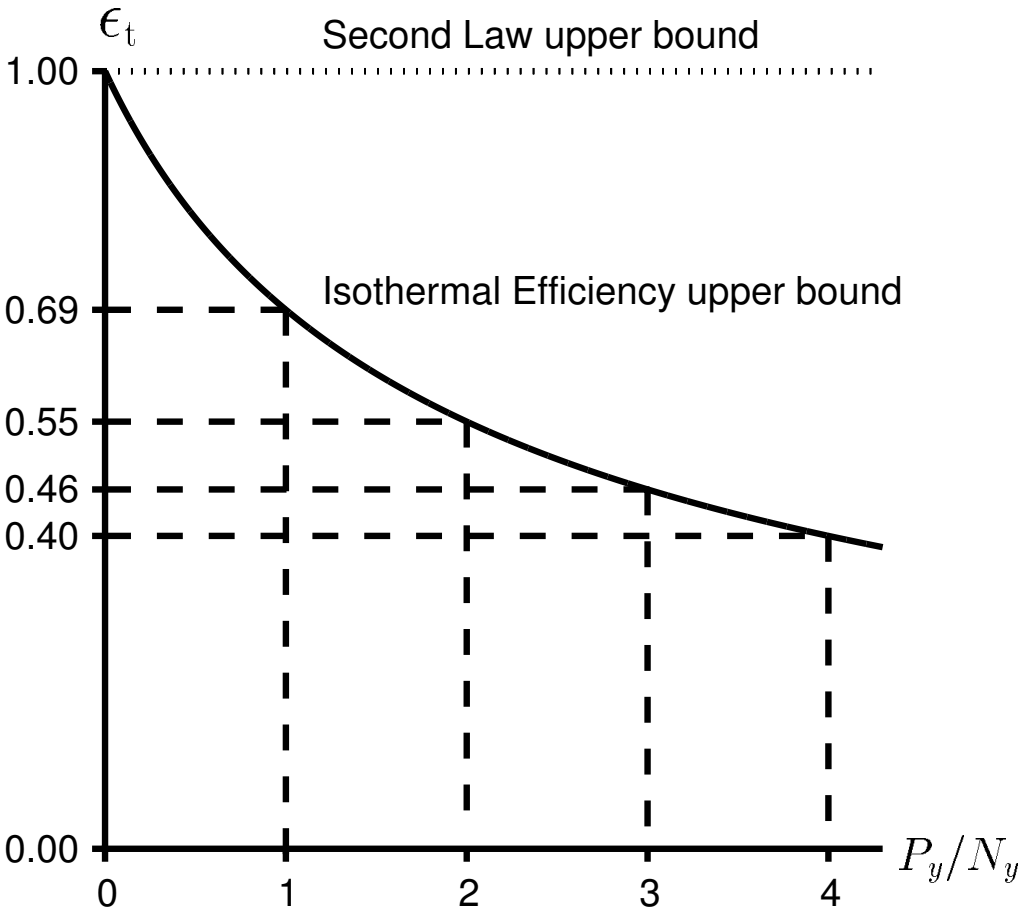

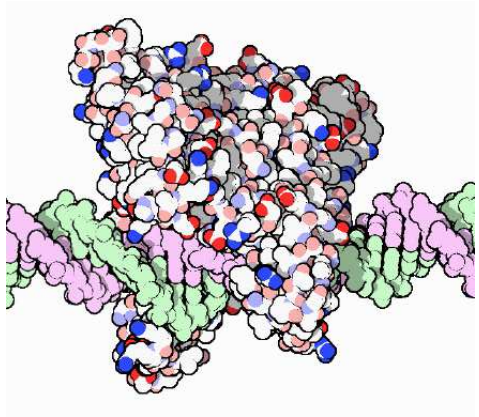

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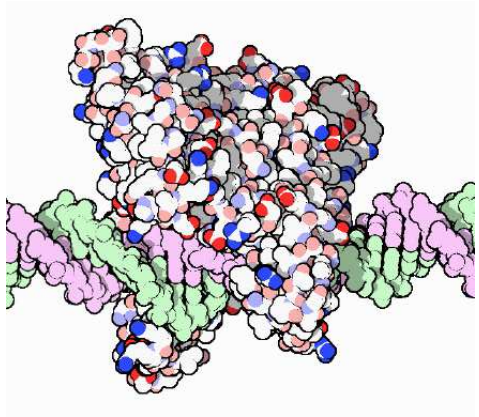

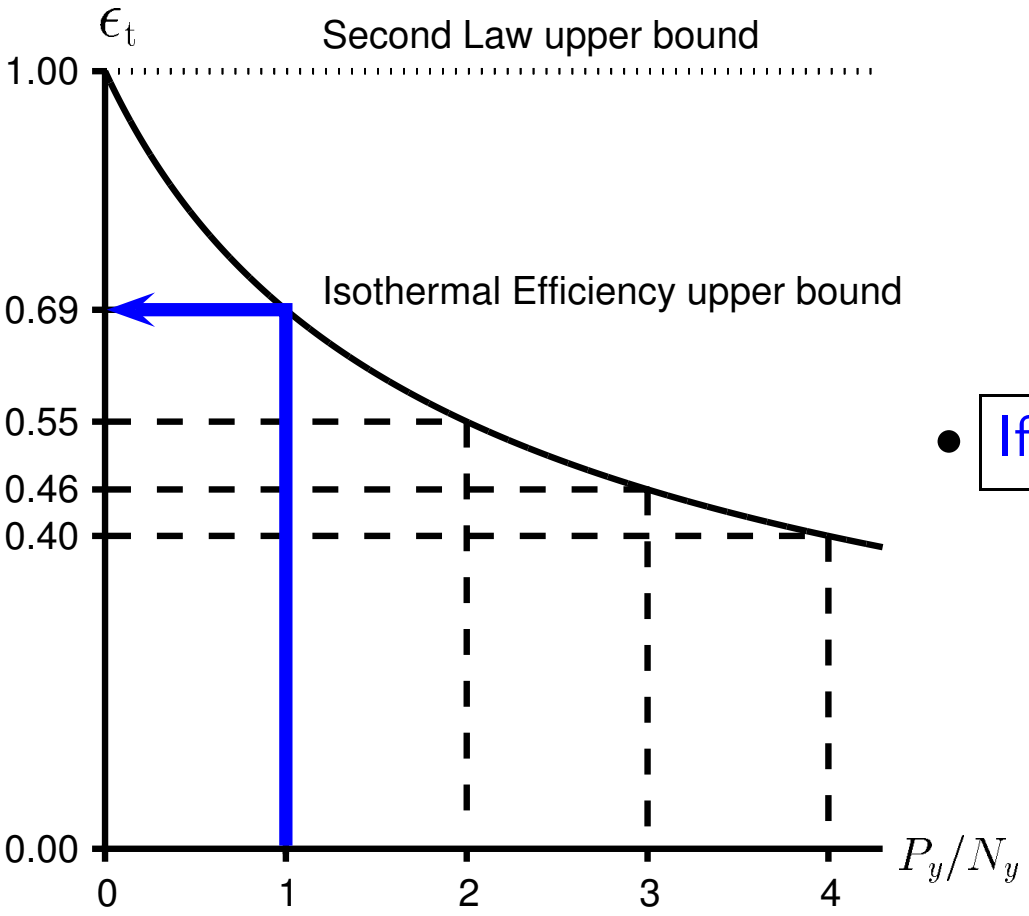

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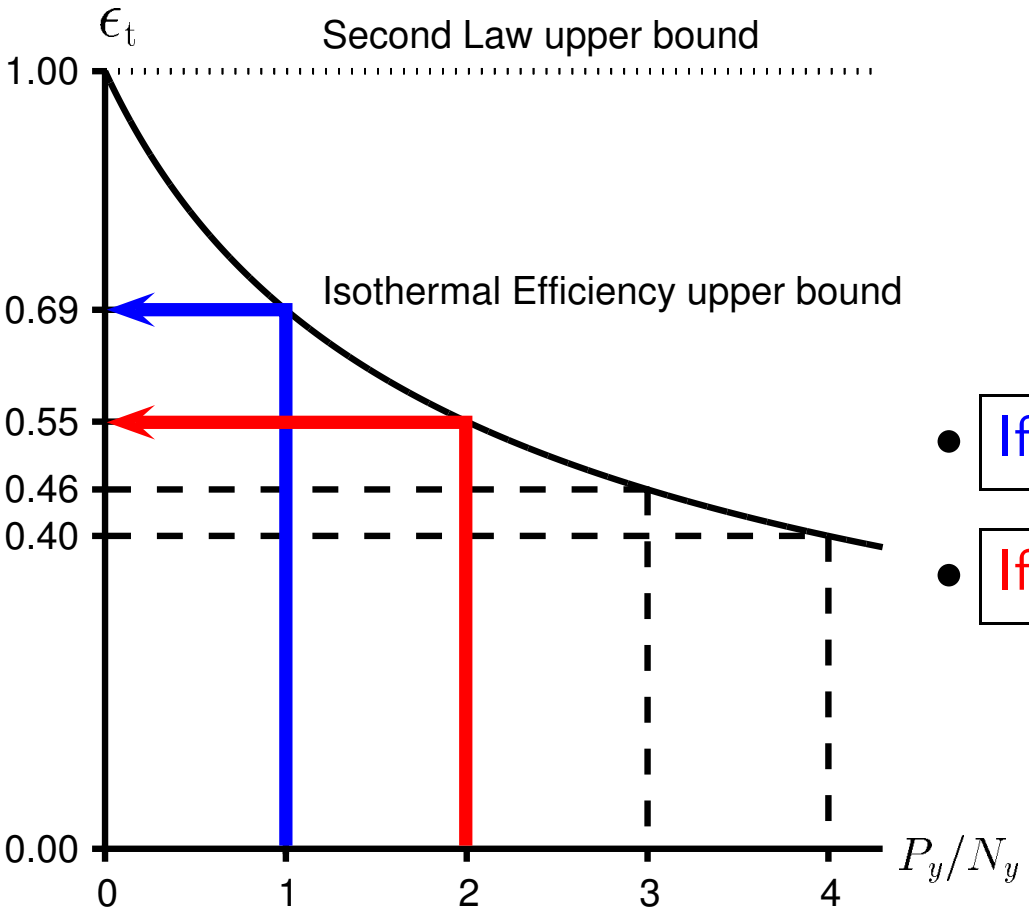

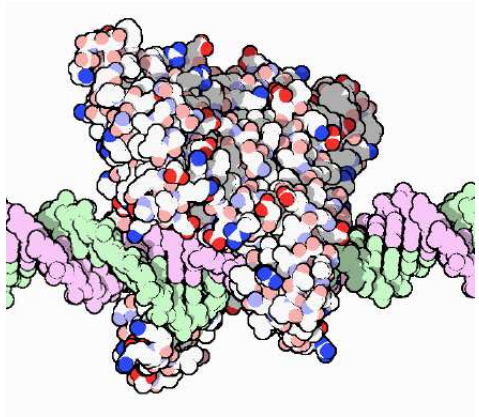

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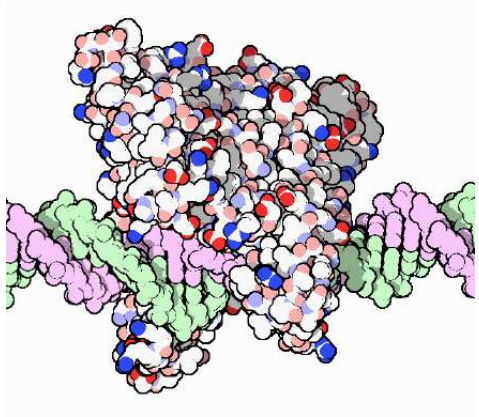

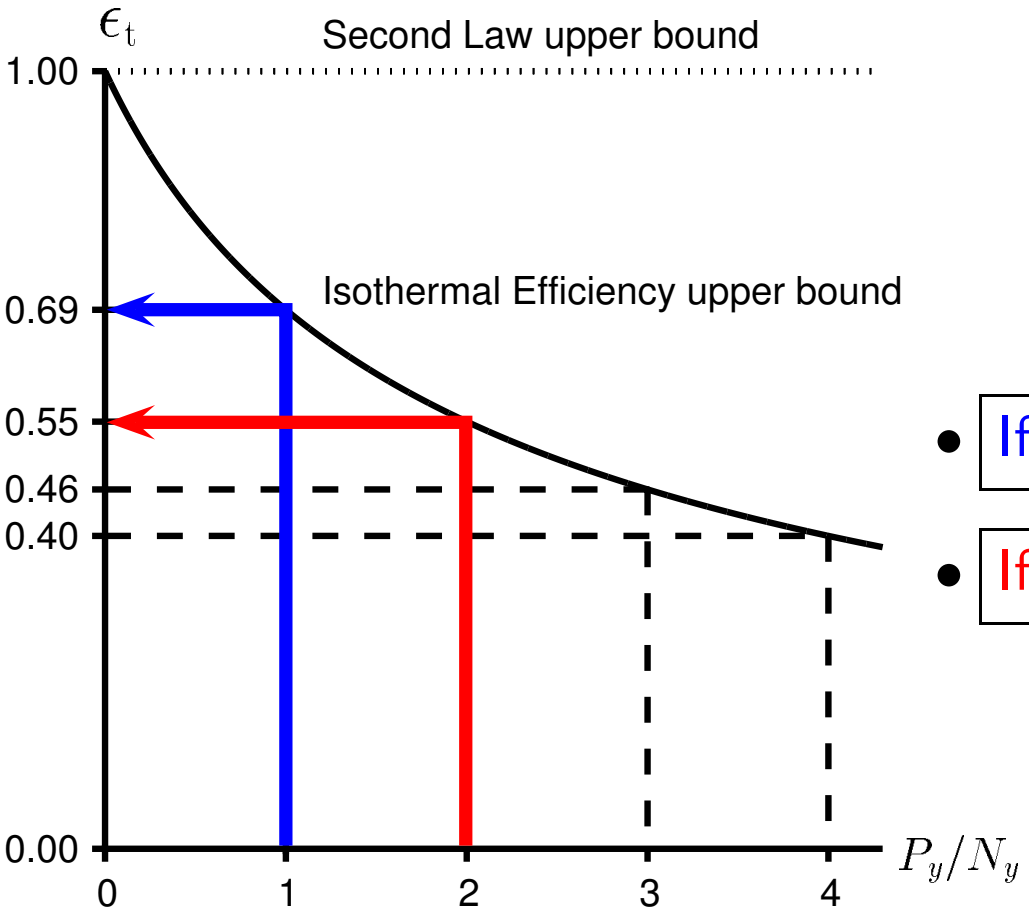

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The theory can explain 55% ecological systems!

Ant Communities and Fire

Environment	State	Evenness	P/N

- The P/N ratio can be computed *BACKWARDS* from the evenness using

$$\epsilon_t = \frac{\ln\left(\frac{P}{N}+1\right)}{\frac{P}{N}}$$

with Newton's method
assuming evenness is maximized for a given P/N.

Ant Communities and Fire

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Farji-Brener.Bettinelli2002 Diversity and Distributions, 8:235-243, 2002

Ant Communities and Fire

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- Class 3 has an evenness of $\frac{\ln(3+1)}{3} = 0.46$, between the Steepe values!

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- Hypothesis: Class 2 and Class 3 are stressed ecosystems

Farji-Brener.Bettinelli2002 Diversity and Distributions, 8:235-243, 2002

Healthy Human Microbiota PART 4

Body Habitat	color key	n	Evennes
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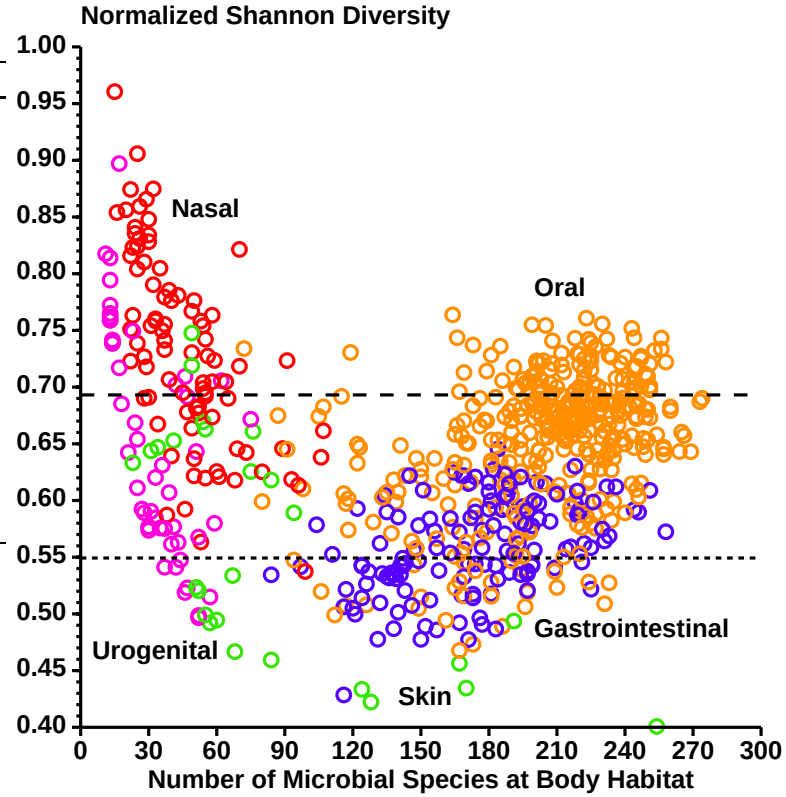

Huttenhower.White2012 Nature, 486:207-214, 2012 http://hmpdacc.org/HMSMCP/

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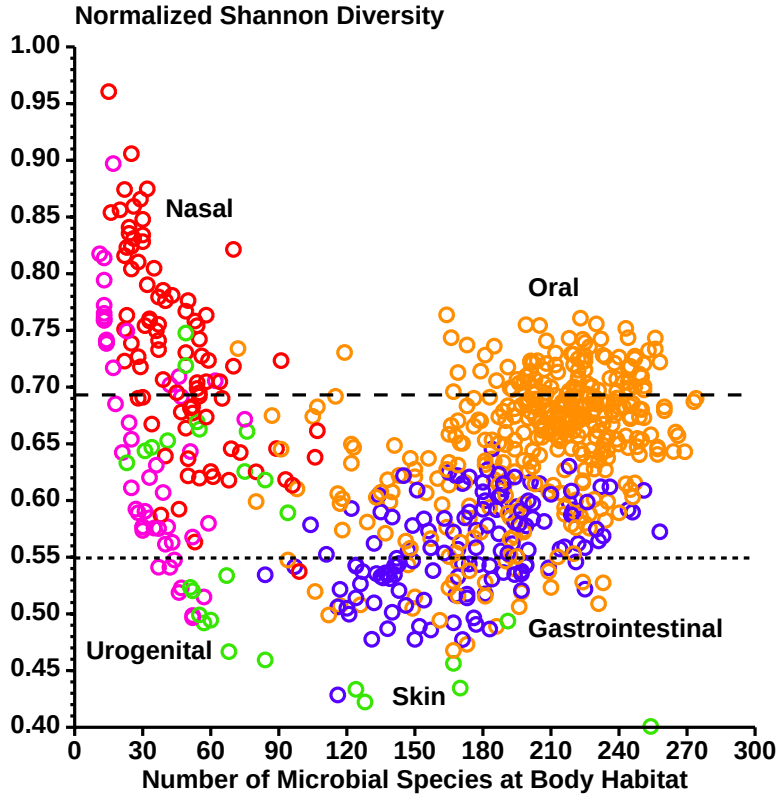

Location	evenness	possible stress
Oral-attached keratinized gingiva = gums attached to teeth	0.57 ± 0.04	brushing teeth

Huttenhower.White2012 Nature, 486:207-214, 2012 http://hmpdacc.org/HMSMCP/

Healthy Human Microbiota PART 4

Body Habitat	color key	n	Evennes
Nasal	red	87	0.73 ± 0.09
Urogenital	purple	56	0.68 ± 0.14
Oral-attached keratinized gingiva	orange	6	0.57 ± 0.04
Oral-buccal mucosa	orange	107	0.60 ± 0.06
Oral-palatine tonsils	orange	6	0.69 ± 0.05
Oral-saliva	orange	3	0.67 ± 0.03
Oral-subgingival plaque	orange	7	0.74 ± 0.02
Oral-supragingival plaque	orange	118	0.69 ± 0.04
Oral-throat	orange	7	0.67 ± 0.05
Oral-tongue dorsum	orange	128	0.66 ± 0.03
Oral	orange	382	0.65 ± 0.06
Skin	green	26	0.56 ± 0.10
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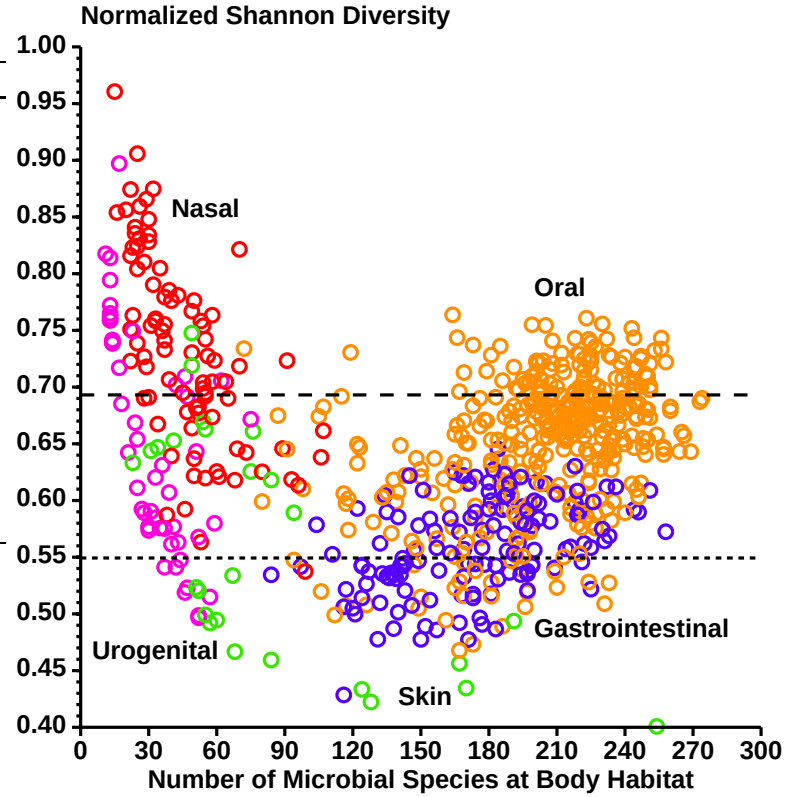

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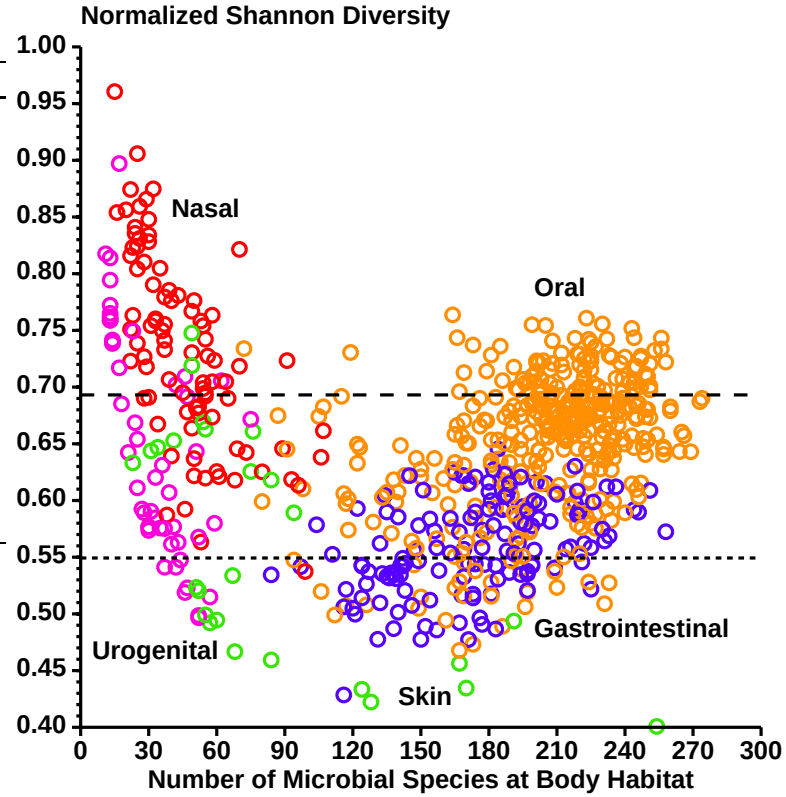

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skin	0.56 ± 0.10	washing

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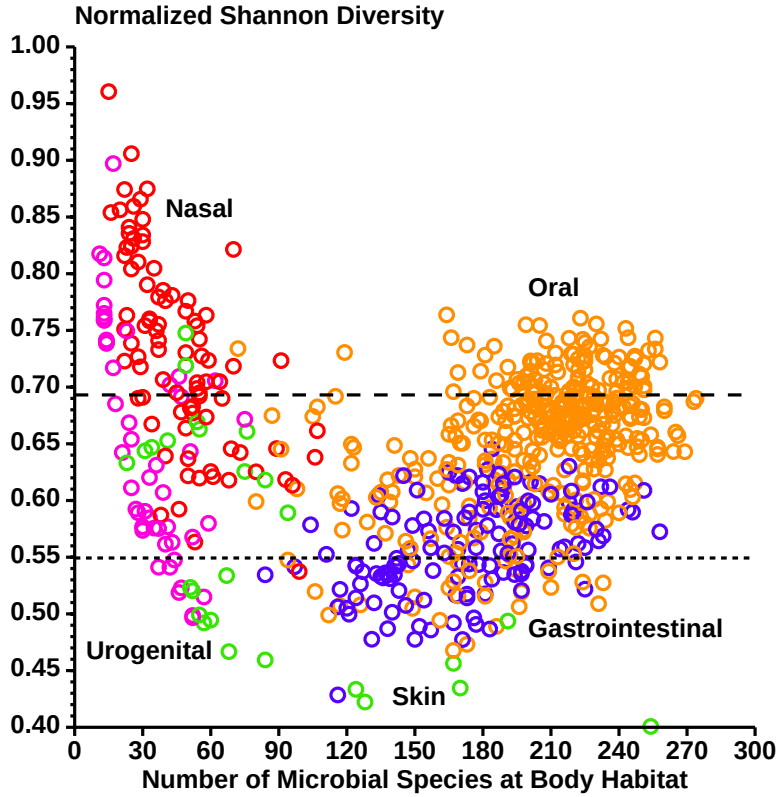

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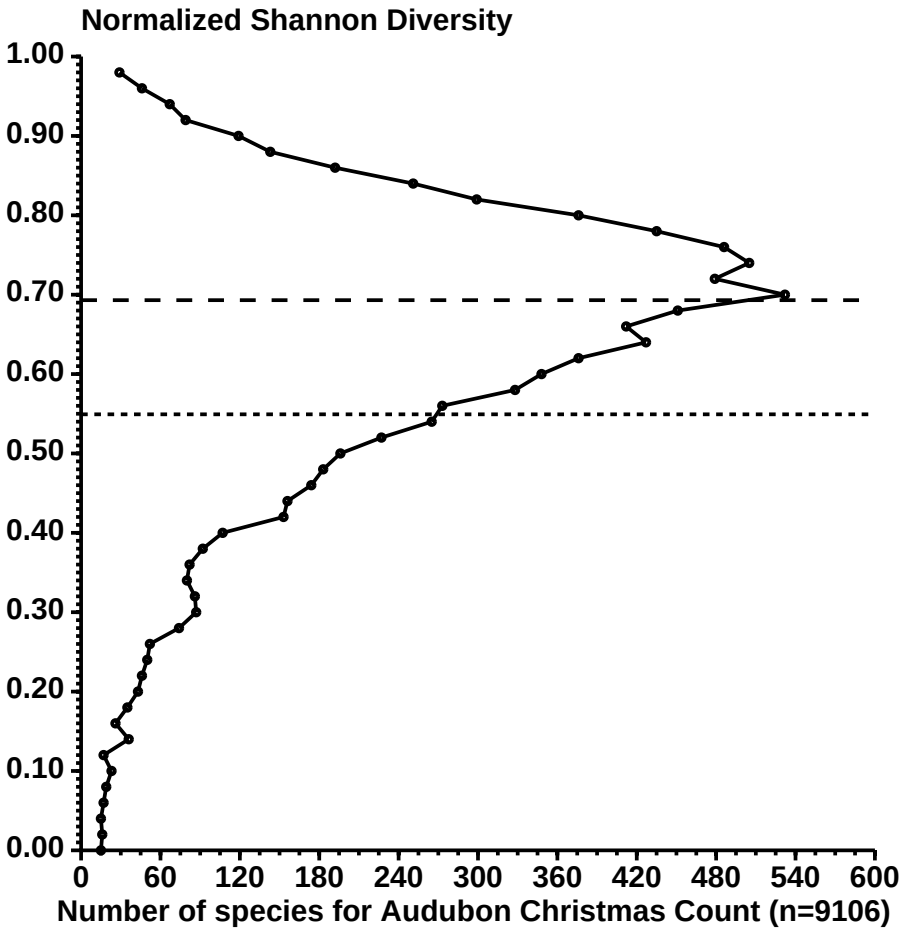
Birds from Audubon Christmas Bird Count



- 1900 to 1950, 9106 bird counts - evenness: 0.64 ± 0.18

Data source: `http://www.christmasbirdcount.org` on 2014 March 31

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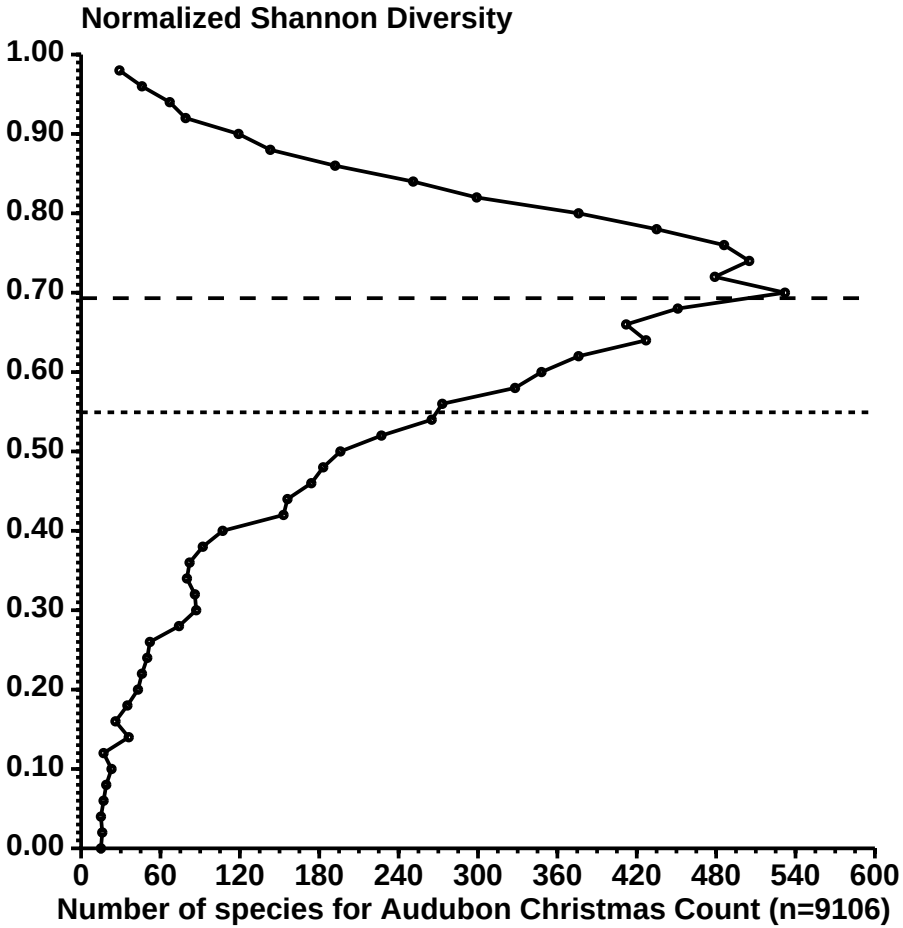

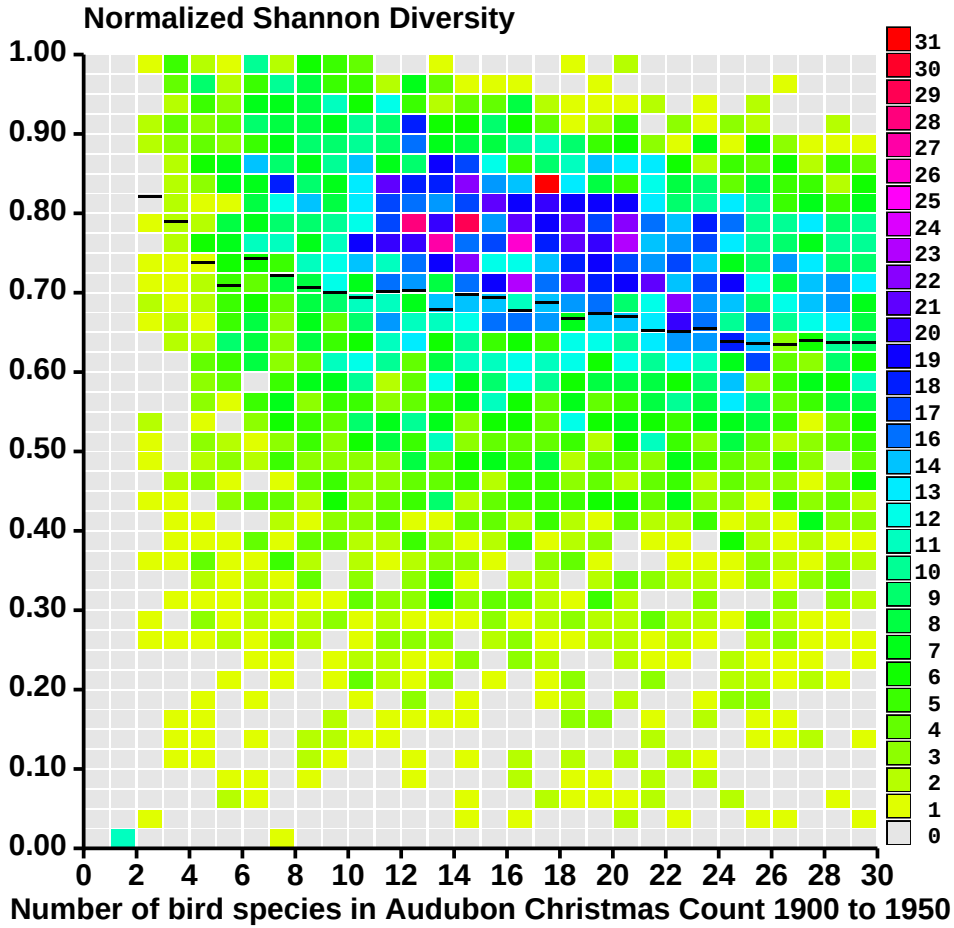

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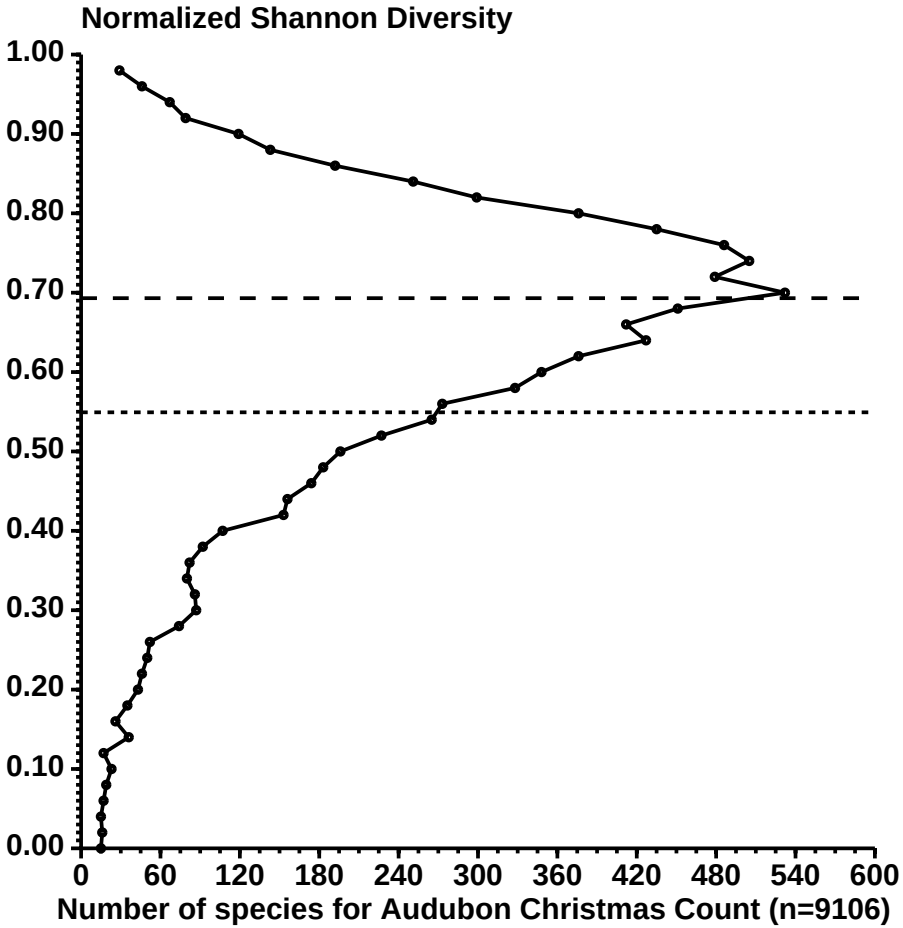

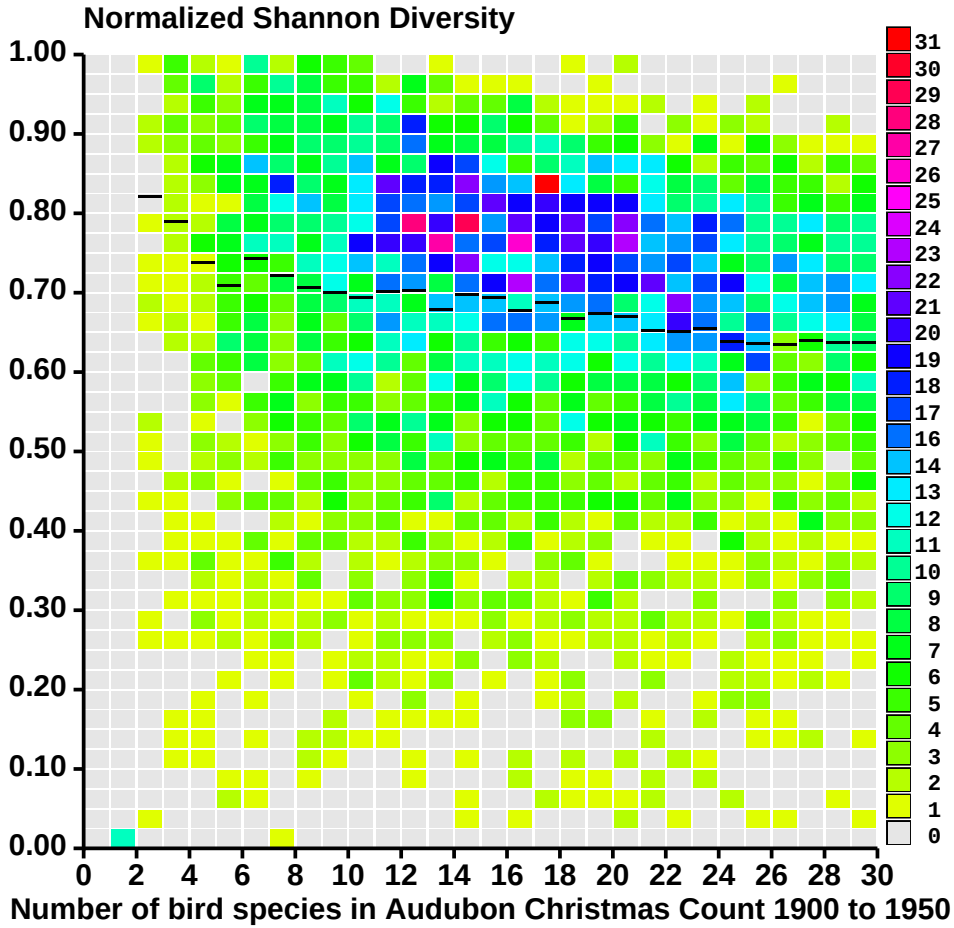

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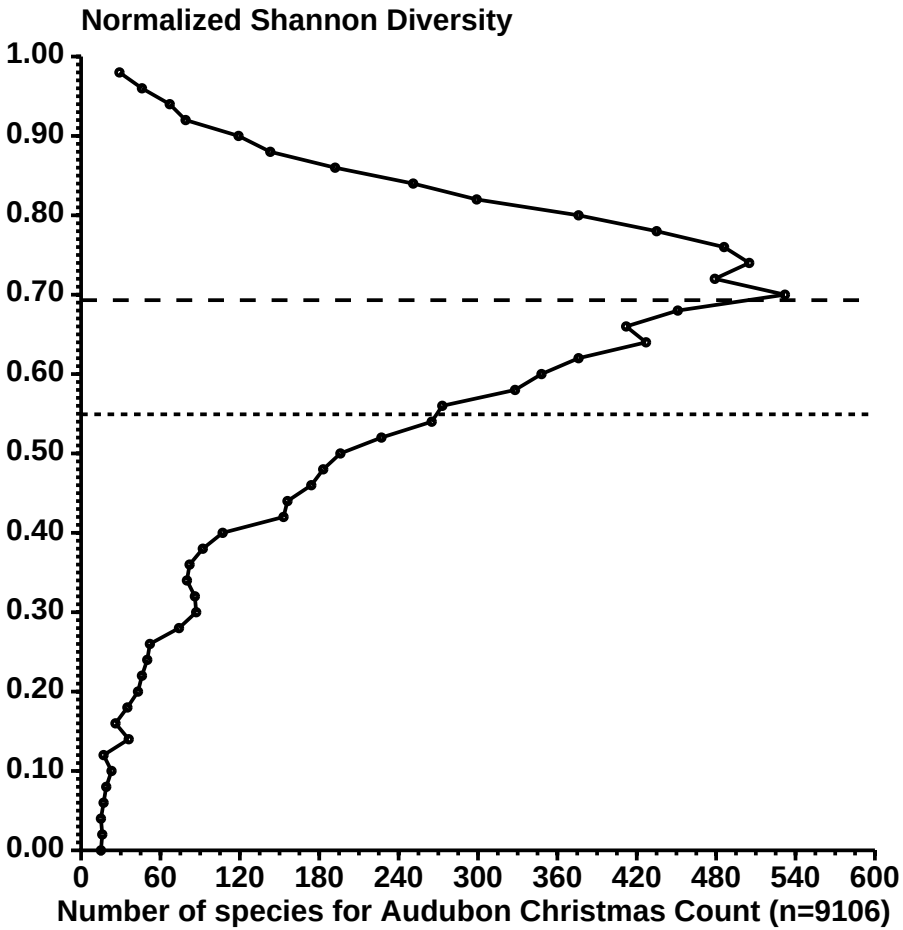

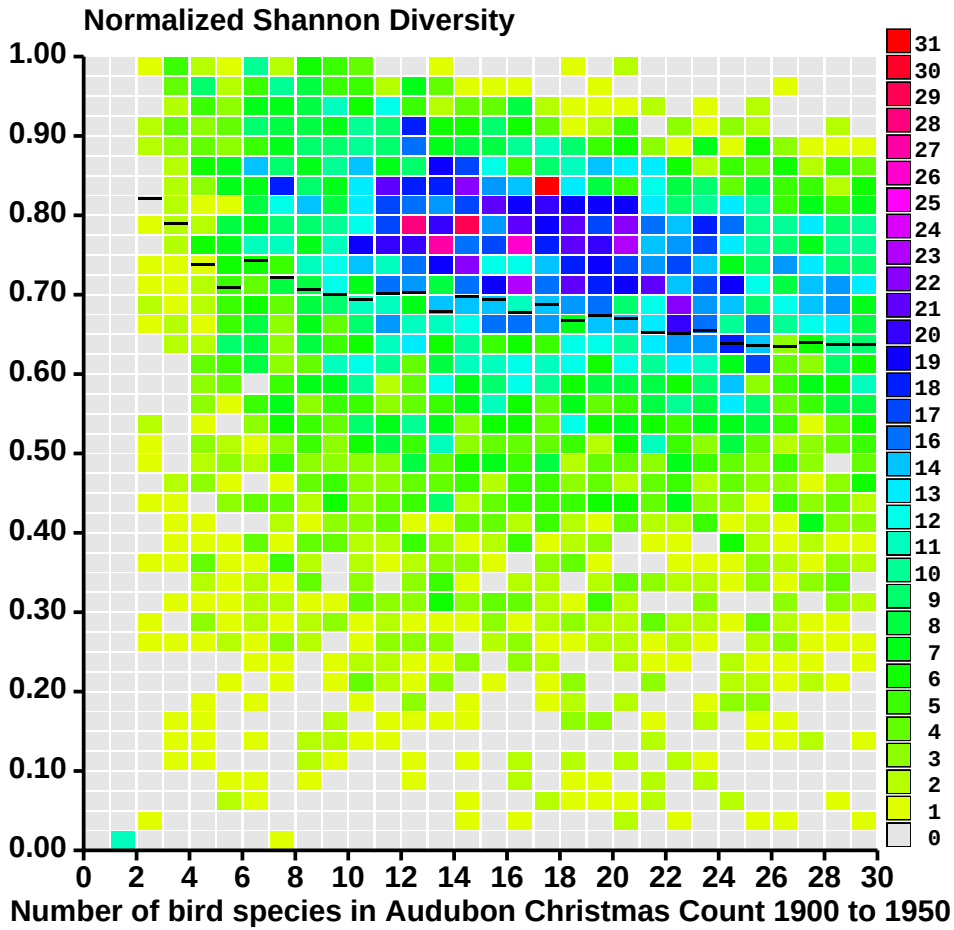

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- Dashes indicate the average for that number of species.

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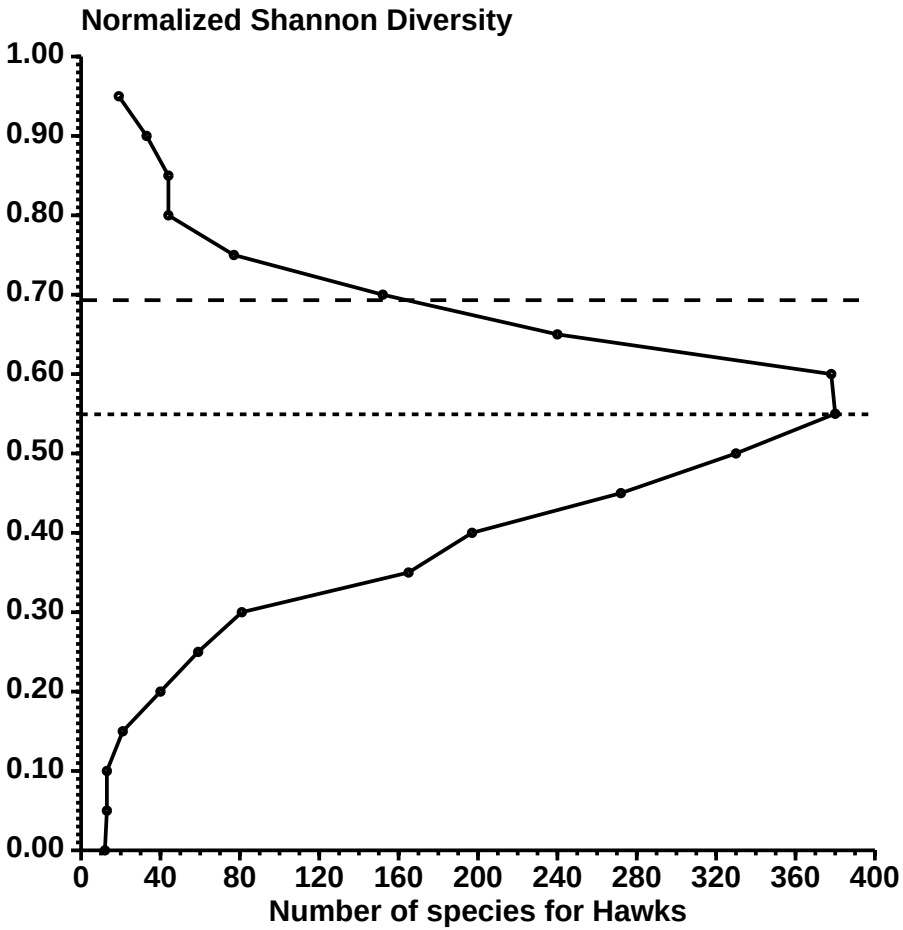
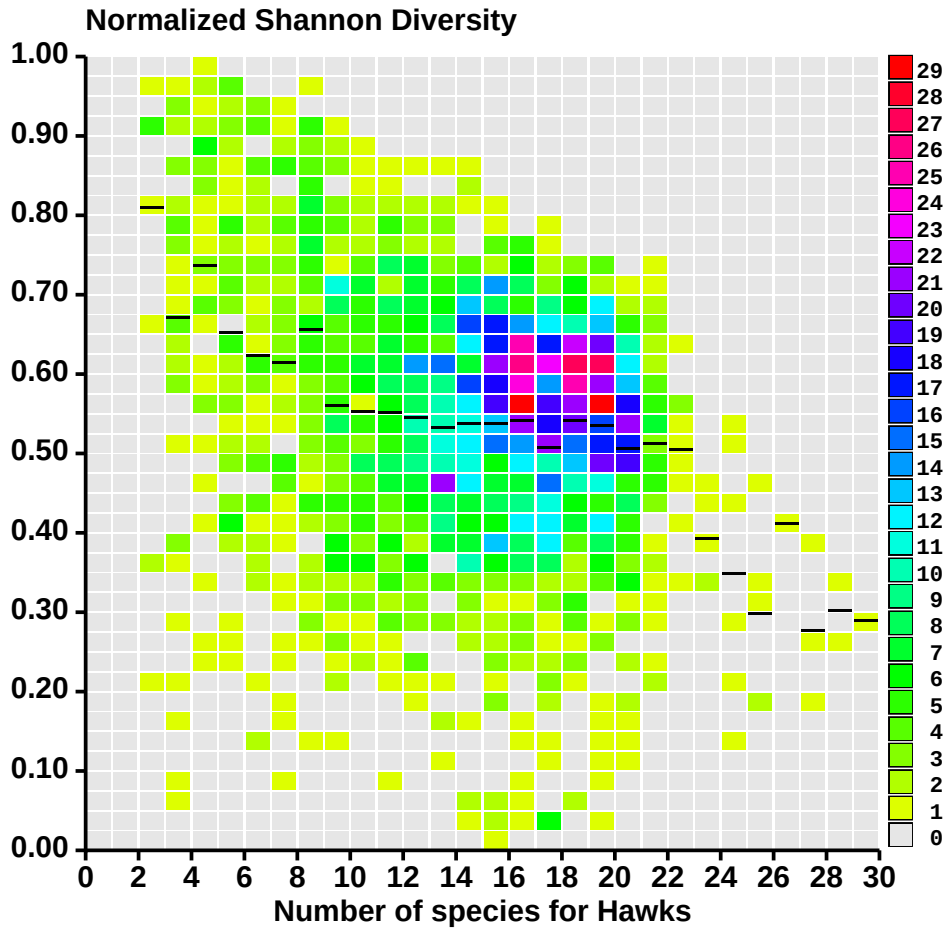
Hawks

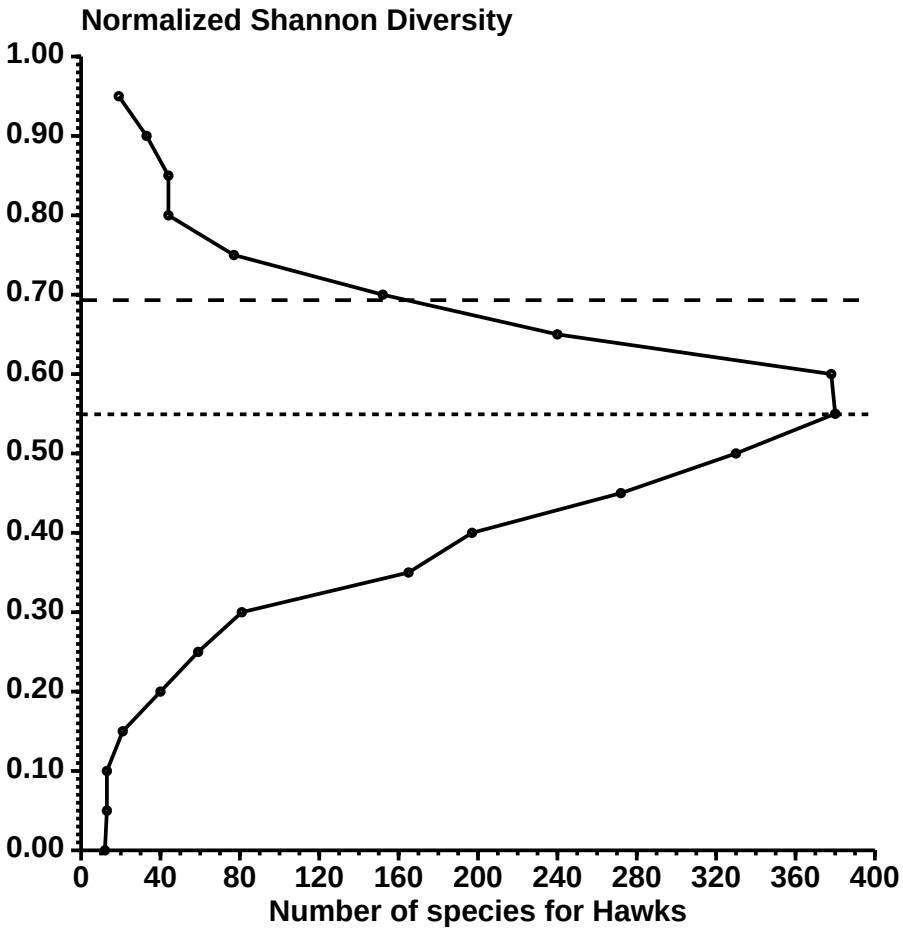


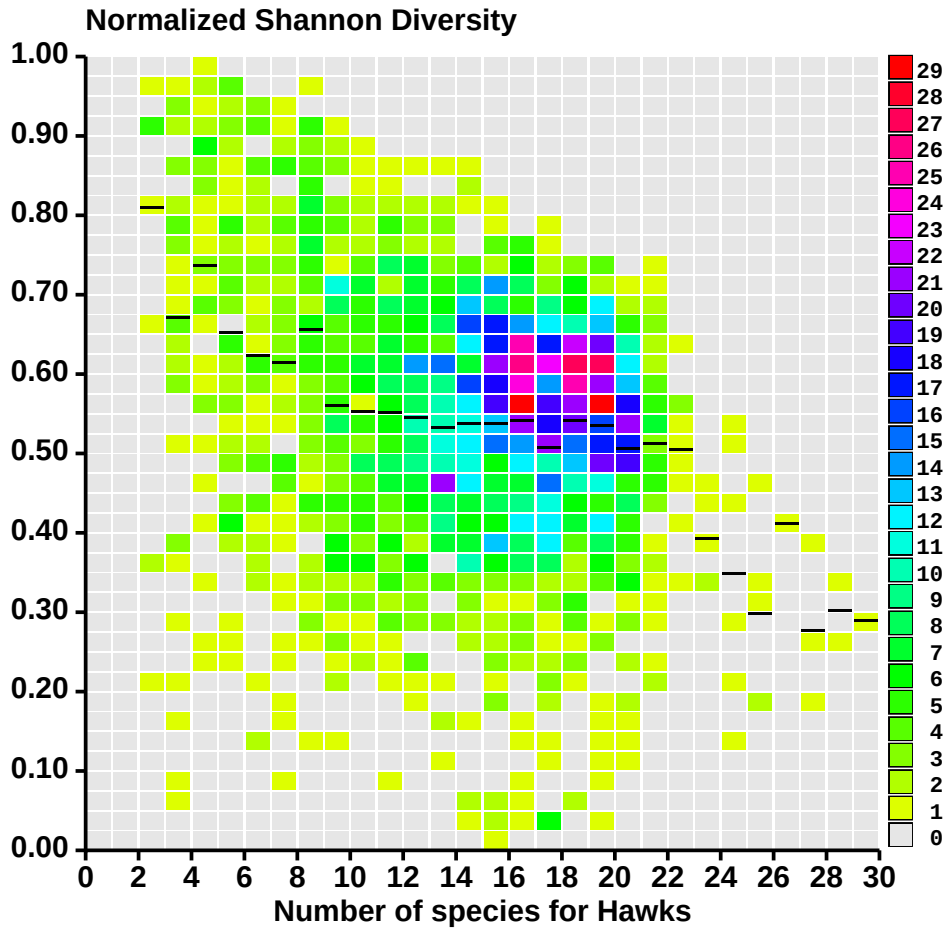


- Hawk counts for 2570 months from 1987 to 2013 in 108 locations of 28 states and provinces in North America

Data source: `http://hawkcount.org` on 2014 March 27 and 28.

Hawks





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- Evenness: 0.55 ± 0.16; Hawks are **pure** Class 2!

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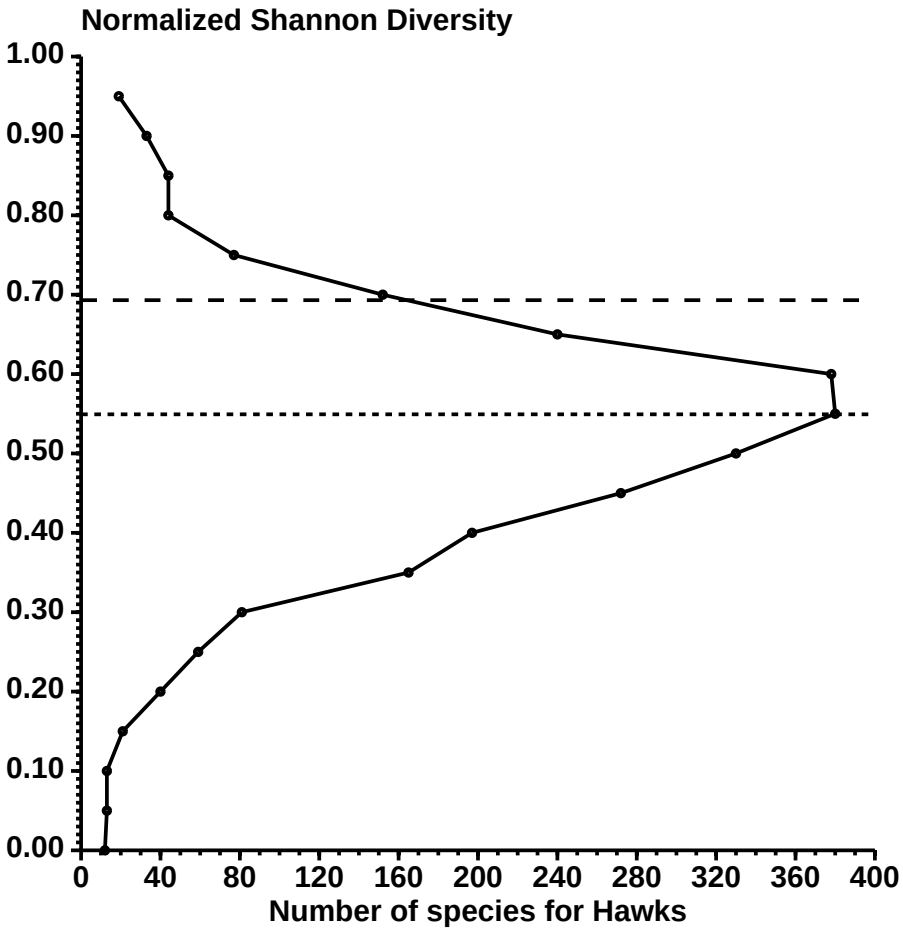
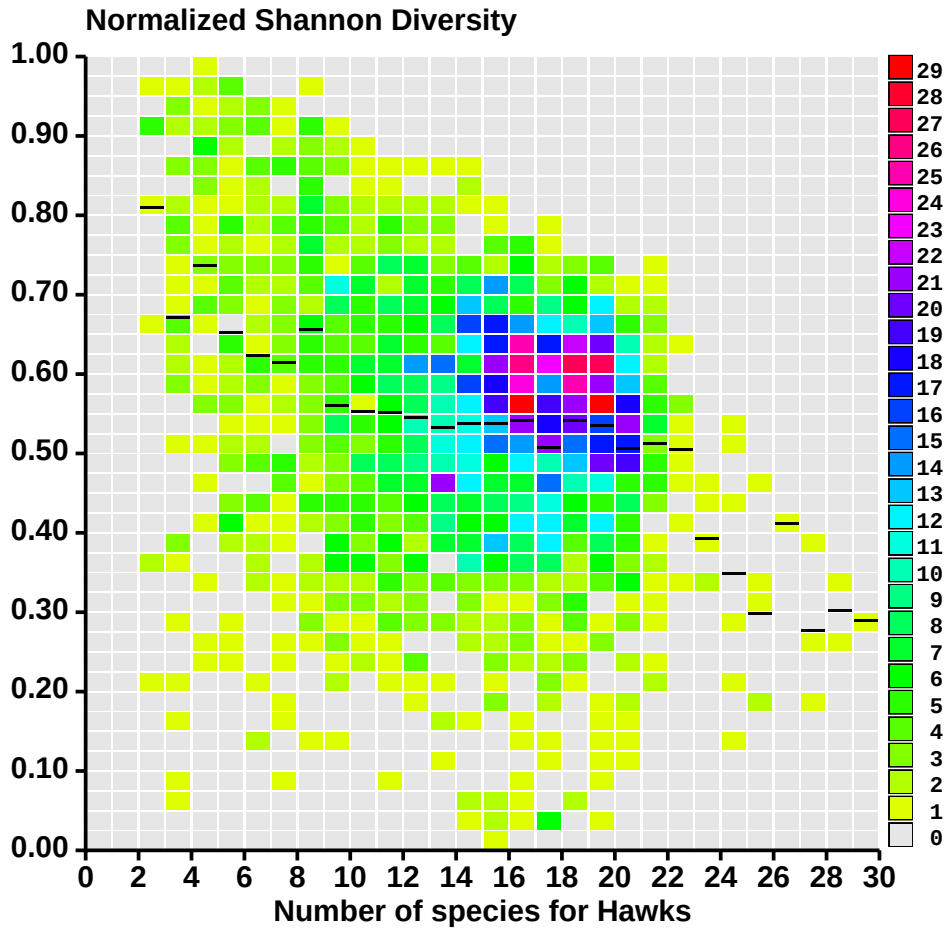
Hawks





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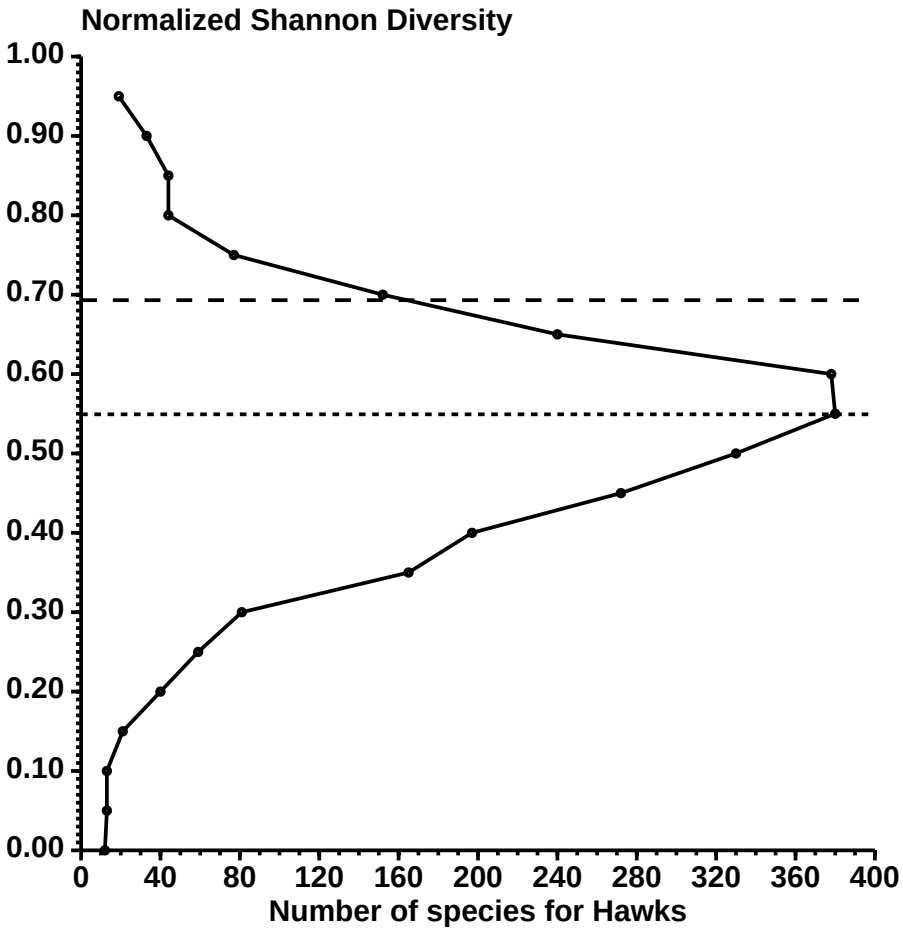

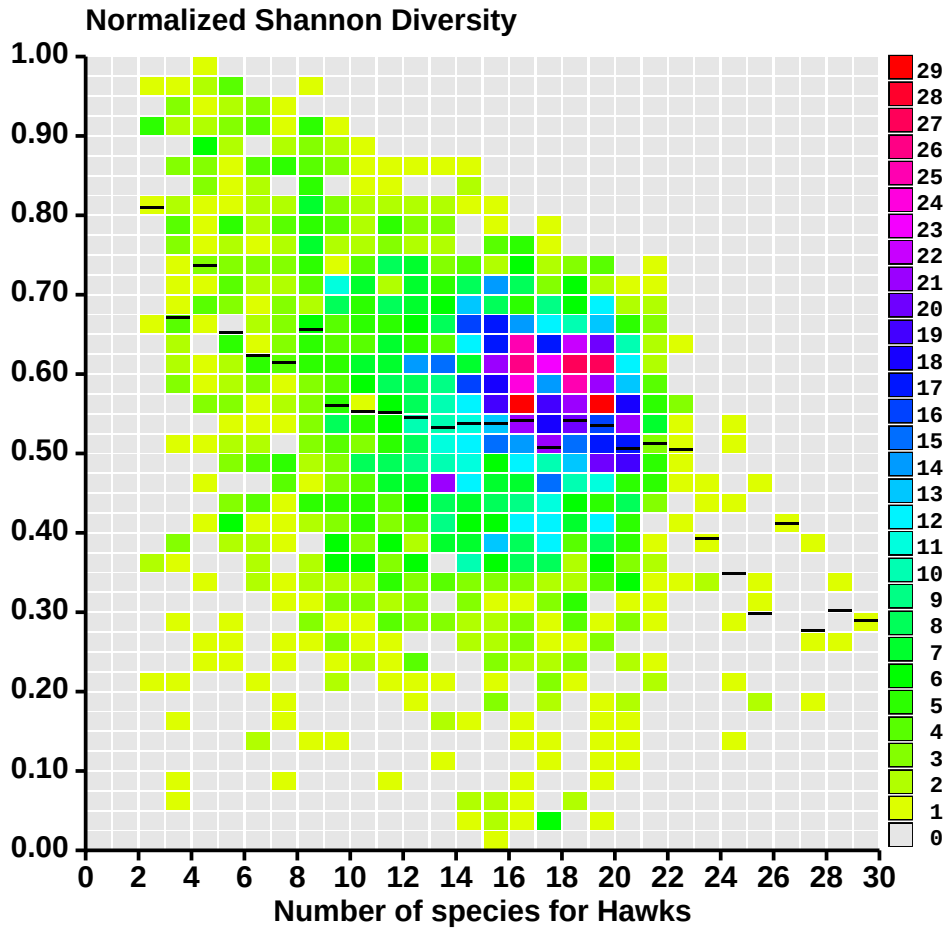

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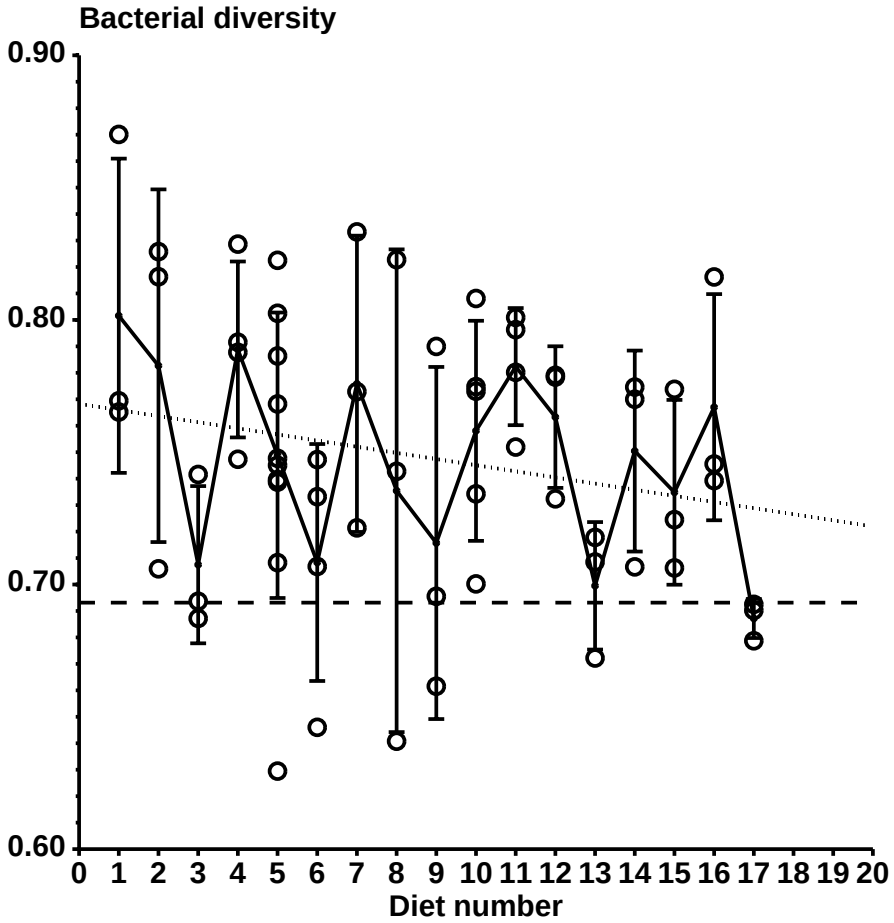
Human gut microbiota gavaged into mice



- Faith *et. al* counted species of bacteria under different diet regimens.

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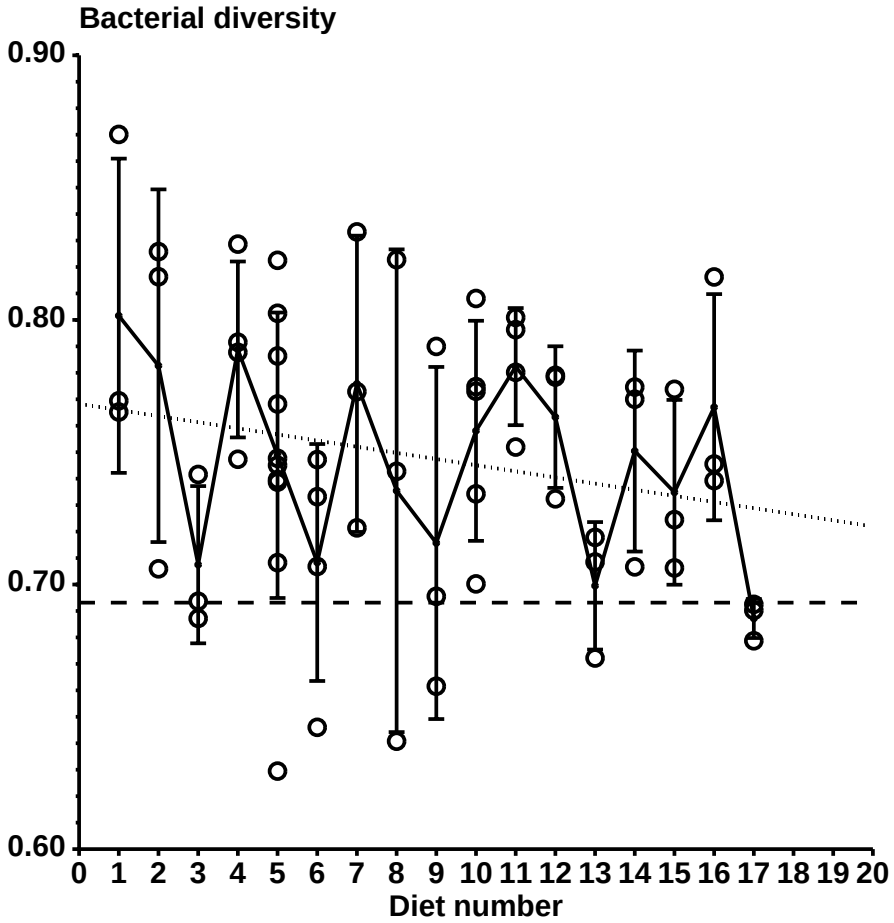

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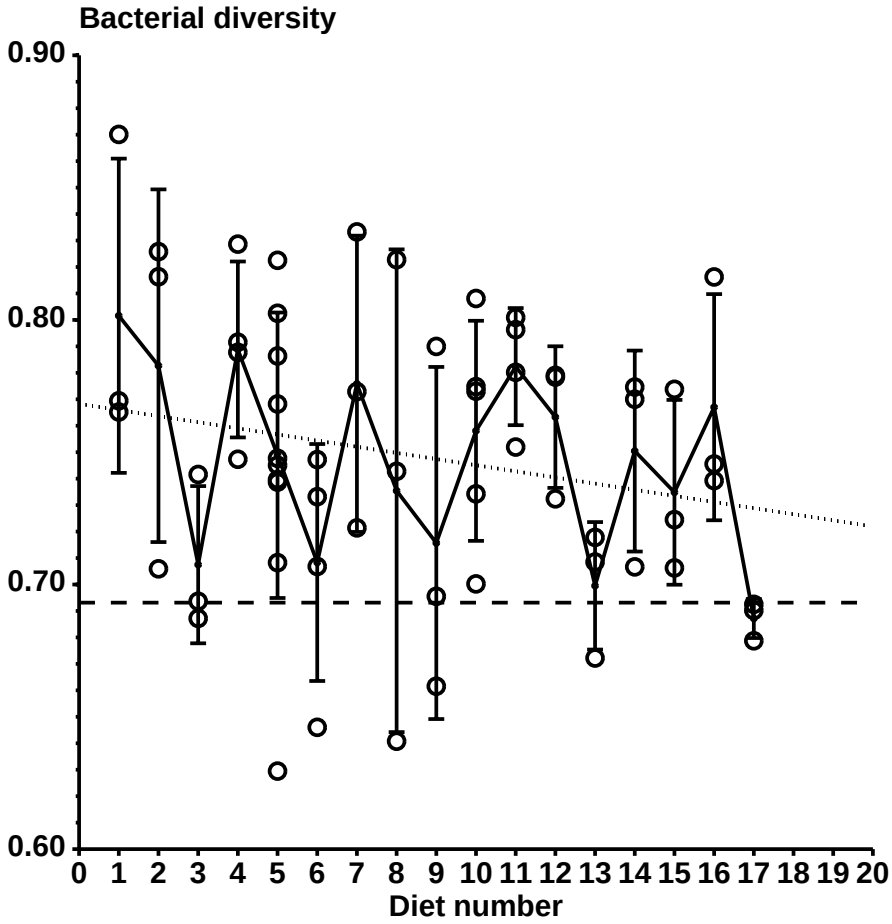

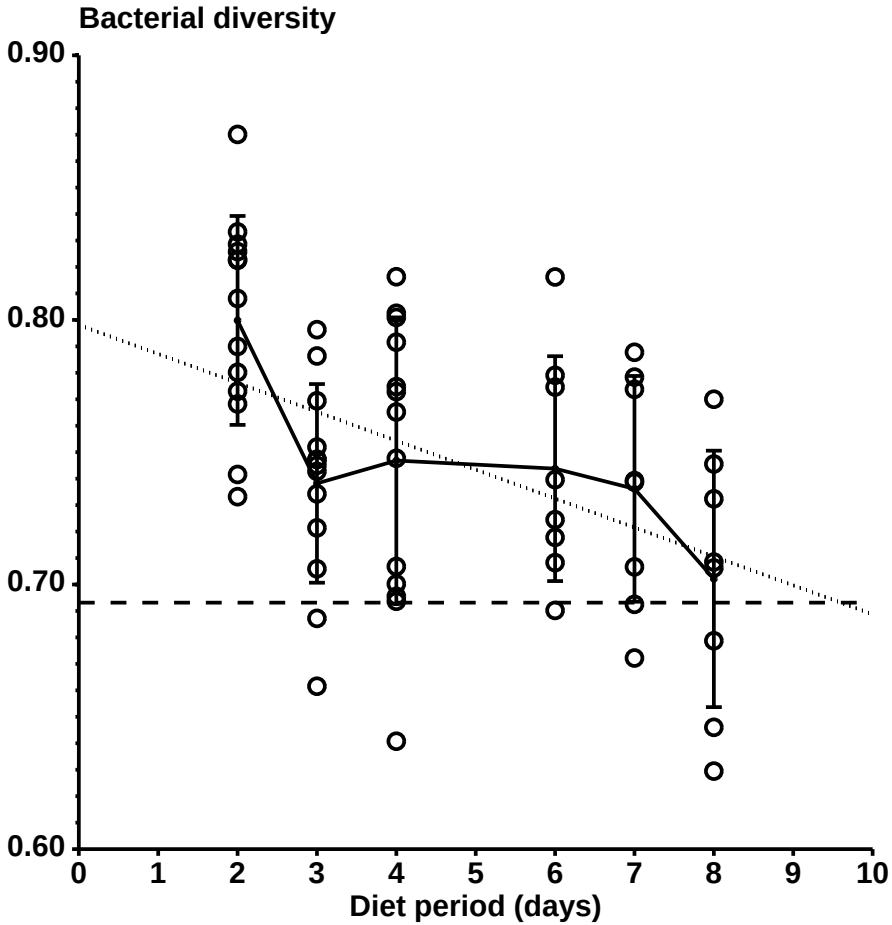

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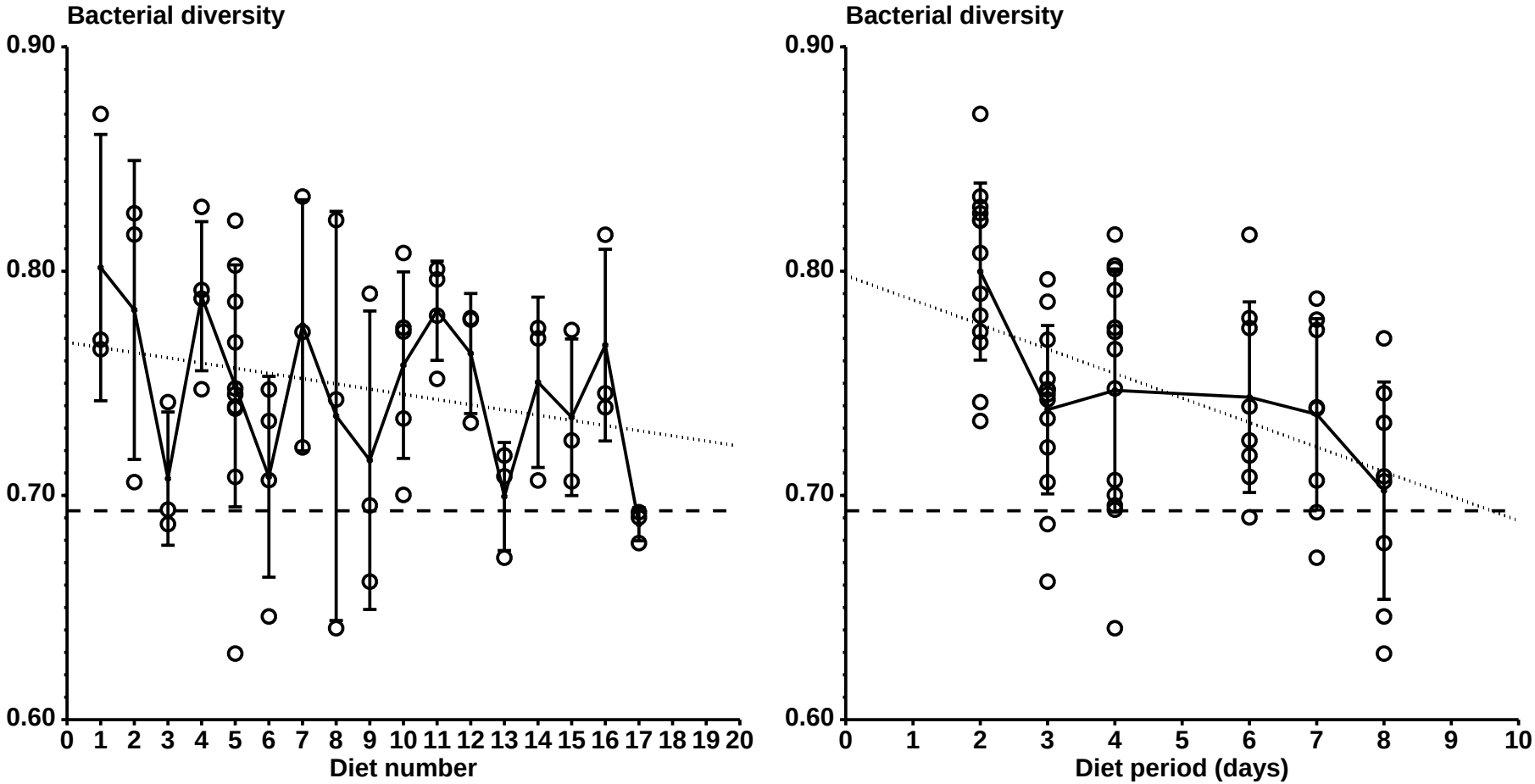

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- bacterial population evenness does not correlate with the diet ($r^2 = 0.04$)
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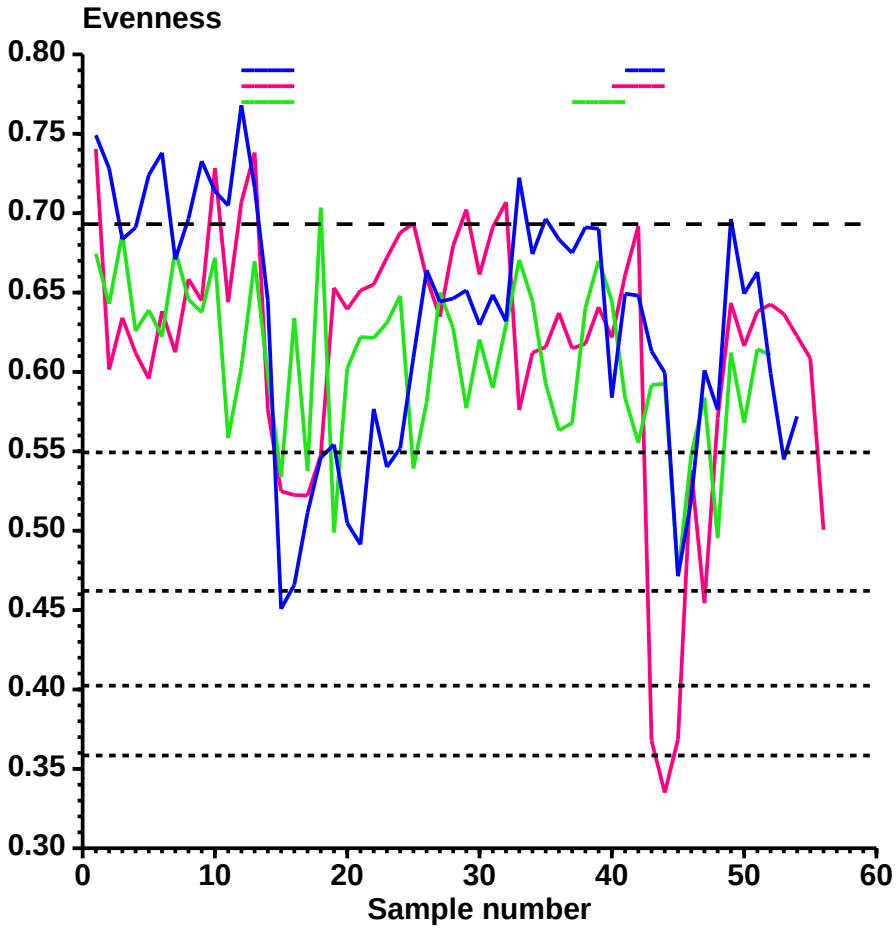
- Populations converge from an evenness of 0.80 ± 0.04 on day 2 to an evenness of 0.70 ± 0.05 on day 8.

Faith.Gordon2011 Science, 333:101-104, 2011

Effect of ciprofloxacin on human gut microbiota diversity



- Normalized Shannon diversity of gut microbiota for three subjects D (age 54, red), E (age 34, green) and F (age 28, blue) is plotted against sample number.

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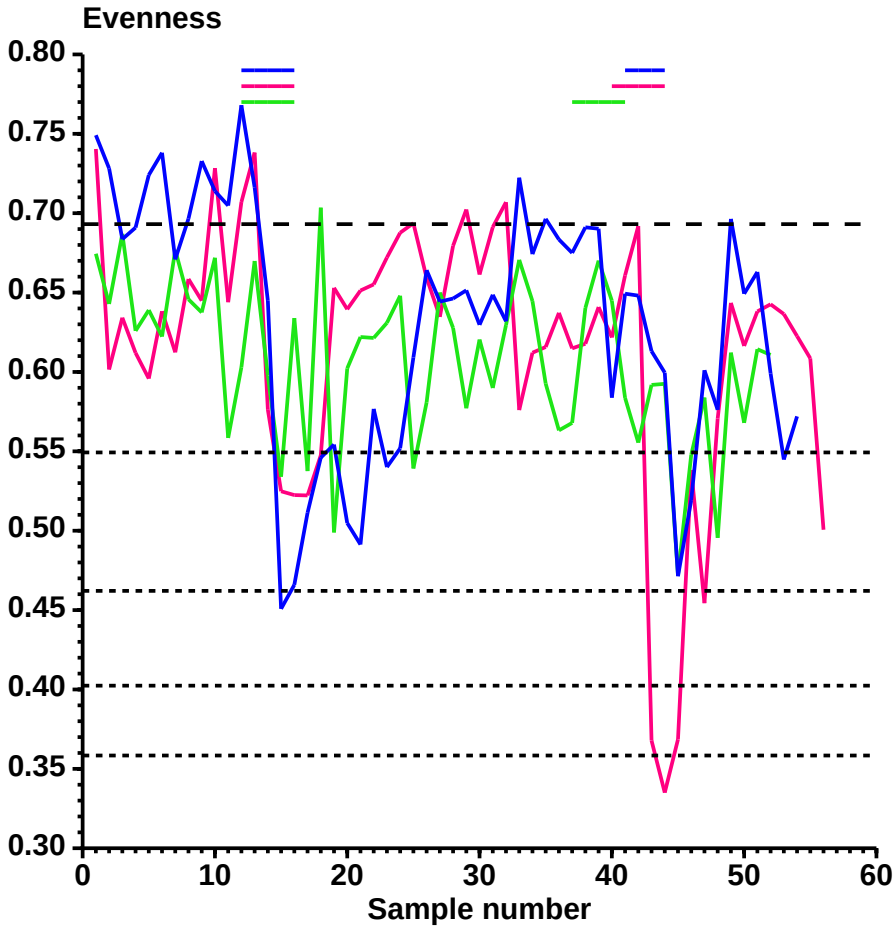

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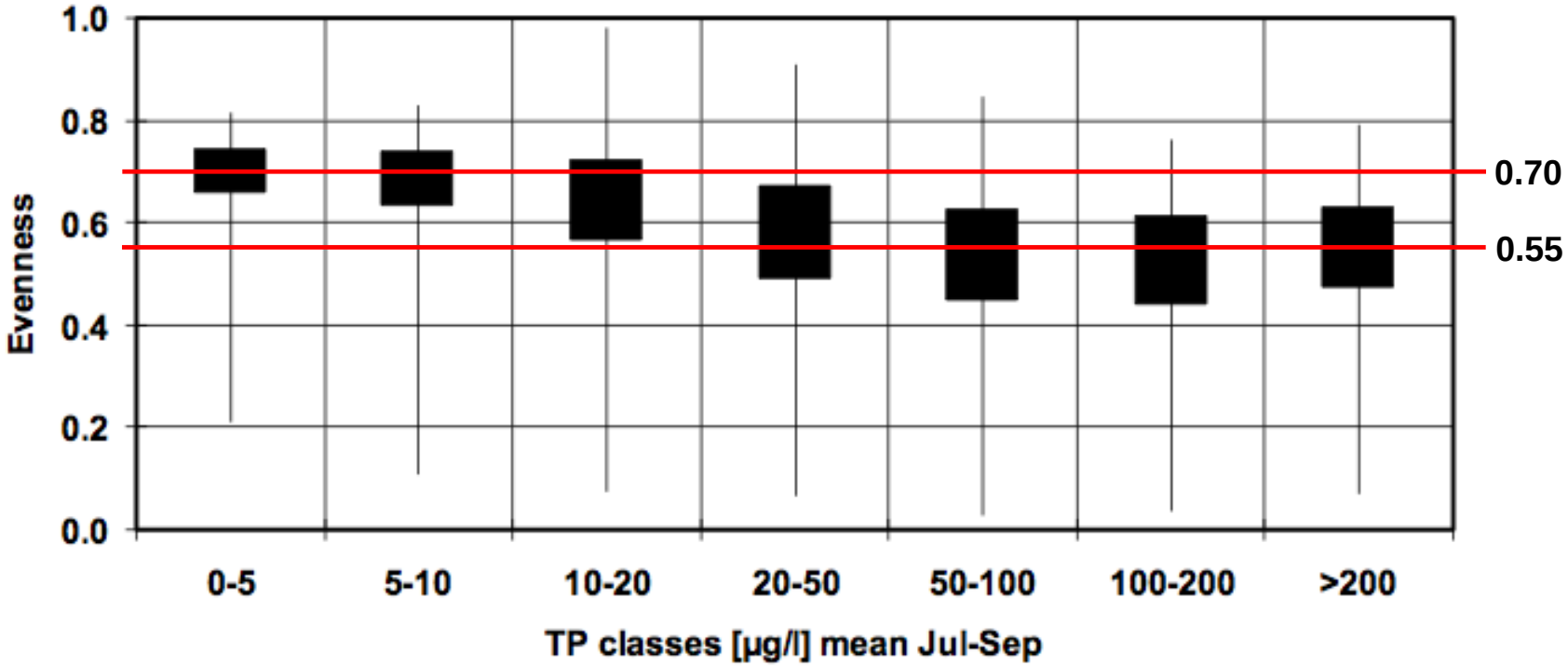
Phytoplankton Responding to Phosphate



- Evenness of phytoplankton species in 1649 European lakes *vs.* total phosphorus concentrations (TP),

From Figure 2.1 of Mischke.Pahissa2011 `http://www.wiser.eu/download/D3.1-2.pdf`

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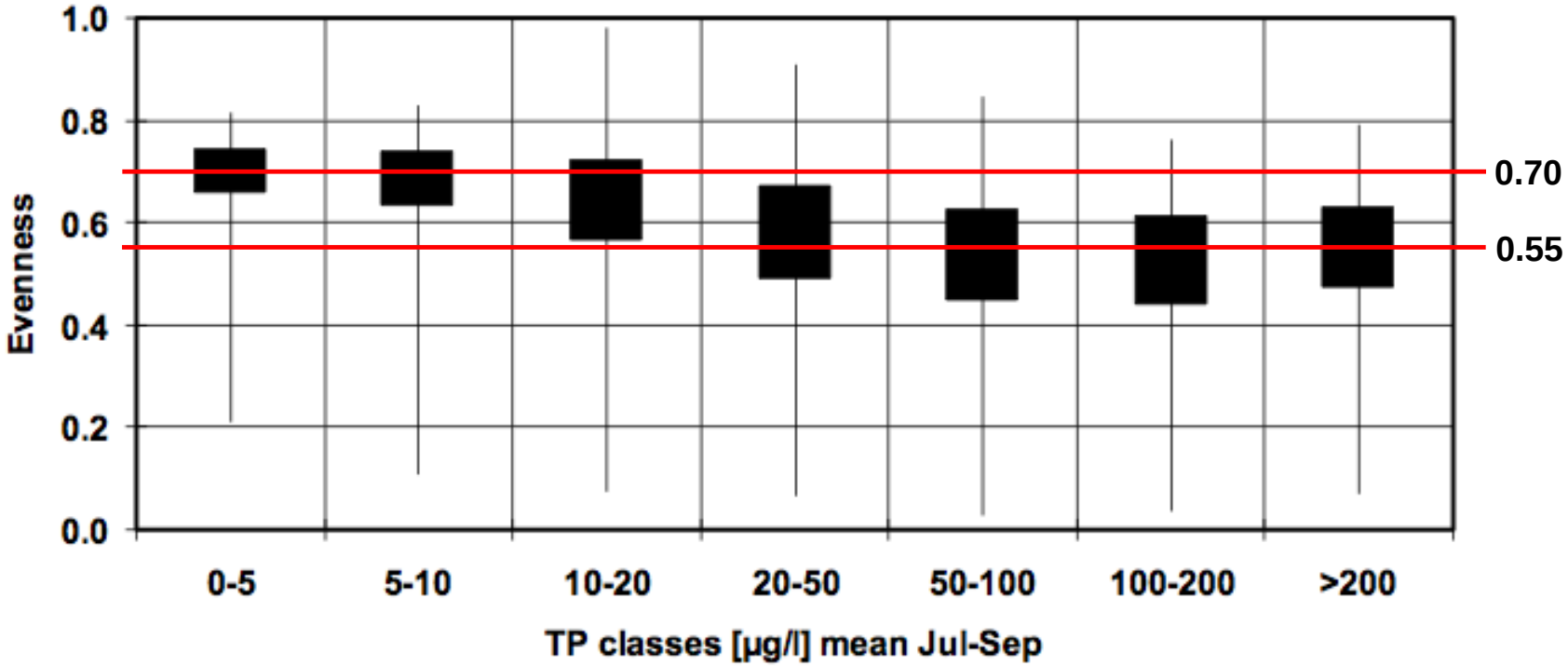

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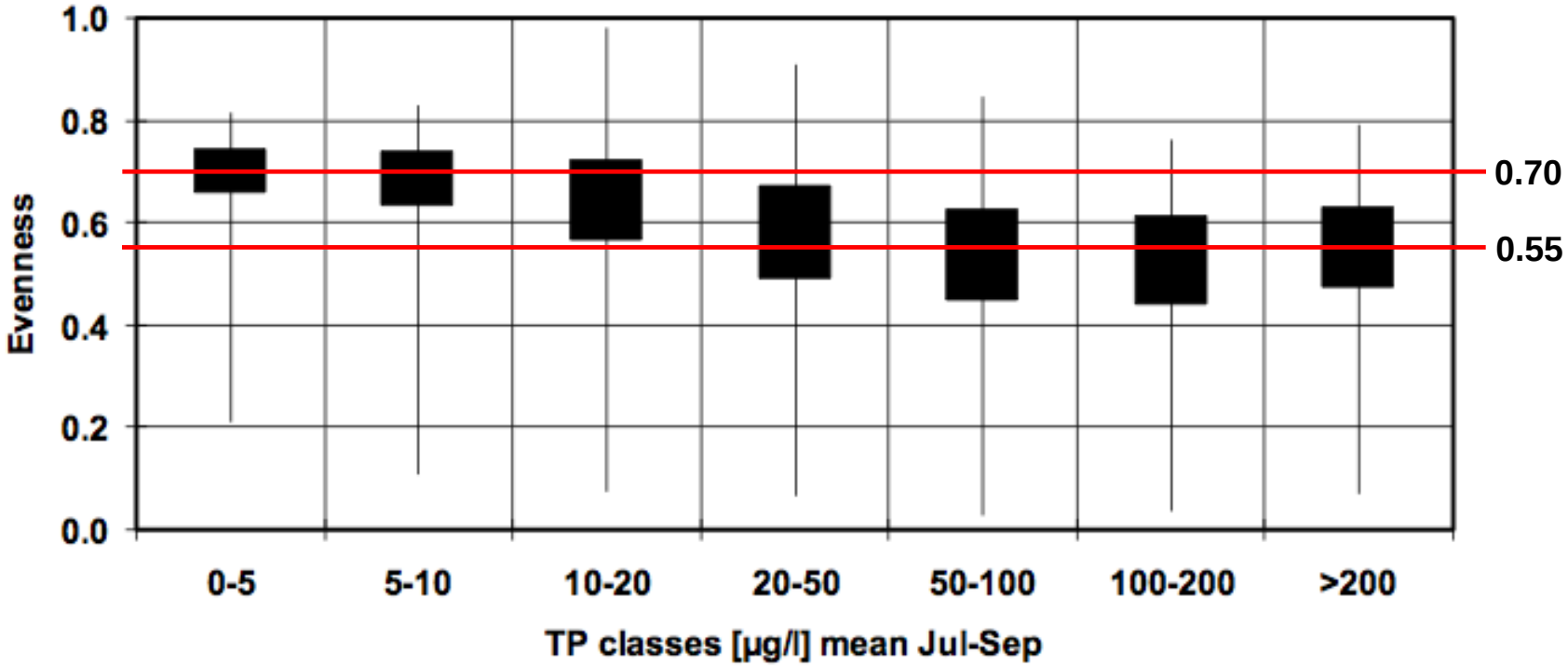

- Evenness of phytoplankton species in 1649 European lakes *vs.* total phosphorus concentrations (TP),
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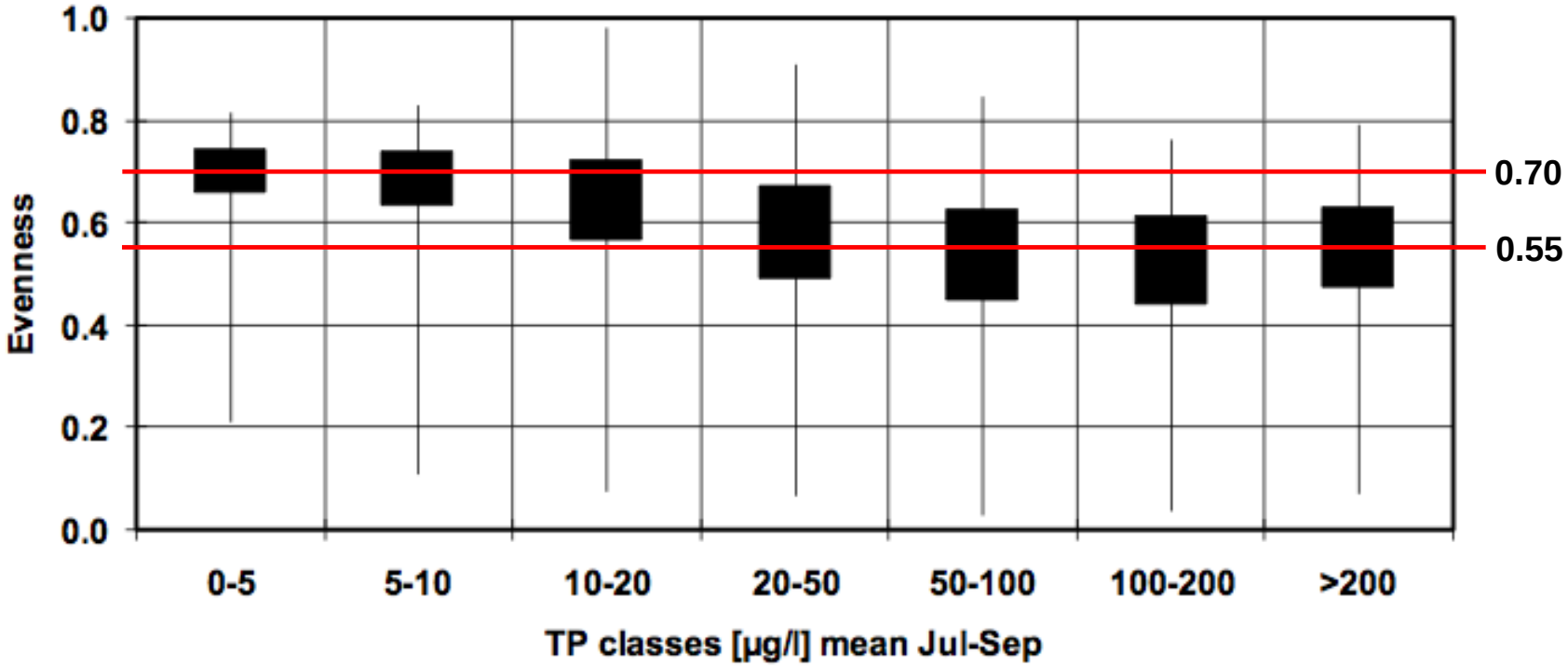

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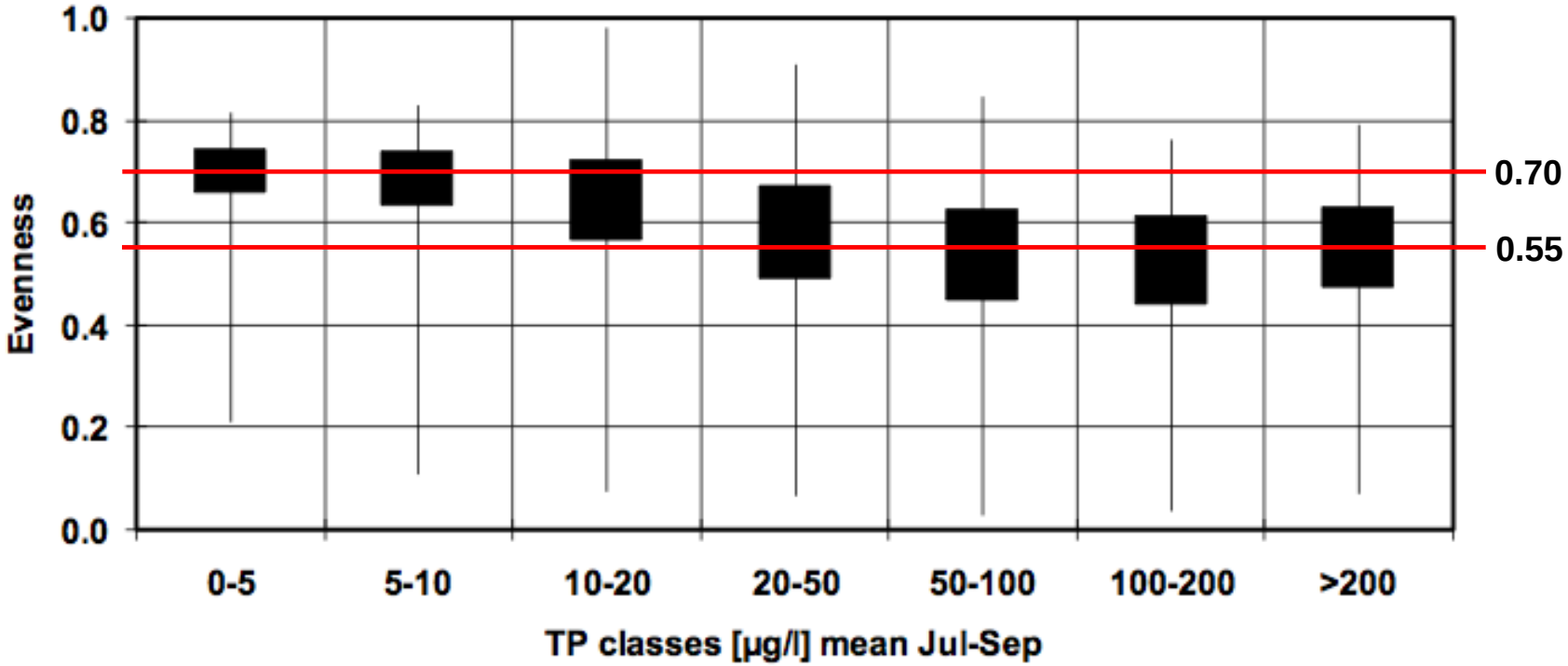

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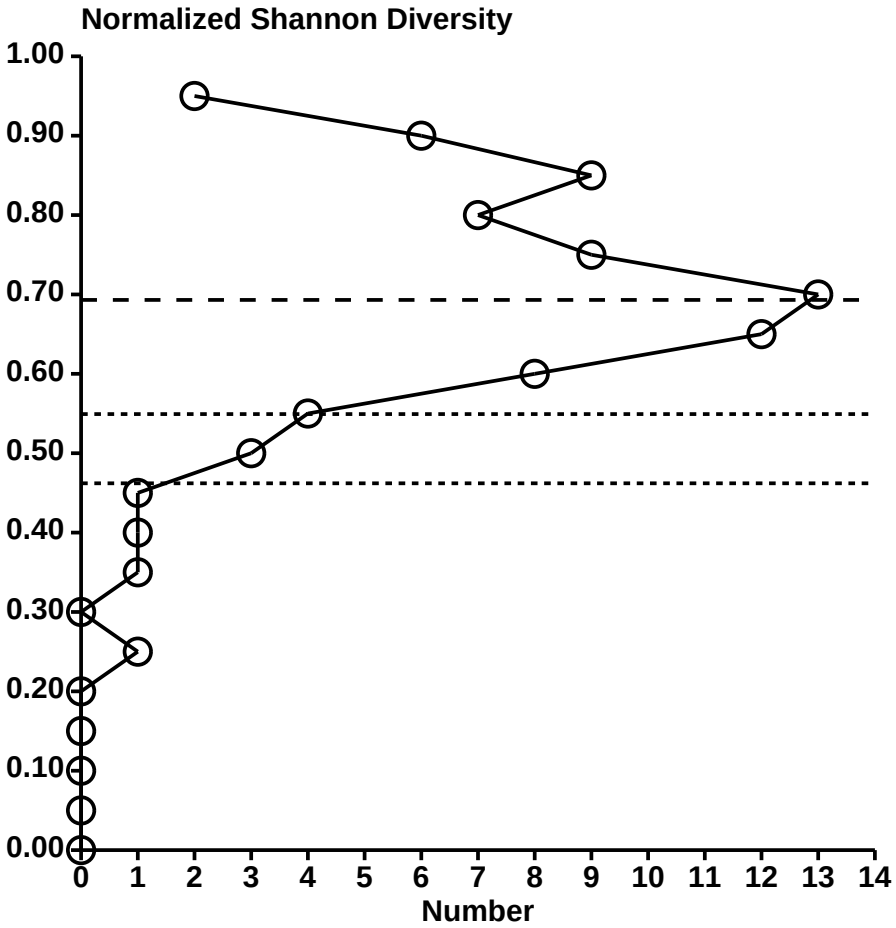
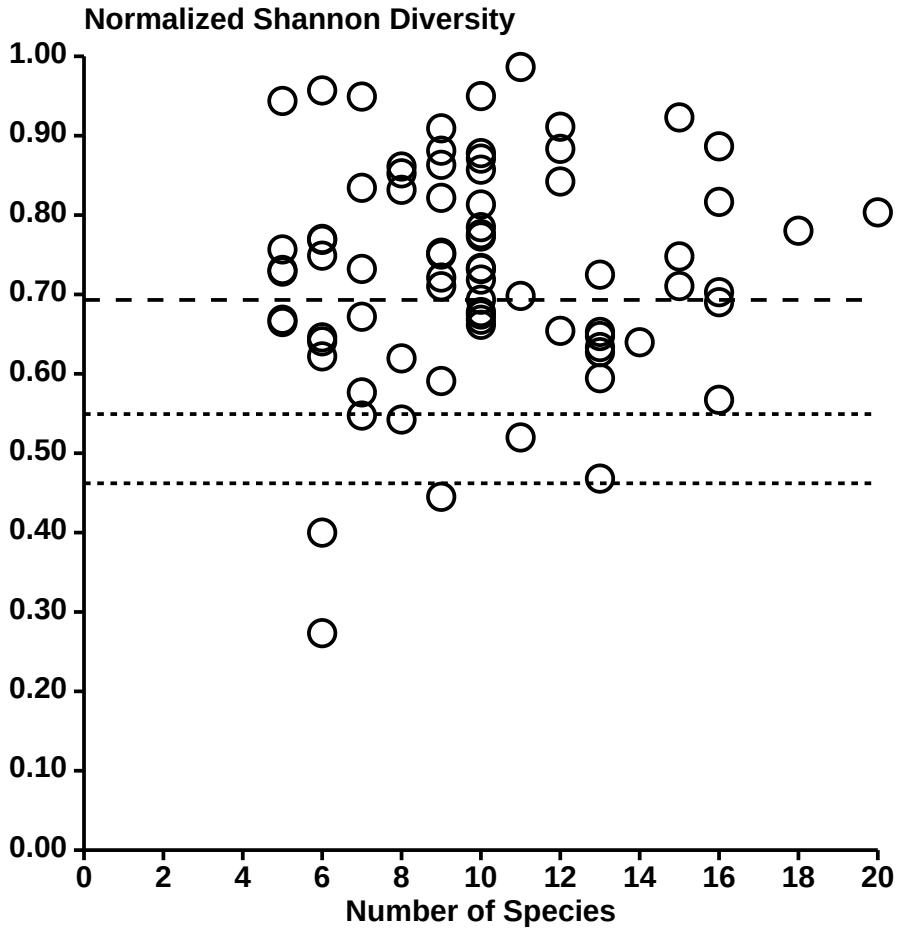
- The phosphorus changes a Class 1 community to Class 2.
- A healthy lake becomes Class 2 during the phytoplankton bloom.

From Figure 2.1 of Mischke.Pahissa2011 `http://www.wiser.eu/download/D3.1-2.pdf`

http://en.wikipedia.org/wiki/File:TARDIS2.jpg

Pennsylvanian Community, 320 to 300 Ma





- Productids, echinoids, bryozoans, crinoids, corals and brachiopods

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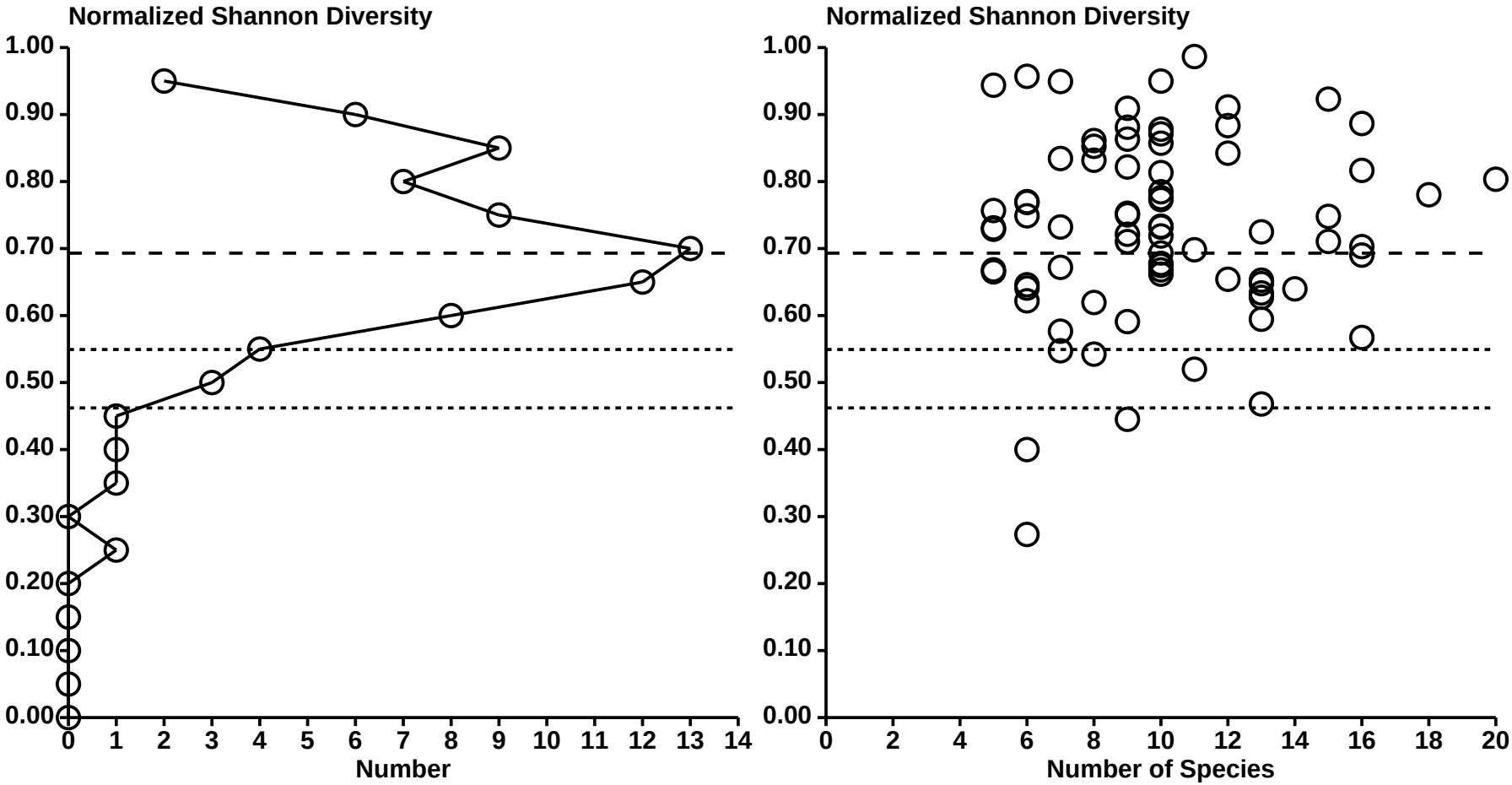

- Productids, echinoids, bryozoans, crinoids, corals and brachiopods
- evenness of 0.73 ± 0.14

Schneider2003 Thesis 2003 http://repositories.lib.utexas.edu/handle/2152/916

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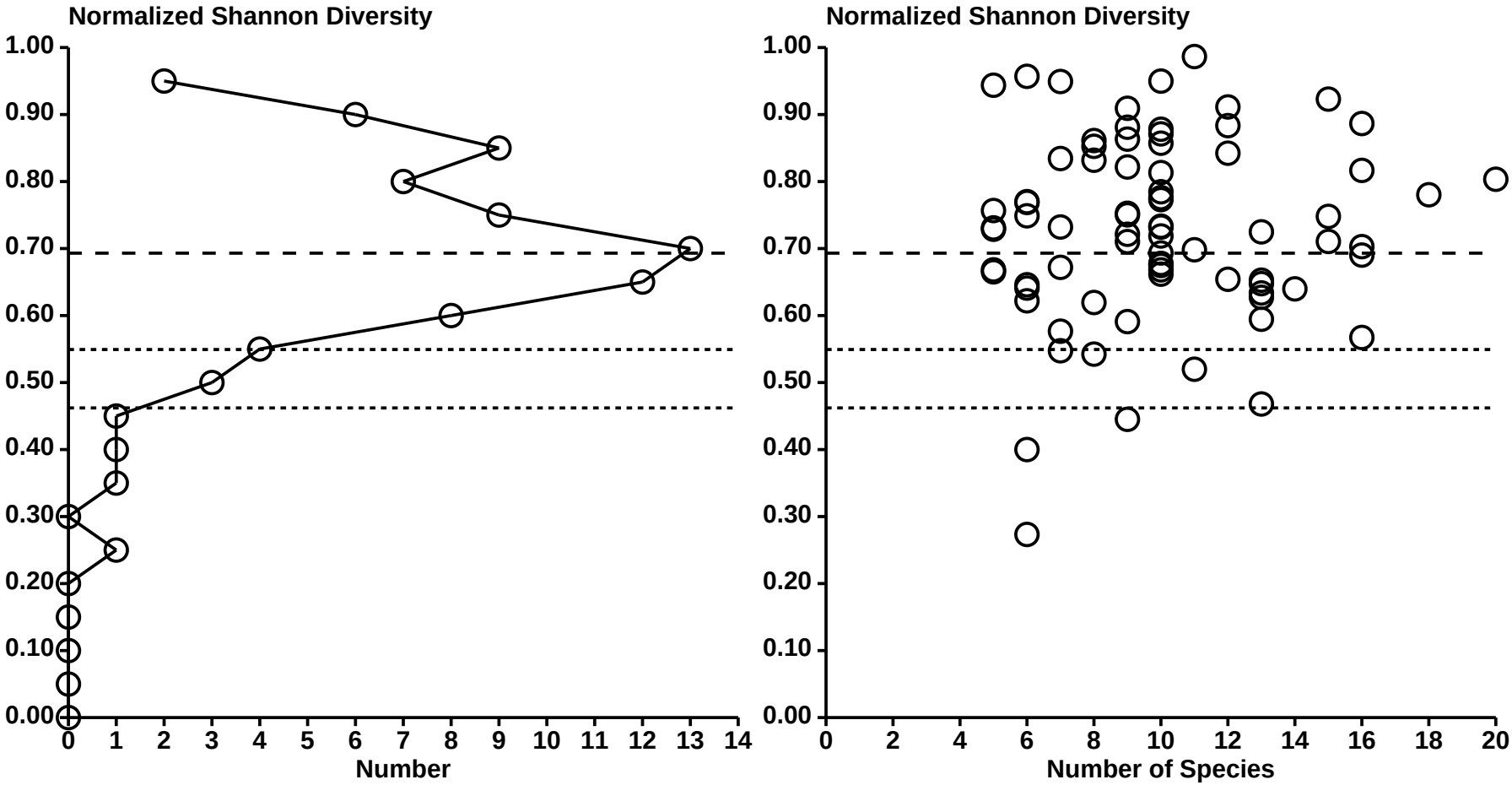
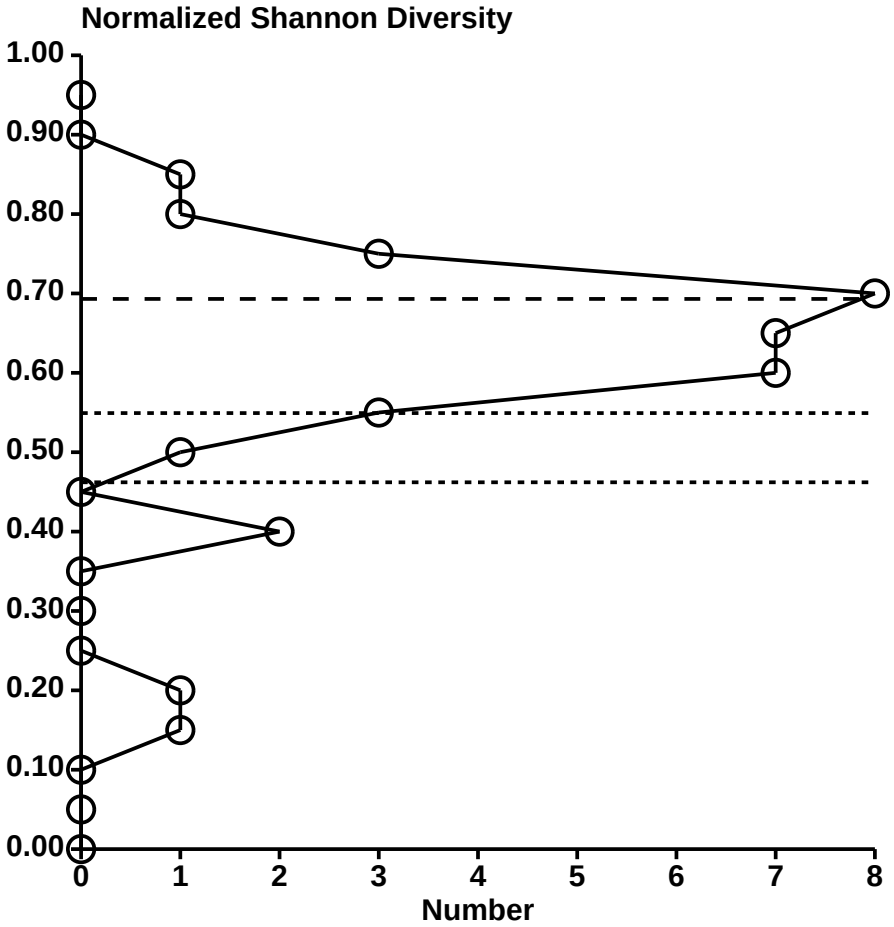
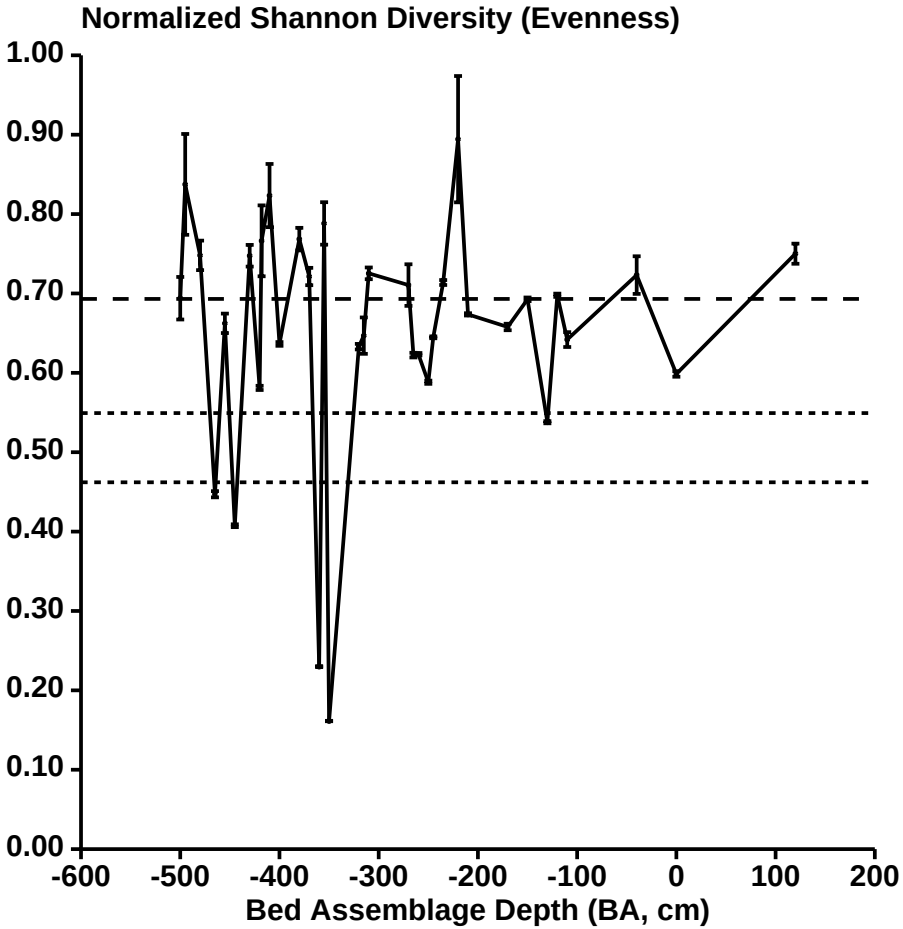


- Productids, echinoids, bryozoans, crinoids, corals and brachiopods
- evenness of 0.73 ± 0.14
- Ancient stable healthy Class 1 ecosystems!

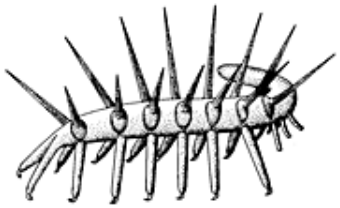
Schneider2003 Thesis 2003 http://repositories.lib.utexas.edu/handle/2152/916

Cambrian Burgess Shale Community, 510 to 505 Ma



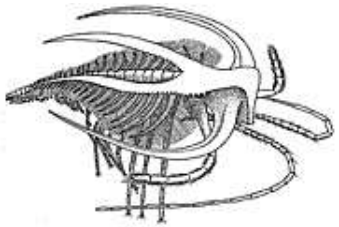


Hallucigenia

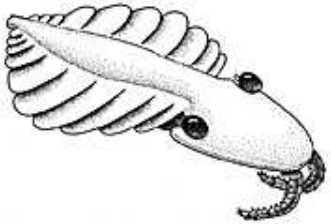


Opabinia

Marrella



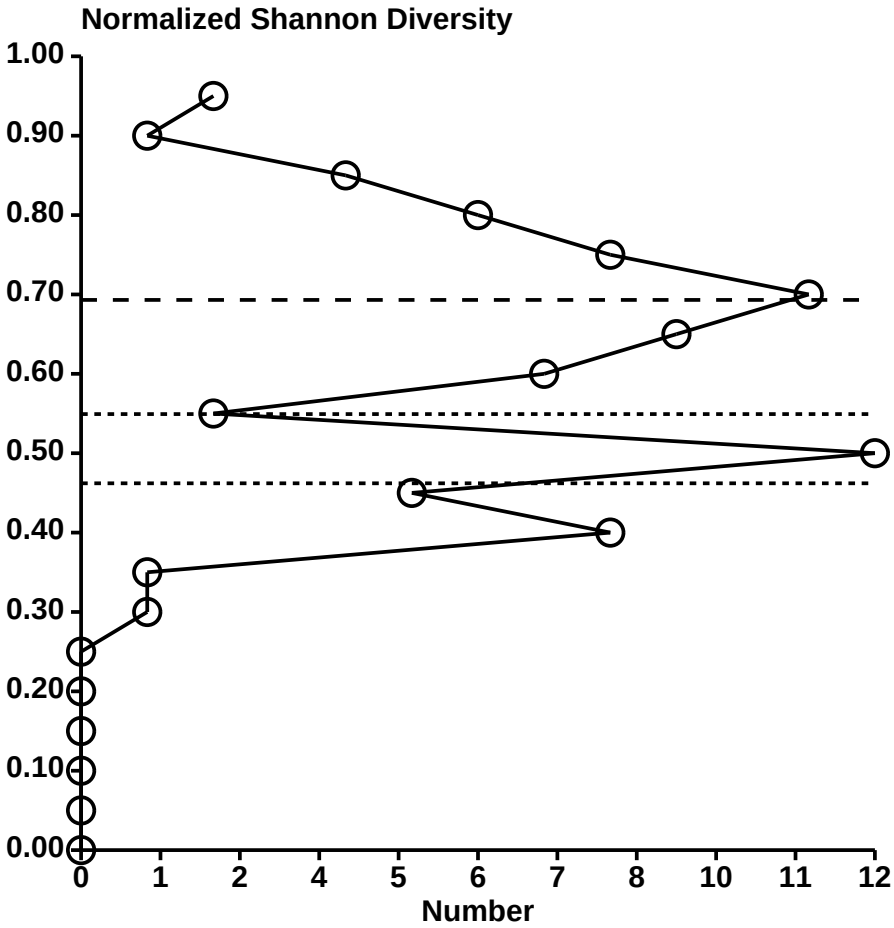
Anomalocaris

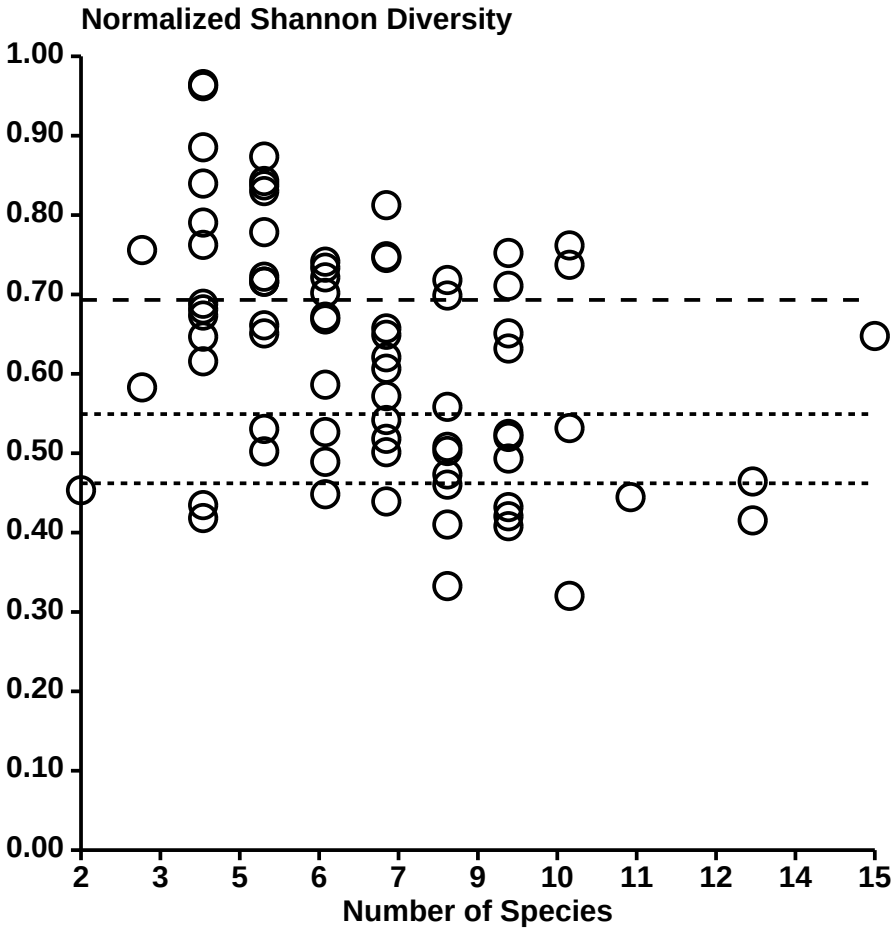


http://paleobiology.si.edu/burgess/burgessSpecimens.html

Caron.Jackson2006 Caron.Jackson2008 http://palaios.ku.edu/2006data.html

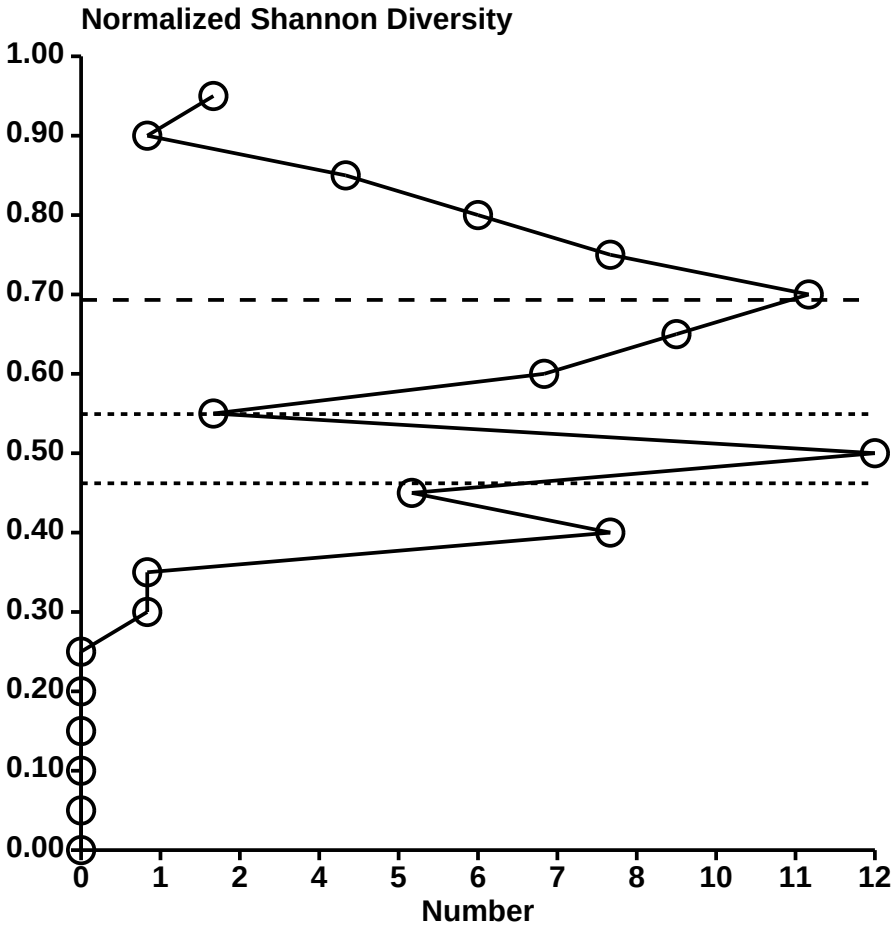
Trilobite to Brachiopod transition, 472 Ma

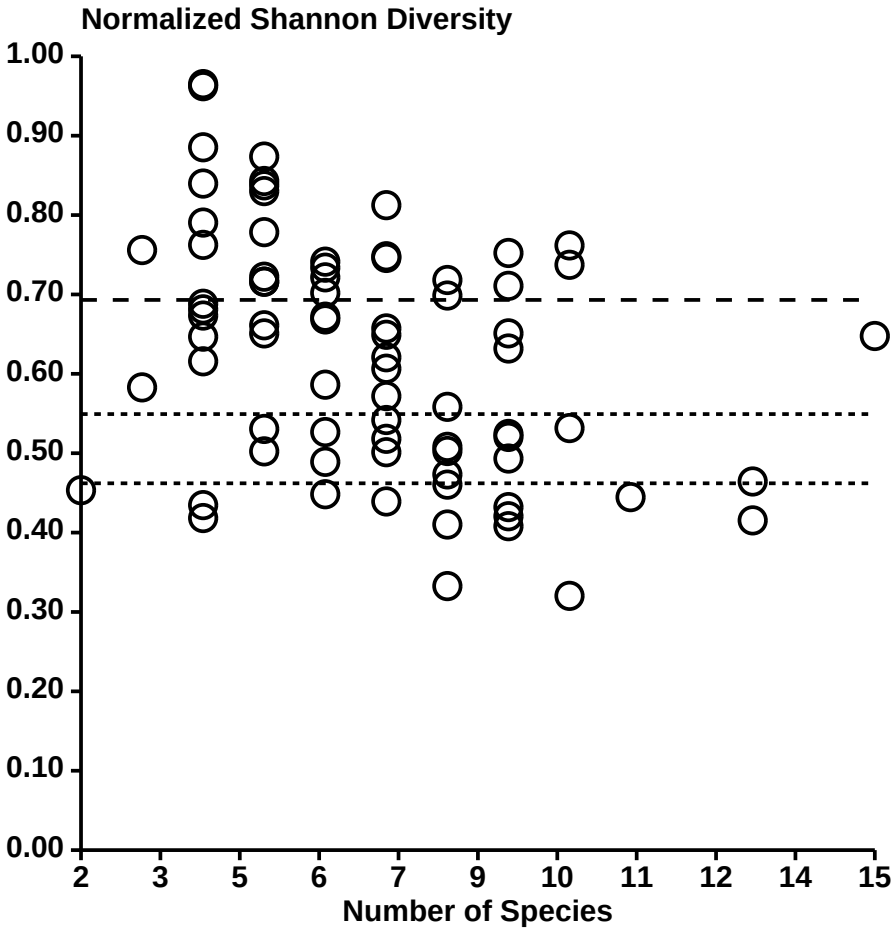




- The community was from the lower to the middle Ordovician.

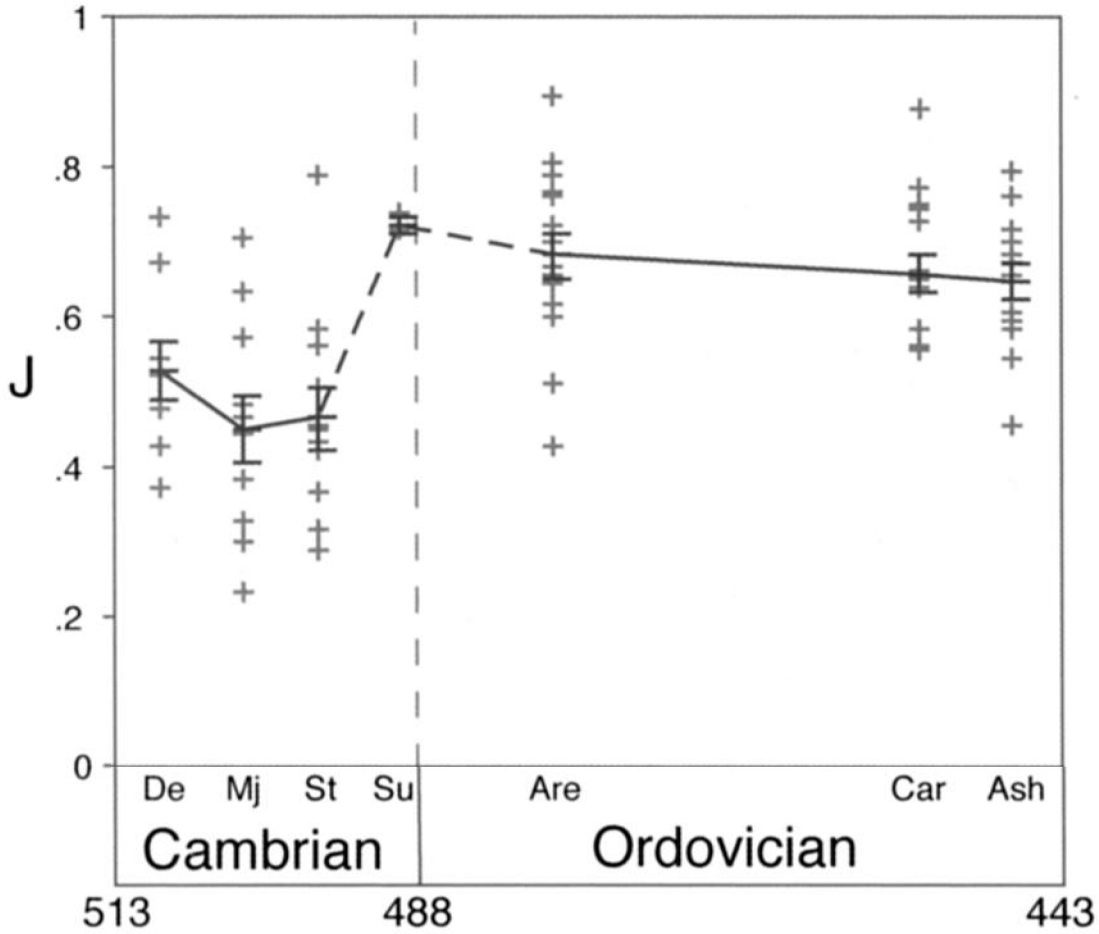
Trilobite to Brachiopod transition, 472 Ma





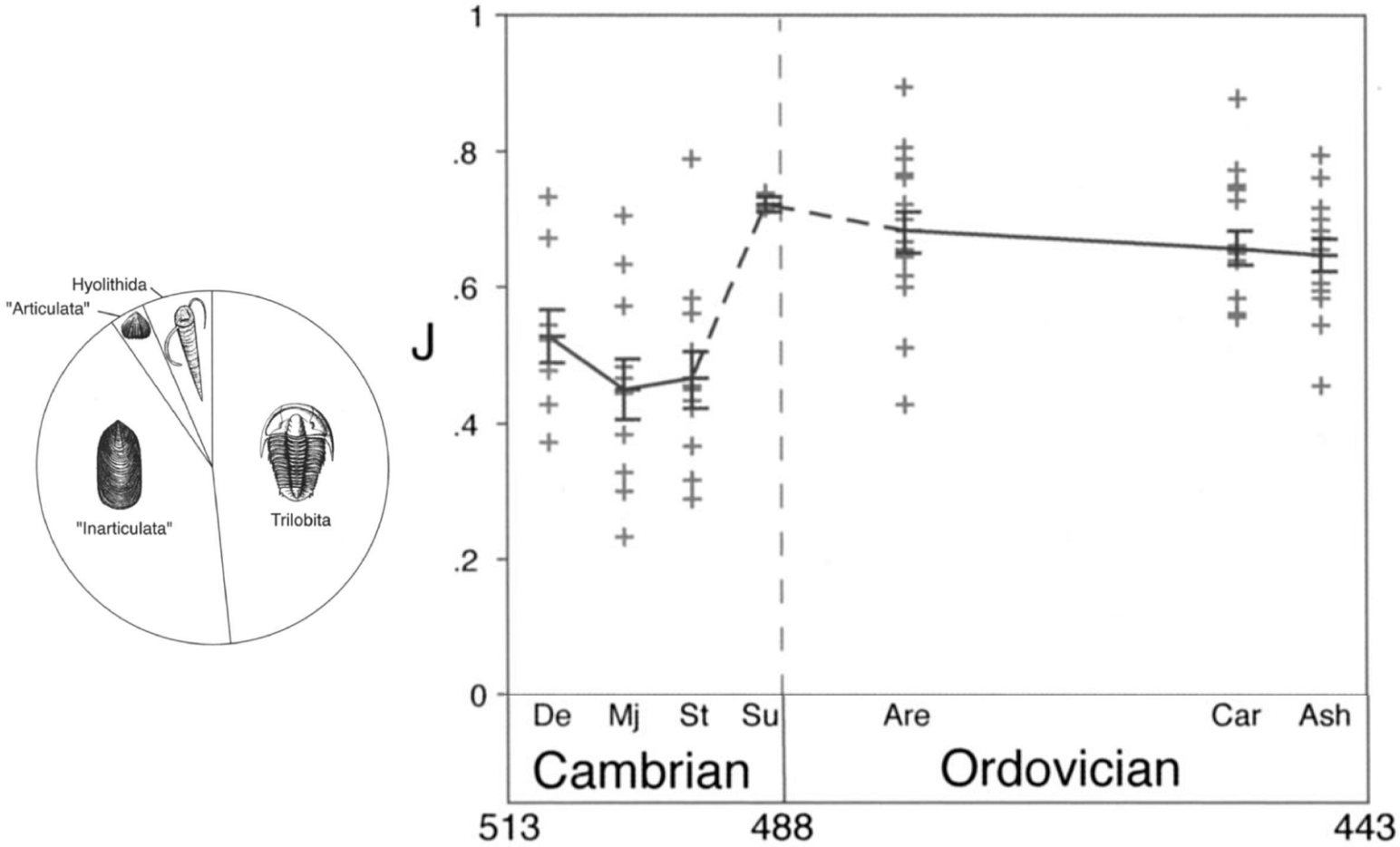
- The community was from the lower to the middle Ordovician.
- The data appear to indicate that the ecologies were either Class 1 or Class 3.

Trilobite to Brachiopod Paleoecosystem Transition at 488 Ma



Peters2004 Paleobiology, 30(3):325-346, 2004

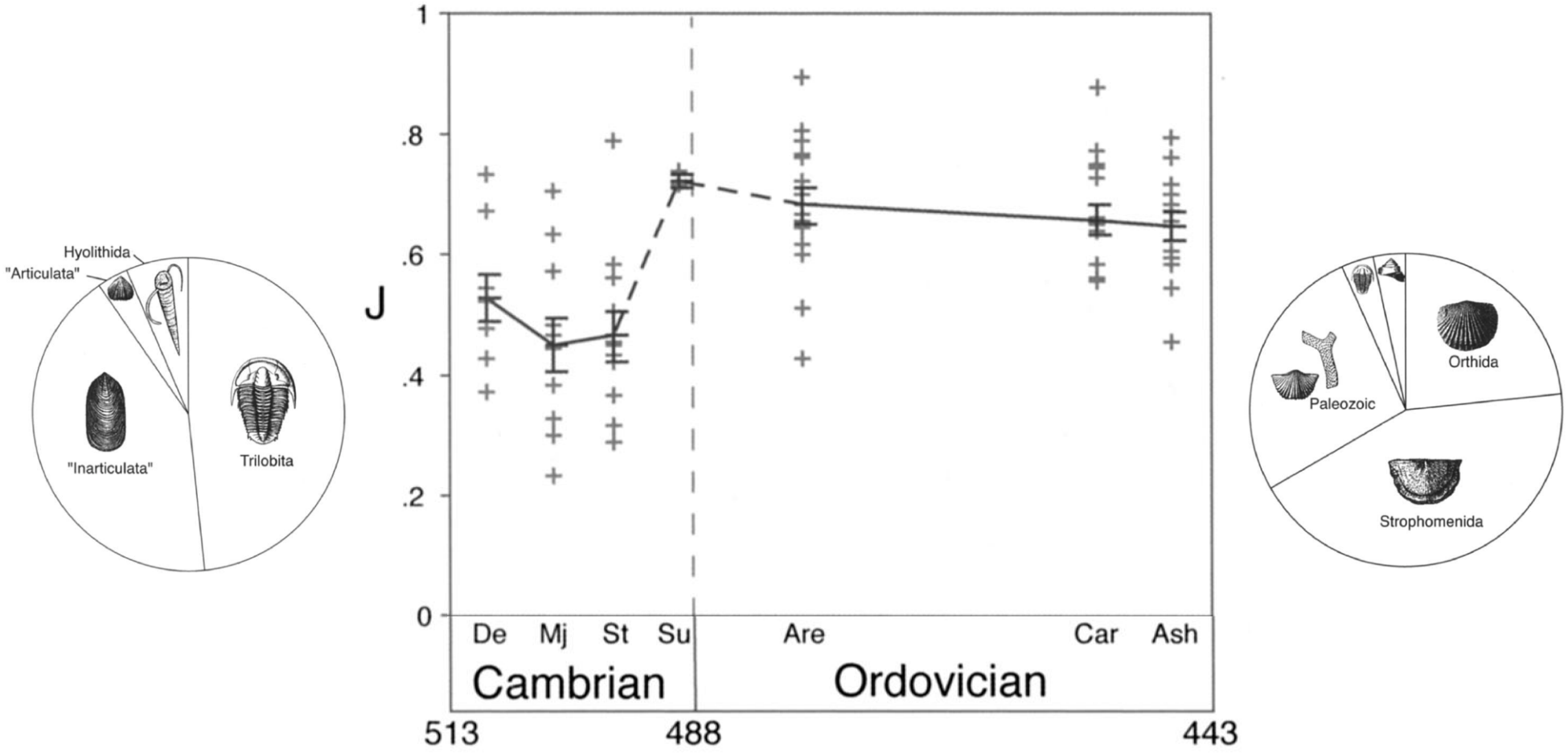
Trilobite to Brachiopod Paleoecosystem Transition at 488 Ma



- Trilobite paleoecosystem was perhaps Class 2 or Class 3.

Peters2004 Paleobiology, 30(3):325-346, 2004

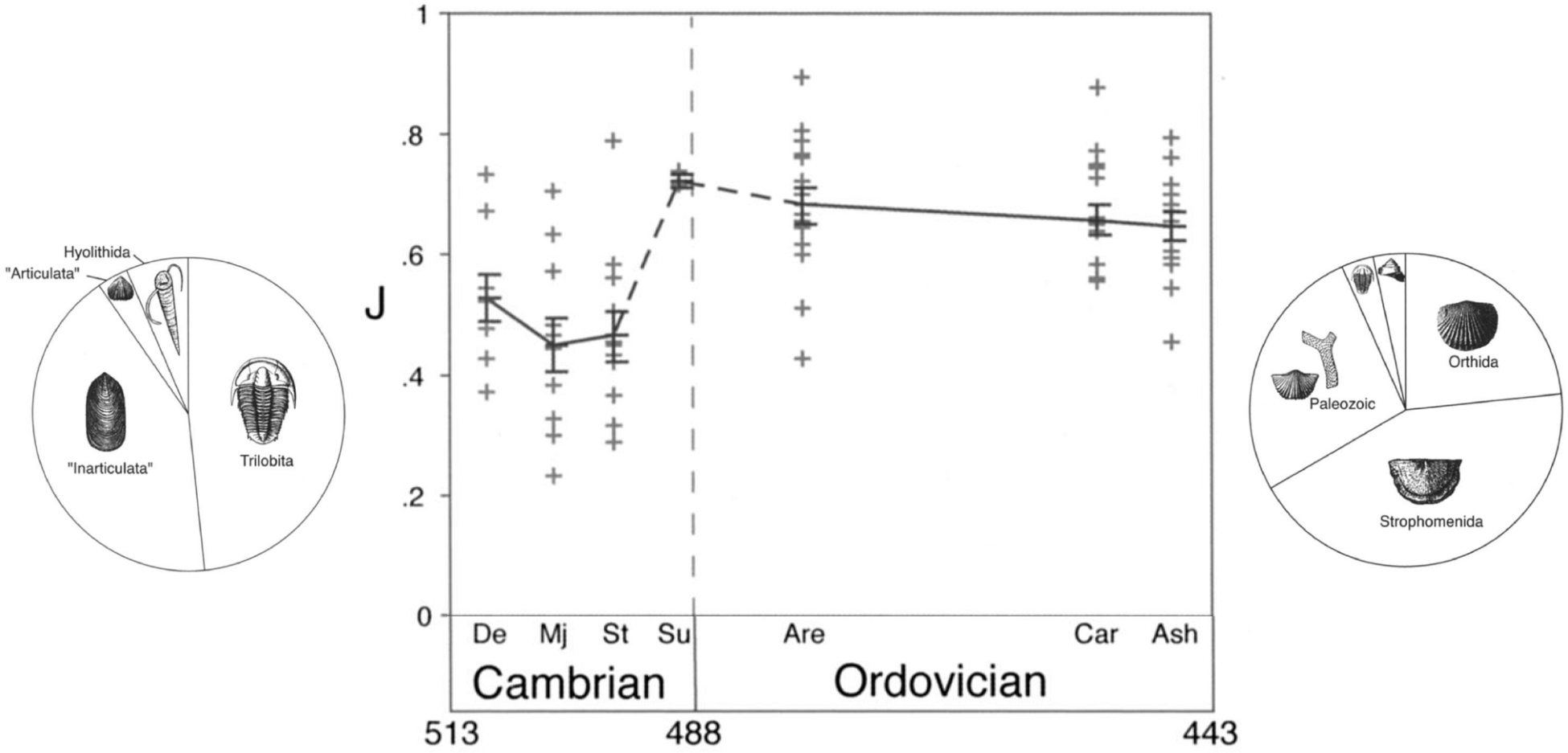
Trilobite to Brachiopod Paleoecosystem Transition at 488 Ma



- Trilobite paleoecosystem was perhaps Class 2 or Class 3.
- Brachiopod paleoecosystem was Class 1

Peters2004 Paleobiology, 30(3):325-346, 2004

Trilobite to Brachiopod Paleoecosystem Transition at 488 Ma



- Trilobite paleoecosystem was perhaps Class 2 or Class 3.
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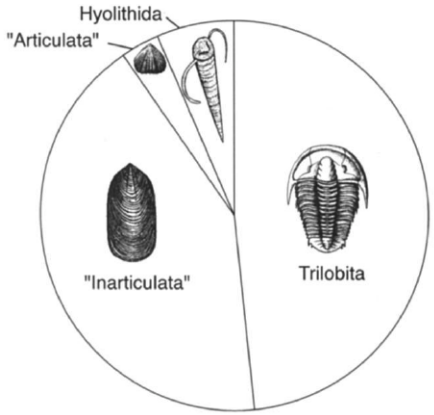
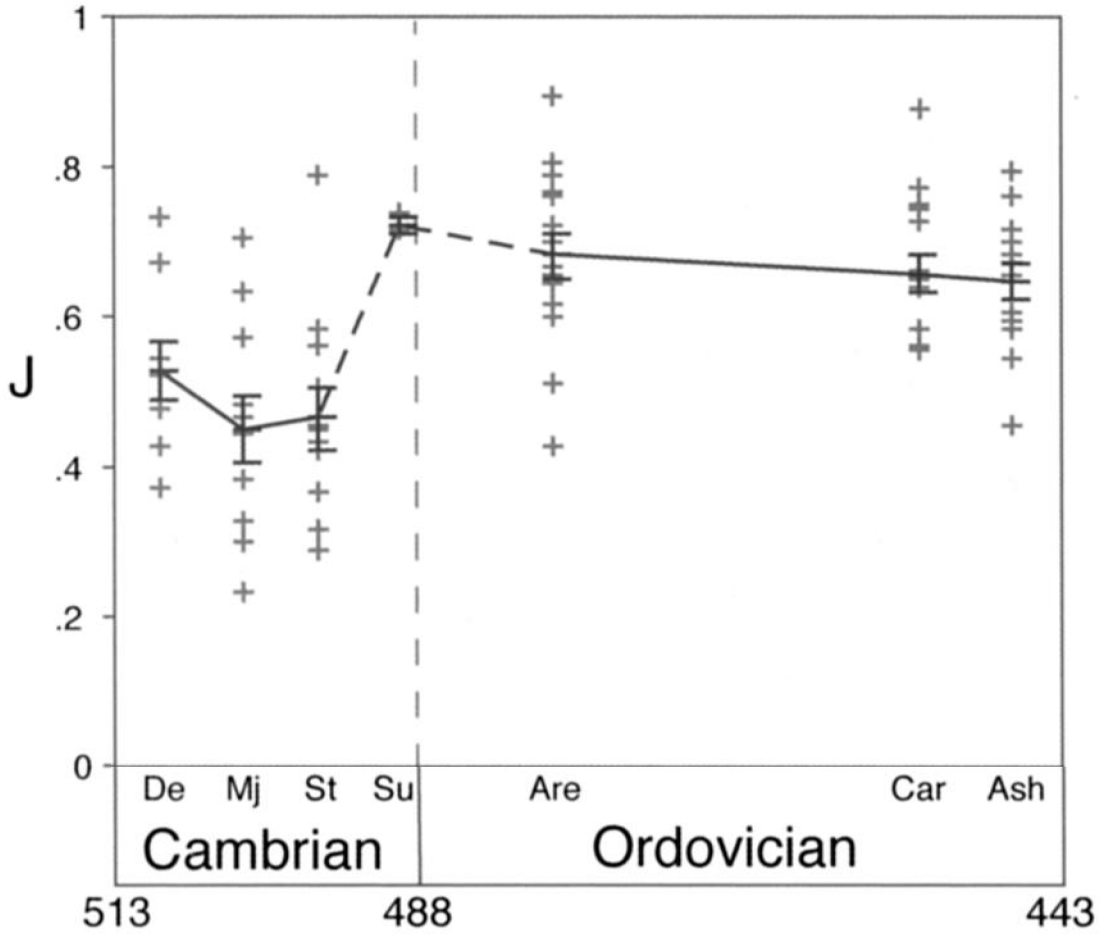
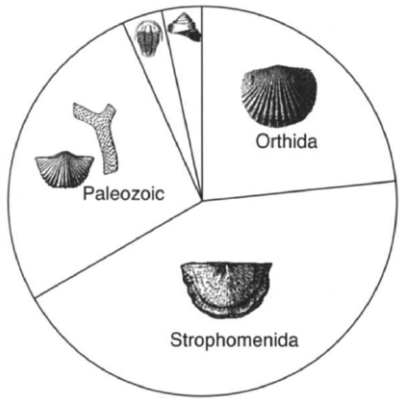
- **Hypotheses 1**: Transition by improvement of the ecosystem

Peters2004 Paleobiology, 30(3):325-346, 2004

Trilobite to Brachiopod Paleoecosystem Transition at 488 Ma



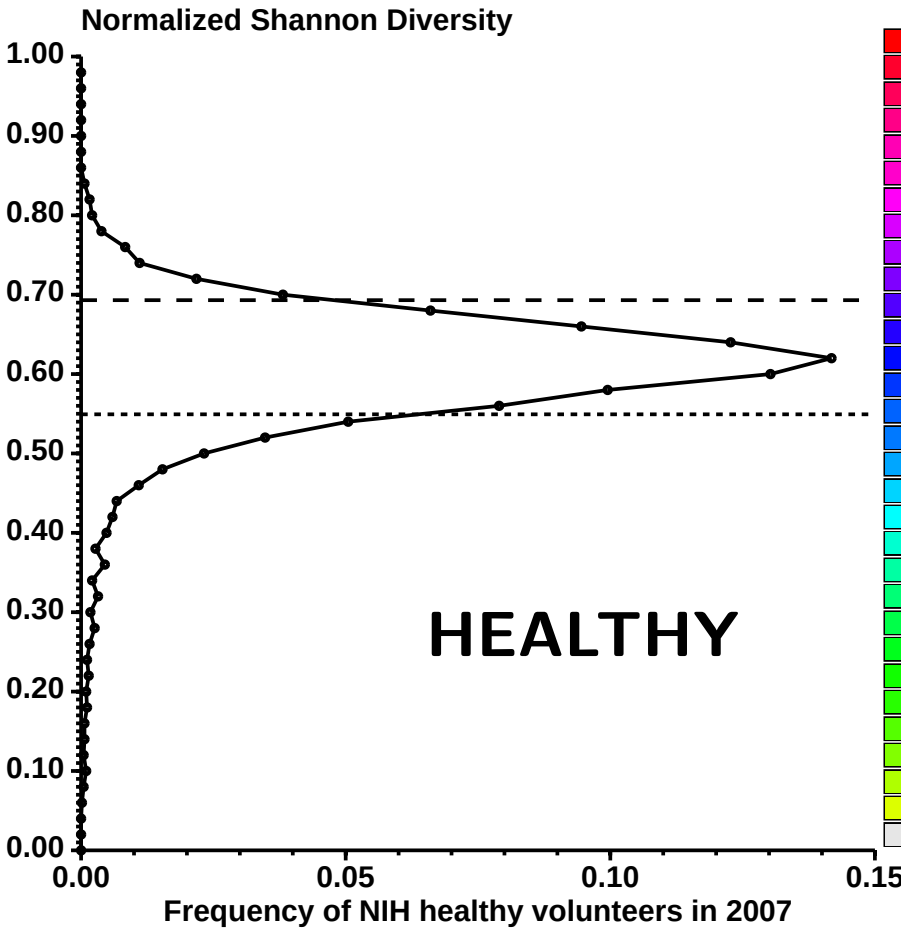


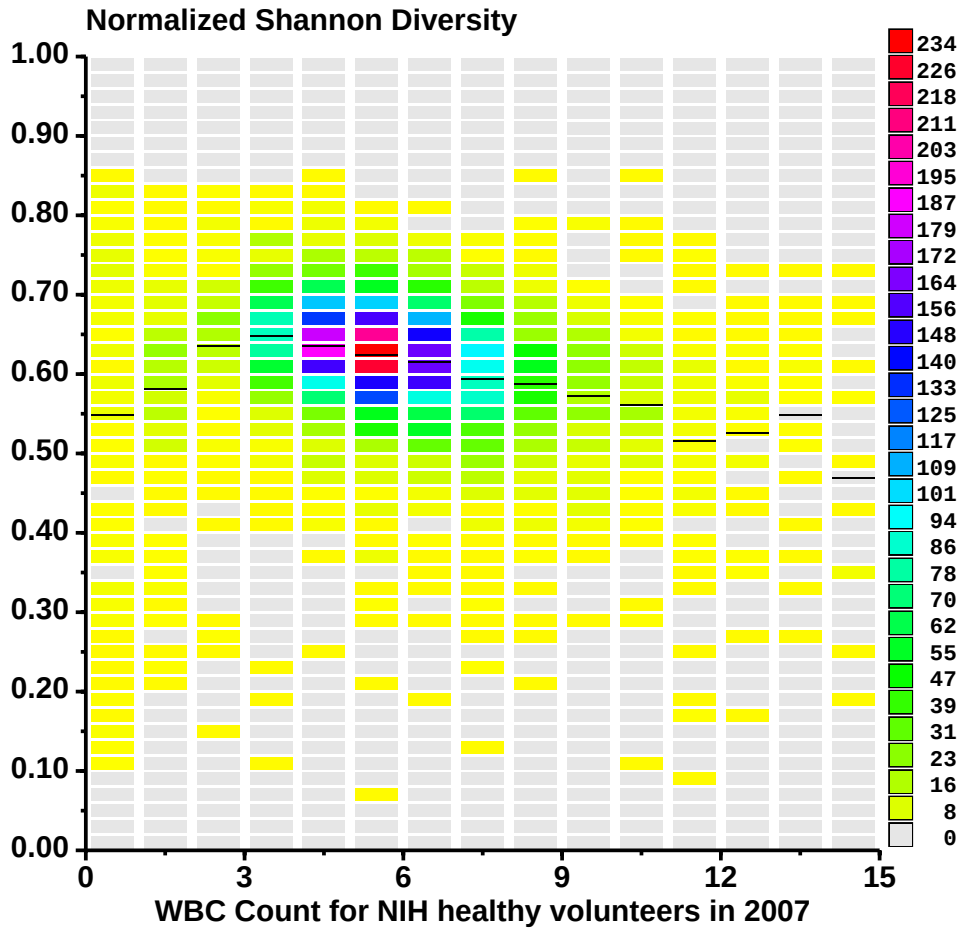


- Trilobite paleoecosystem was perhaps Class 2 or Class 3.
- Brachiopod paleoecosystem was Class 1
- **Hypotheses 1**: Transition by improvement of the ecosystem
- **Hypotheses 2**: Other factor(s) and brachiopods were more efficient.

Peters2004 Paleobiology, 30(3):325-346, 2004

White blood cell counts: healthy people

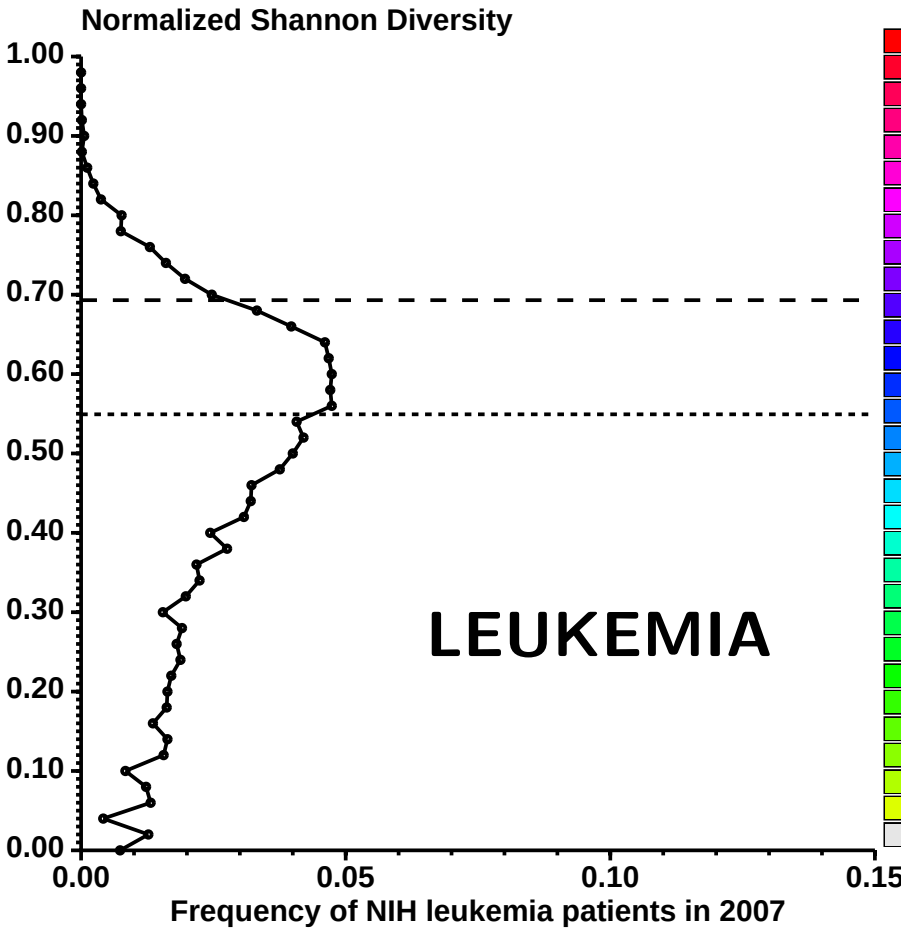


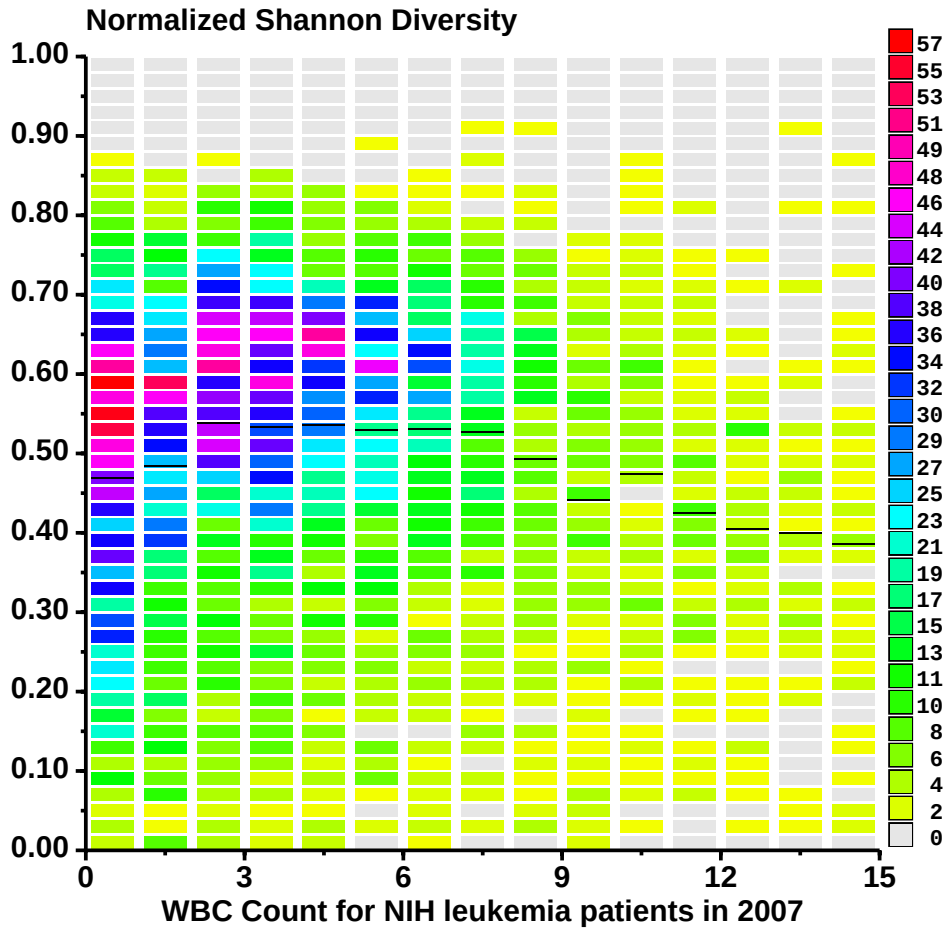


- CBC with differential: (Neutrophil, Eosinophil, Basophil, Lymphocyte and Monocyte) were obtained for healthy volunteers ($n = 6241$) and leukemia patients ($n = 6924$). Data peak at 0.61 ± 0.8. at NIH in 2007.

Data were obtained from `http://btris.nih.gov/` in March 2013

White blood cell counts: leukemia patients

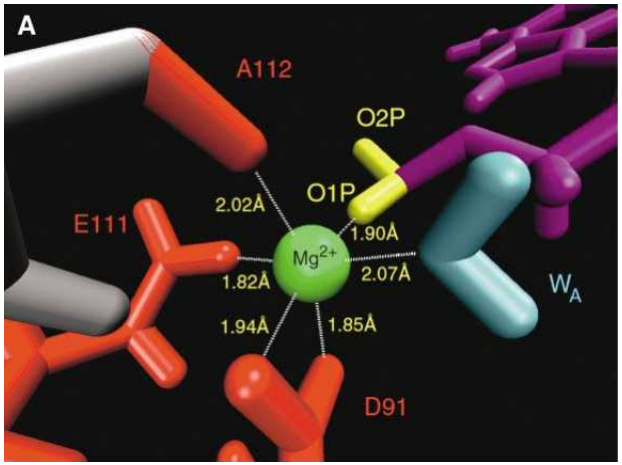




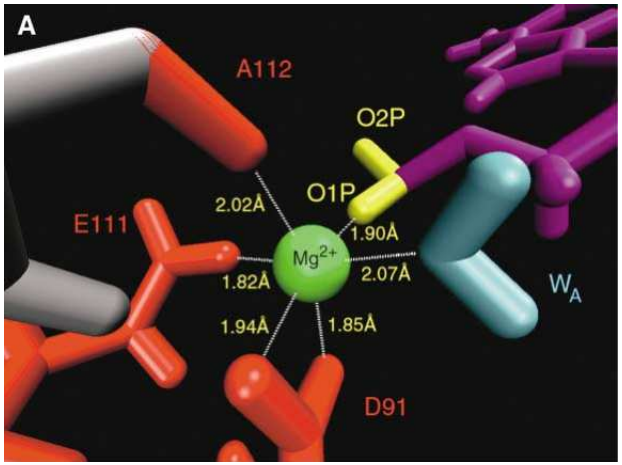
- CBC with differential: (Neutrophil, Eosinophil, Basophil, Lymphocyte and Monocyte) were obtained for healthy volunteers ($n = 6241$) and leukemia patients ($n = 6924$). Data peak at 0.61 ± 0.8. at NIH in 2007.
- Leukemia patients still peak ~ 0.6 but the distribution strongly spreads to lower evenness suggesting this is a Class 2 disease.

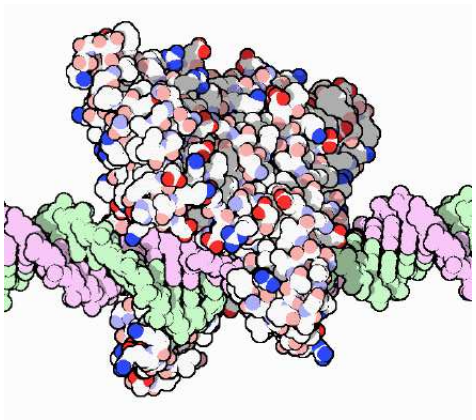
Data were obtained from `http://btris.nih.gov/` in March 2013

Three Principles

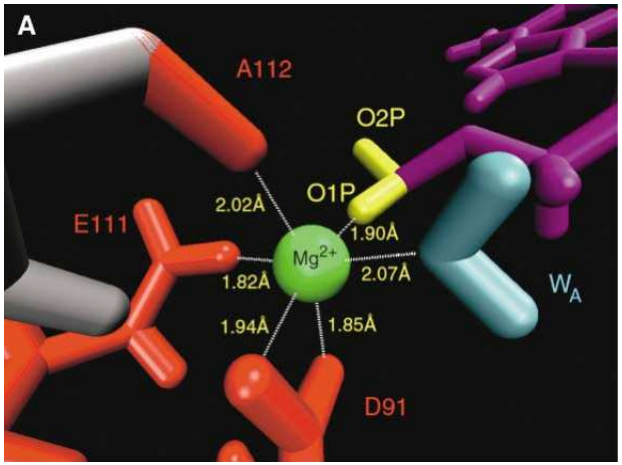


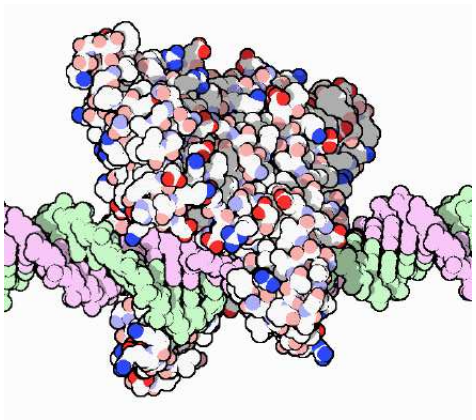
Three Principles

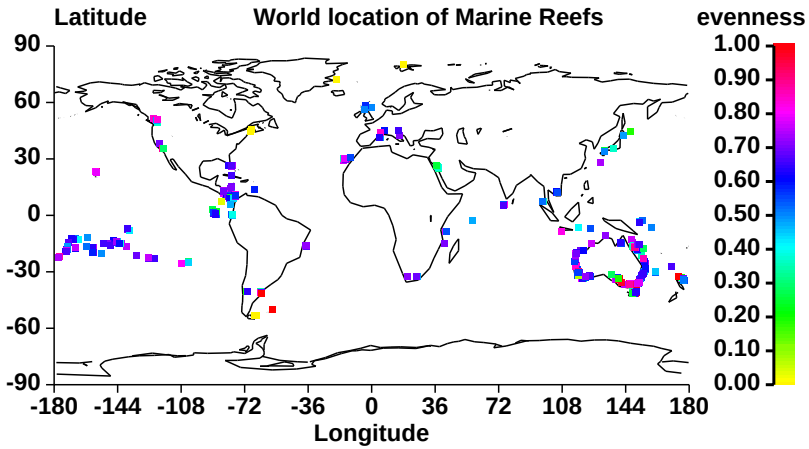




Three Principles







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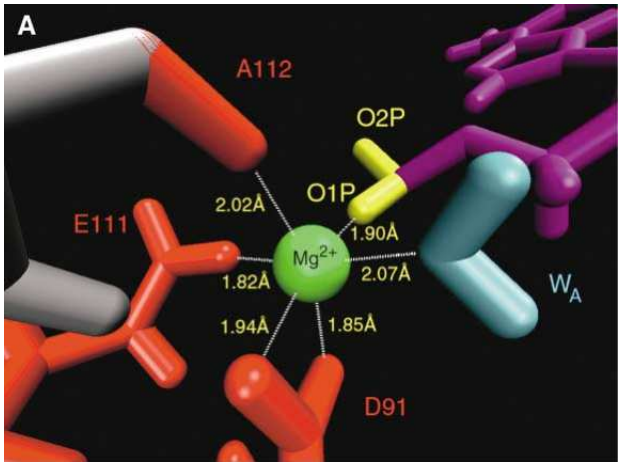
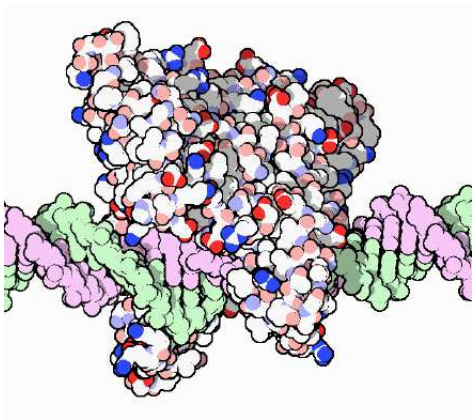
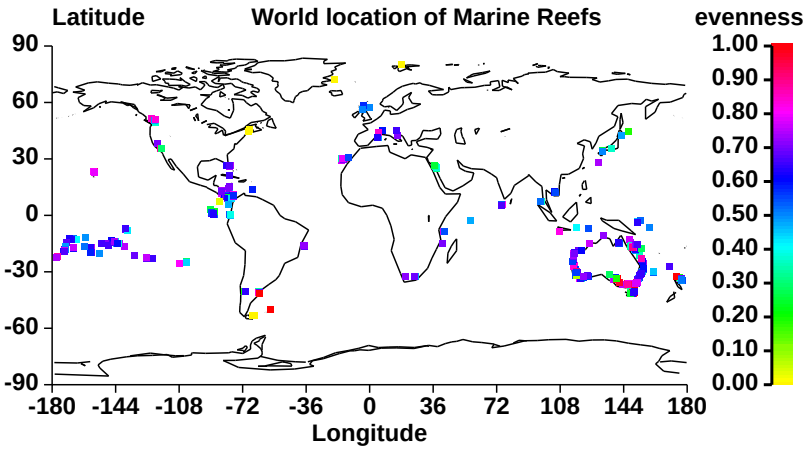
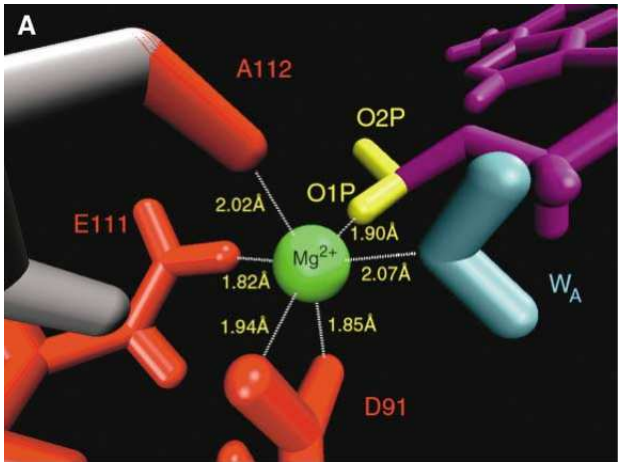


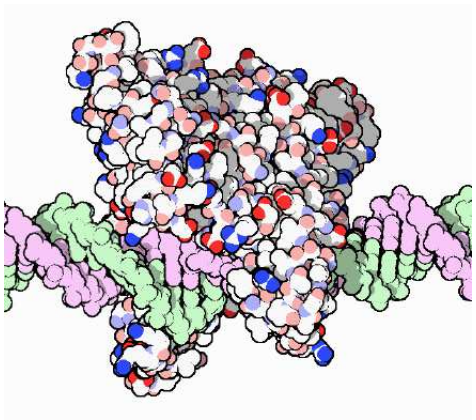


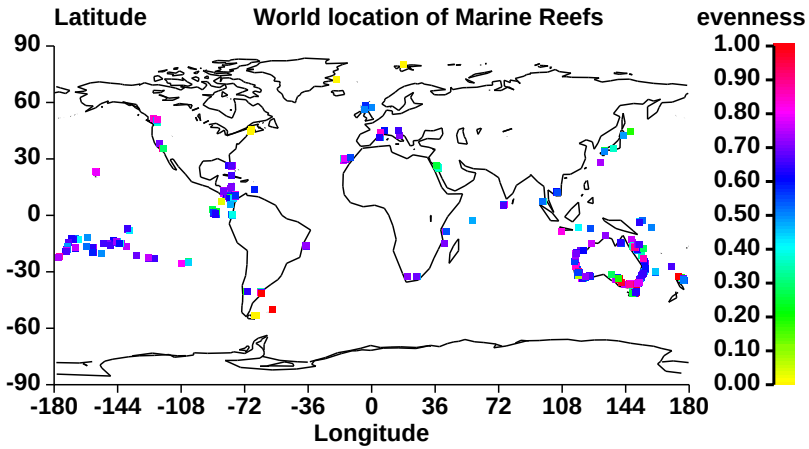


Three Principles of Biological States

Three Principles

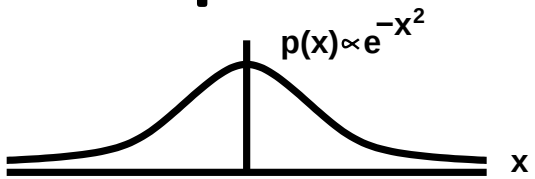




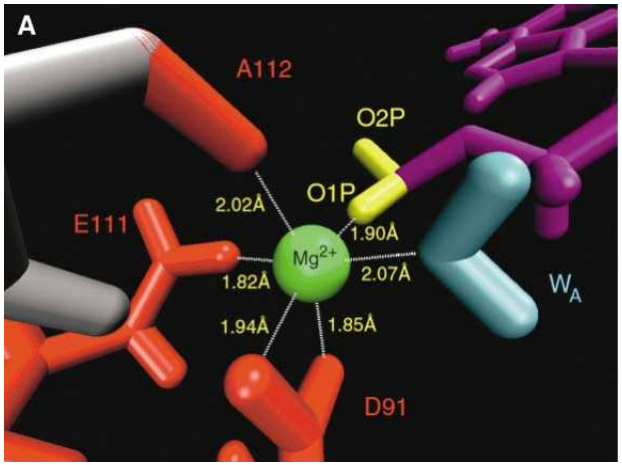


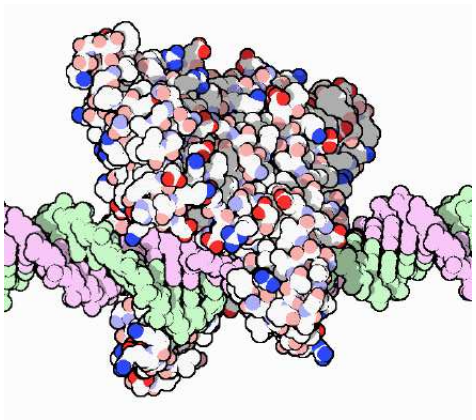
Three Principles of Biological States

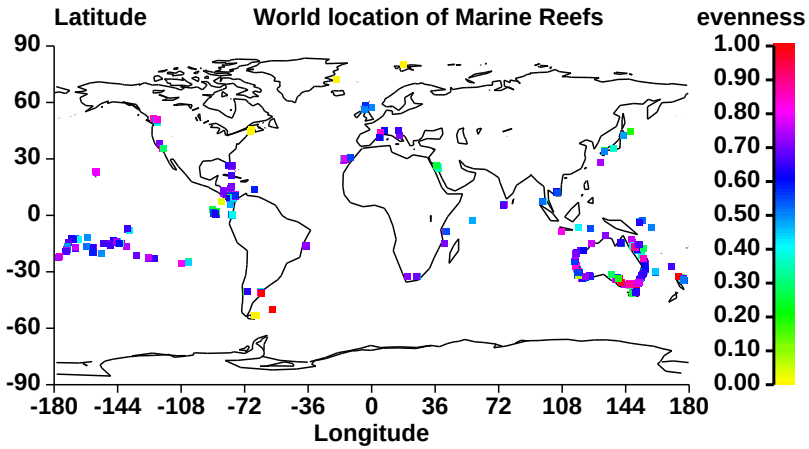
- Noise



Three Principles







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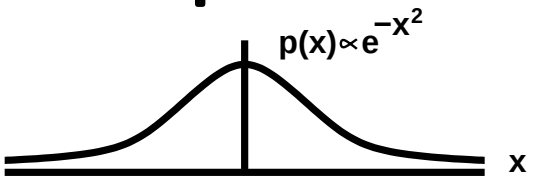
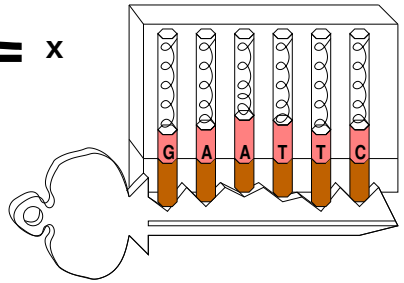
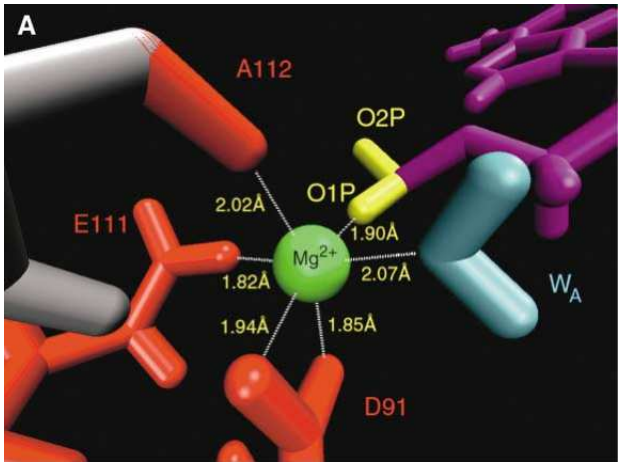
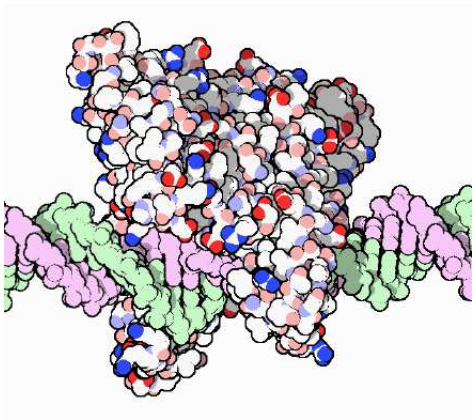


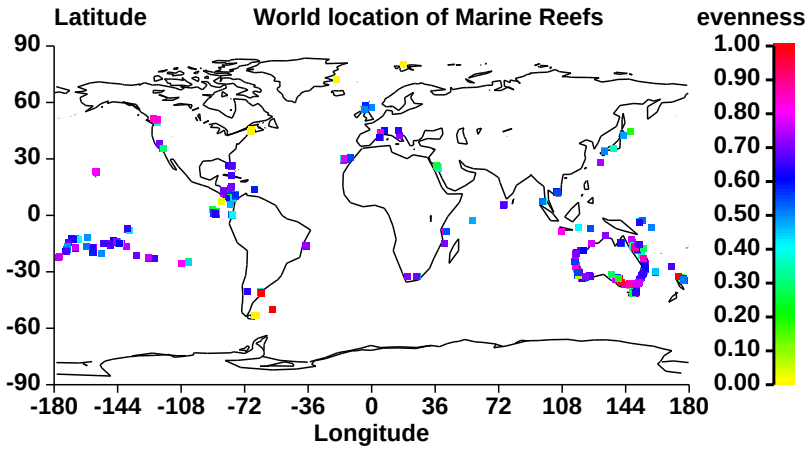
- High dimensionality



Three Principles







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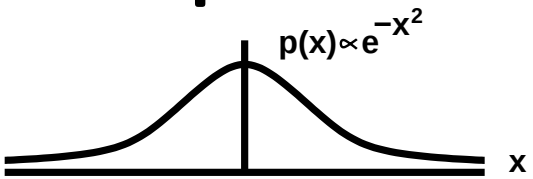

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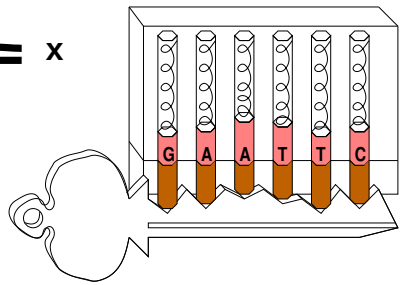
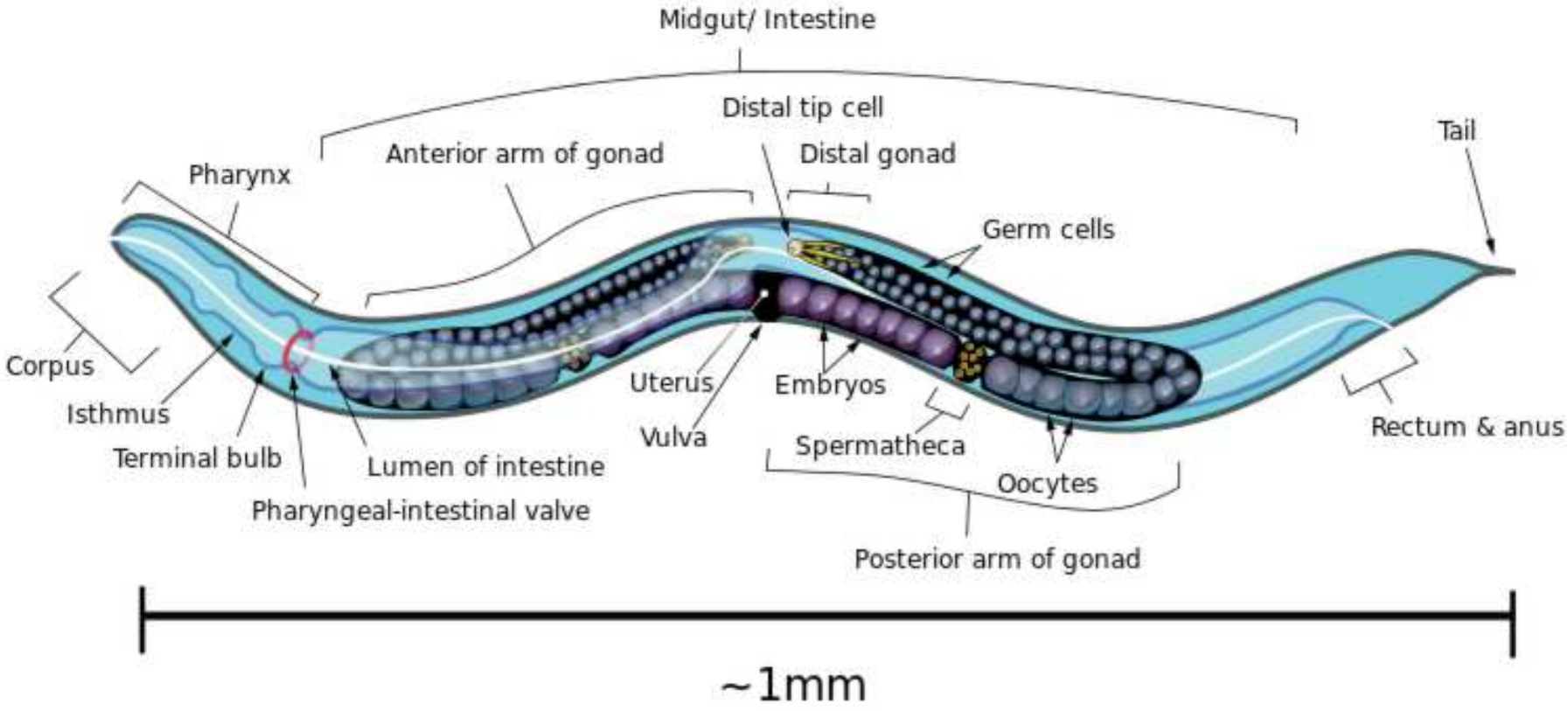


- Separation of states

These Principles imply that the isothermal efficiency will be: 0.69, 0.55, 0.46 . . .

Caenorhabditis elegans



http://en.wikipedia.org/wiki/Caenorhabditis_elegans

Caenorhabditis elegans cell divisions

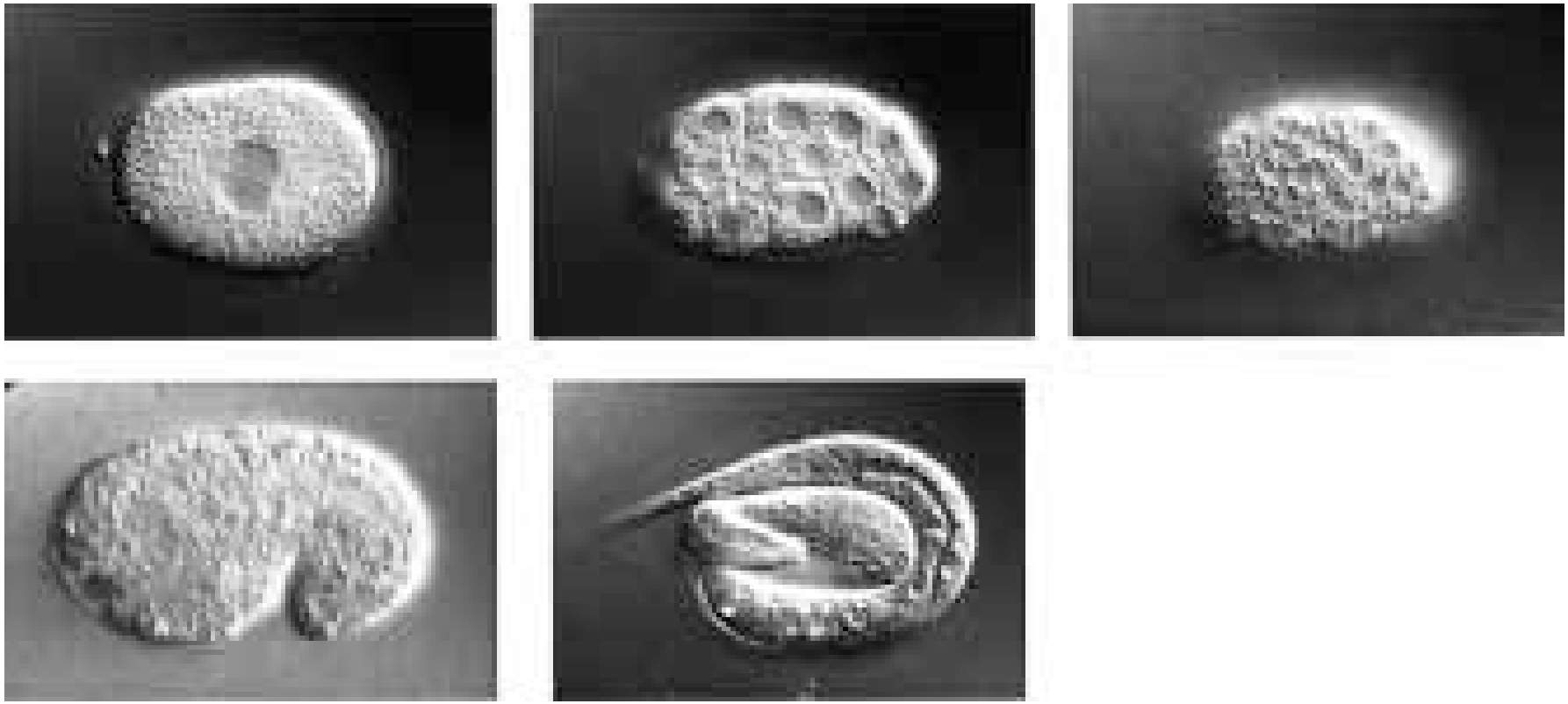
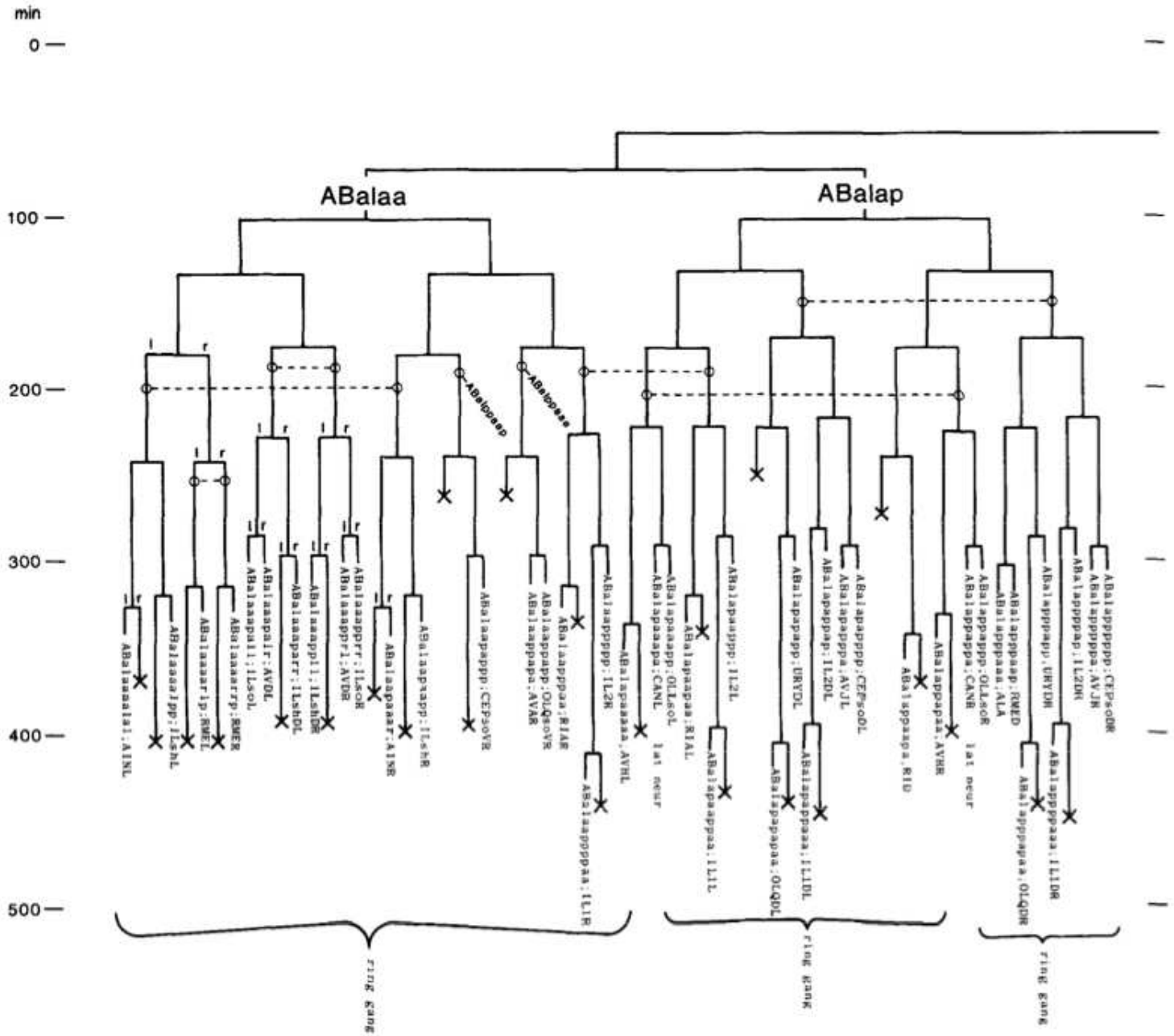


Figure 18. The egg, seen in Nomarski optics, from pronuclear fusion to hatching.

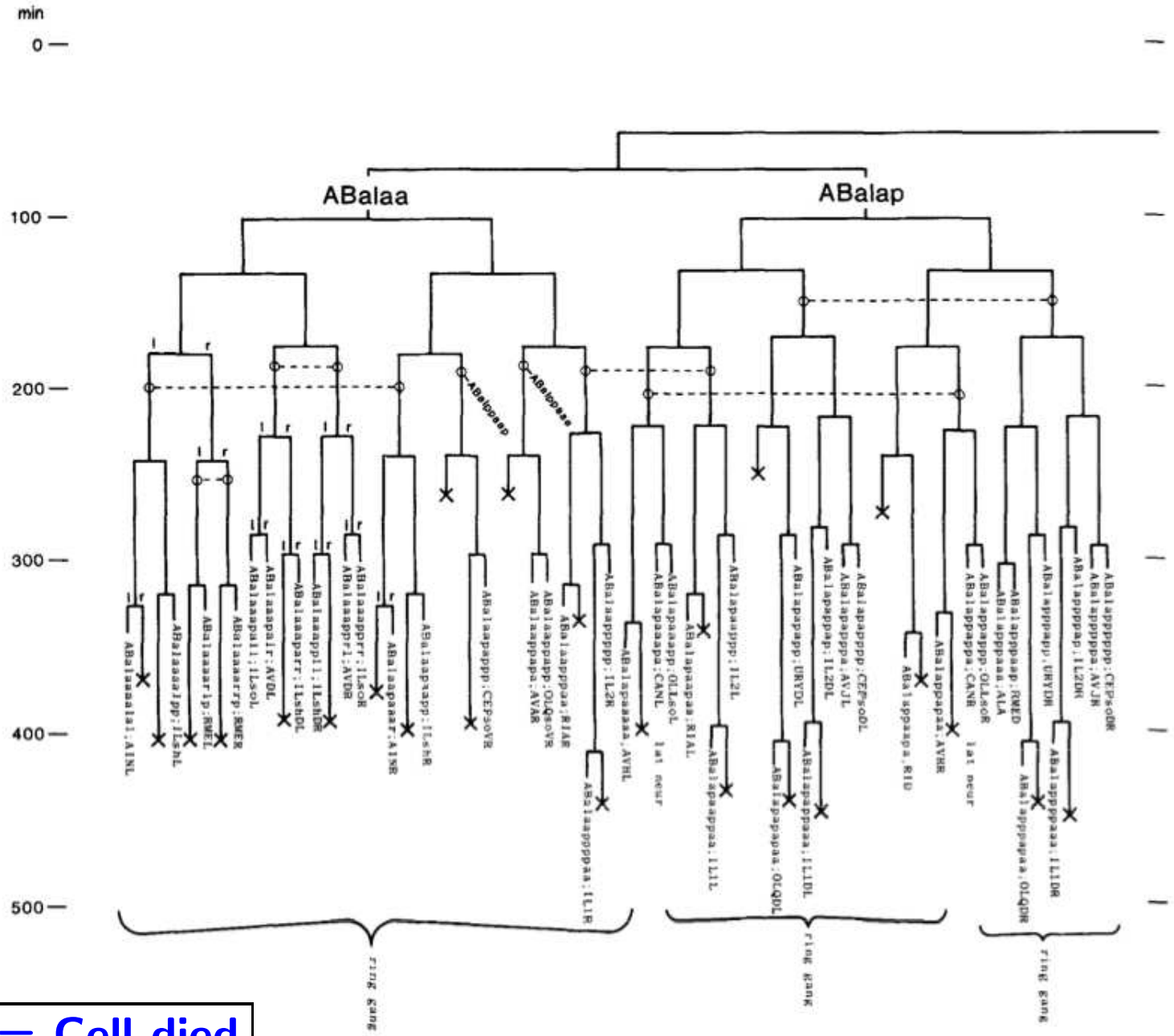
J. E. Sulston, Nobel Lecture, 2002 `http://tinyurl.com/Sulston2002`

Caenorhabditis elegans Lineage



J. E. Sulston *et. al* Developmental Biology 100, 64-119 (1983)

Caenorhabditis elegans Lineage



X = Cell died

J. E. Sulston *et. al* Developmental Biology 100, 64-119 (1983)

Caenorhabditis elegans Lineage Evenness

Sex	Stage	Deaths Counted	Number of Cell Types, M	Cells Counted	H (bits)	Evenness$\pm$SD	Δ from $\ln 2$	Z
hermaphrodite	L1	+	22	671	3.192	0.721 ± 0.008	0.028	3.630
hermaphrodite	L1	-	21	558	3.051	0.701 ± 0.009	0.007	0.855
hermaphrodite	adult	+	20	1090	3.136	0.728 ± 0.005	0.035	7.682
hermaphrodite	adult	-	19	959	2.962	0.700 ± 0.005	0.007	1.494
male	L1	+	22	671	3.189	0.720 ± 0.008	0.027	3.557
male	L1	-	21	560	3.046	0.699 ± 0.009	0.006	0.709
male	adult	+	20	1179	3.096	0.719 ± 0.004	0.026	6.188
male	adult	-	19	1031	2.917	0.690 ± 0.004	-0.003	-0.760

The Embryonic Cell Lineage of the Nematode Caenorhabditis elegans
J. E. Sulston, E. Schierenberg, J. G. White, and J. N. Thomson
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- Including dead cells always gives a large deviation from theory: $Z > 3$ St. dev.

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- Without dead cells the deviation fits the theory: $Z < 2$ St.dev.

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male	adult	-	19	1031	2.917	0.690 ± 0.004	-0.003	-0.760

The Embryonic Cell Lineage of the Nematode Caenorhabditis elegans
J. E. Sulston, E. Schierenberg, J. G. White, and J. N. Thomson
Developmental Biology 100, 64-119 (1983)

- Including dead cells always gives a large deviation from theory: $Z > 3$ St. dev.
- Without dead cells the deviation fits the theory: $Z < 2$ St.dev.
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Caenorhabditis elegans Lineage Evenness

Sex	Stage	Deaths Counted	Number of Cell Types, M	Cells Counted	H (bits)	Evenness±SD	Δ from $\ln 2$	Z
hermaphrodite	L1	+	22	671	3.192	0.721 ± 0.008	0.028	3.630
hermaphrodite	L1	-	21	558	3.051	0.701 ± 0.009	0.007	0.855
hermaphrodite	adult	+	20	1090	3.136	0.728 ± 0.005	0.035	7.682
hermaphrodite	adult	-	19	959	2.962	0.700 ± 0.005	0.007	1.494
male	L1	+	22	671	3.189	0.720 ± 0.008	0.027	3.557
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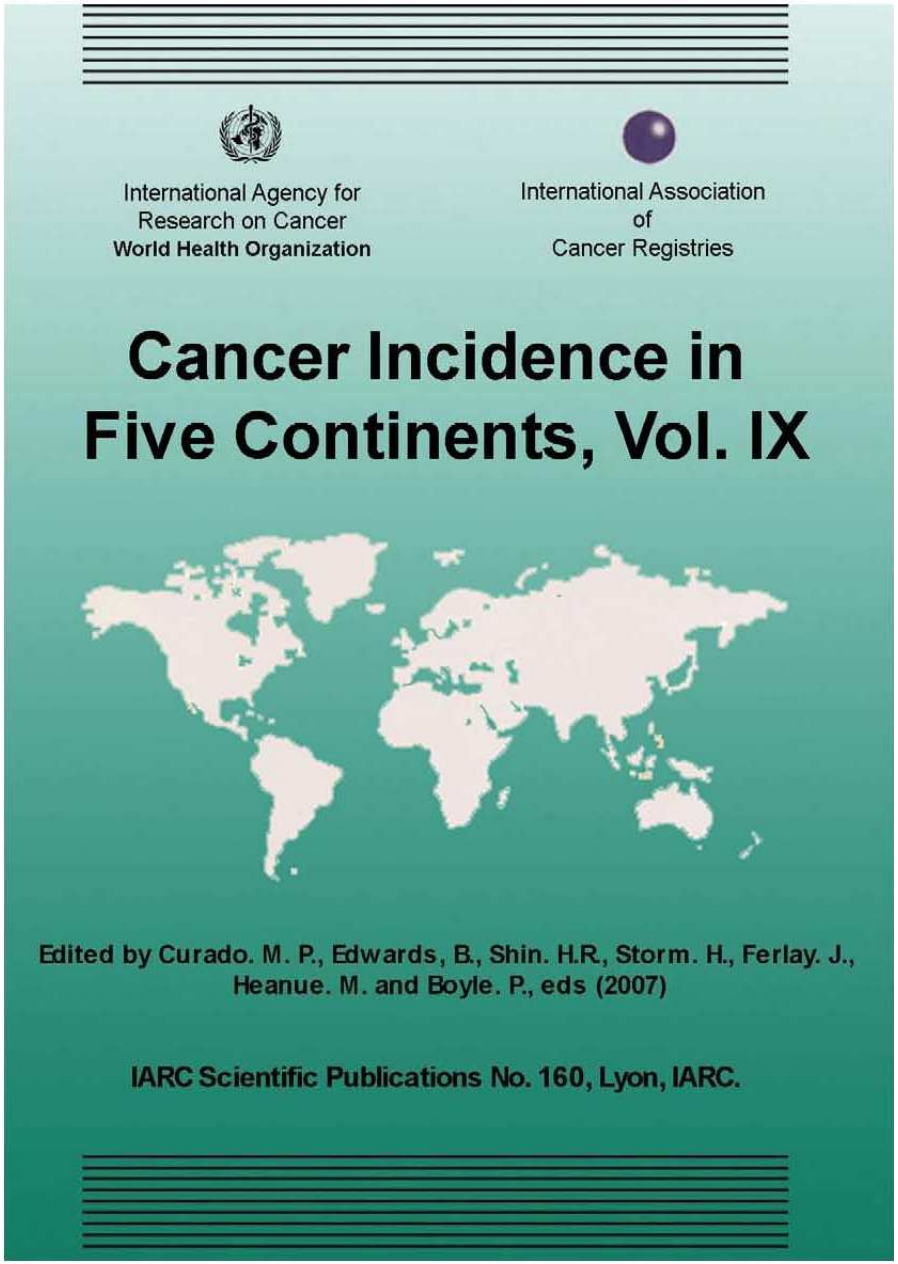
- Dead cells are not part of the coding space.
- Dead cells as a cell type would violate the theory!
- Maybe cells die to avoid exceeding the channel capacity **X = Cell died**

Cancer Incidence WHO data



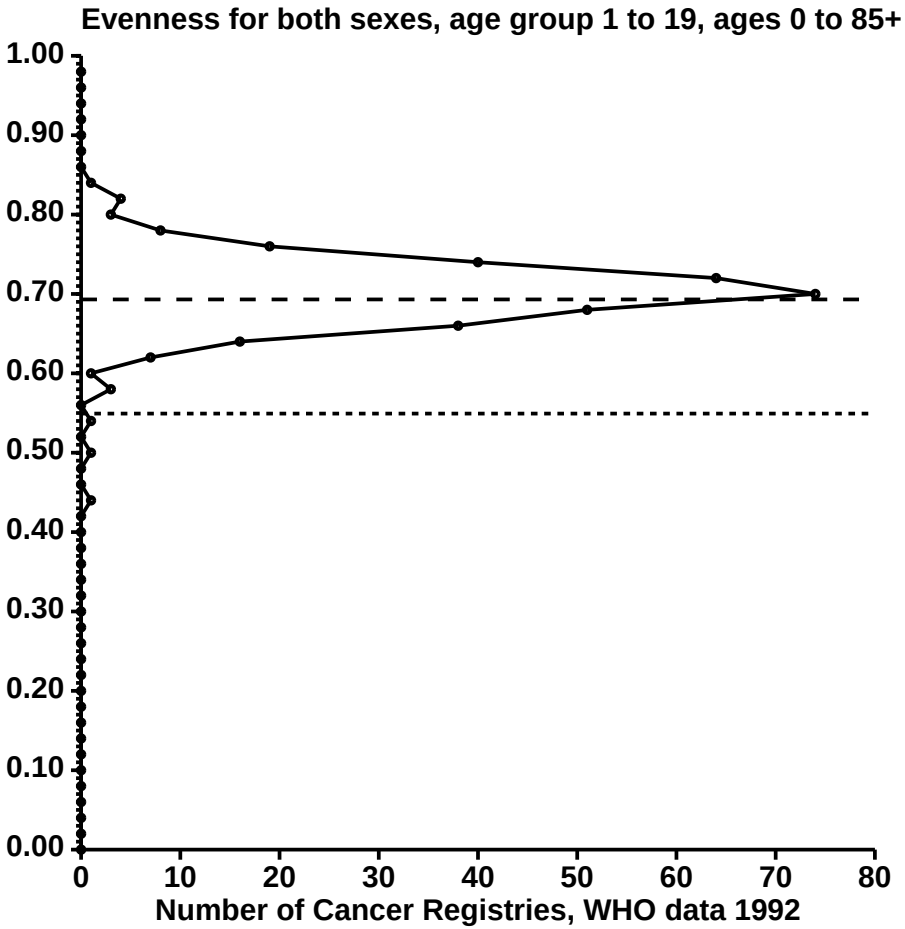
http://ci5.iarc.fr/

Cancer Incidence WHO data

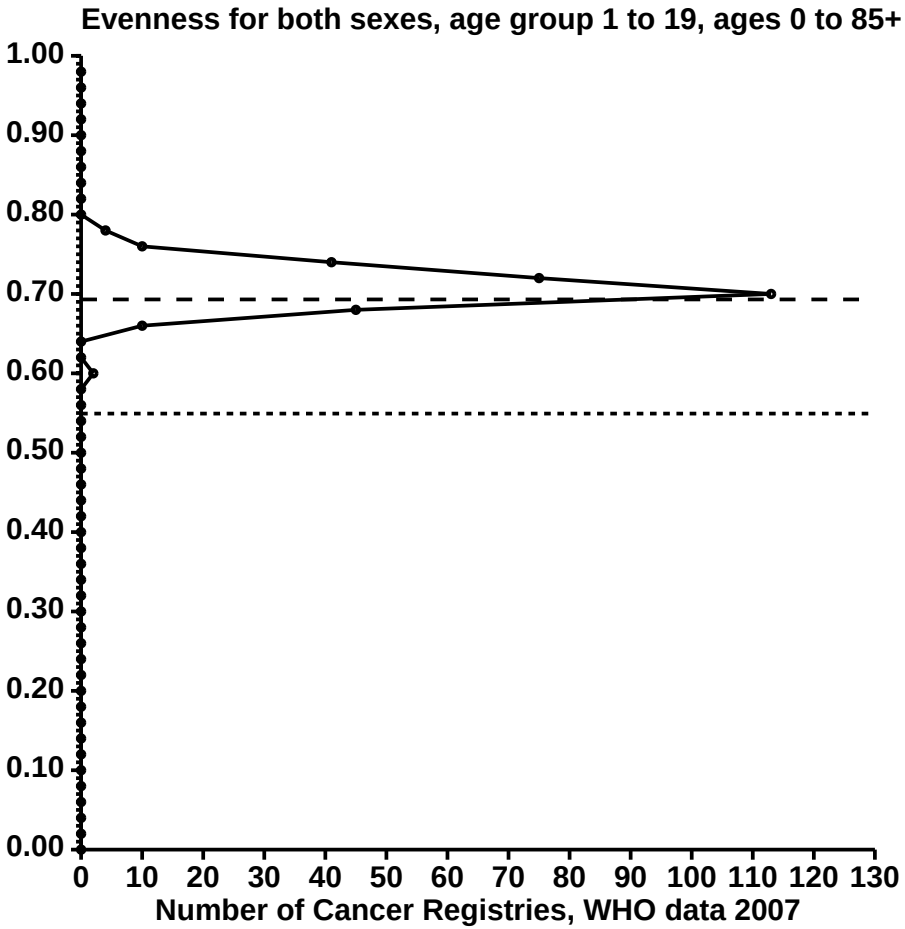
Table 3.1 Classification used in incidence tables

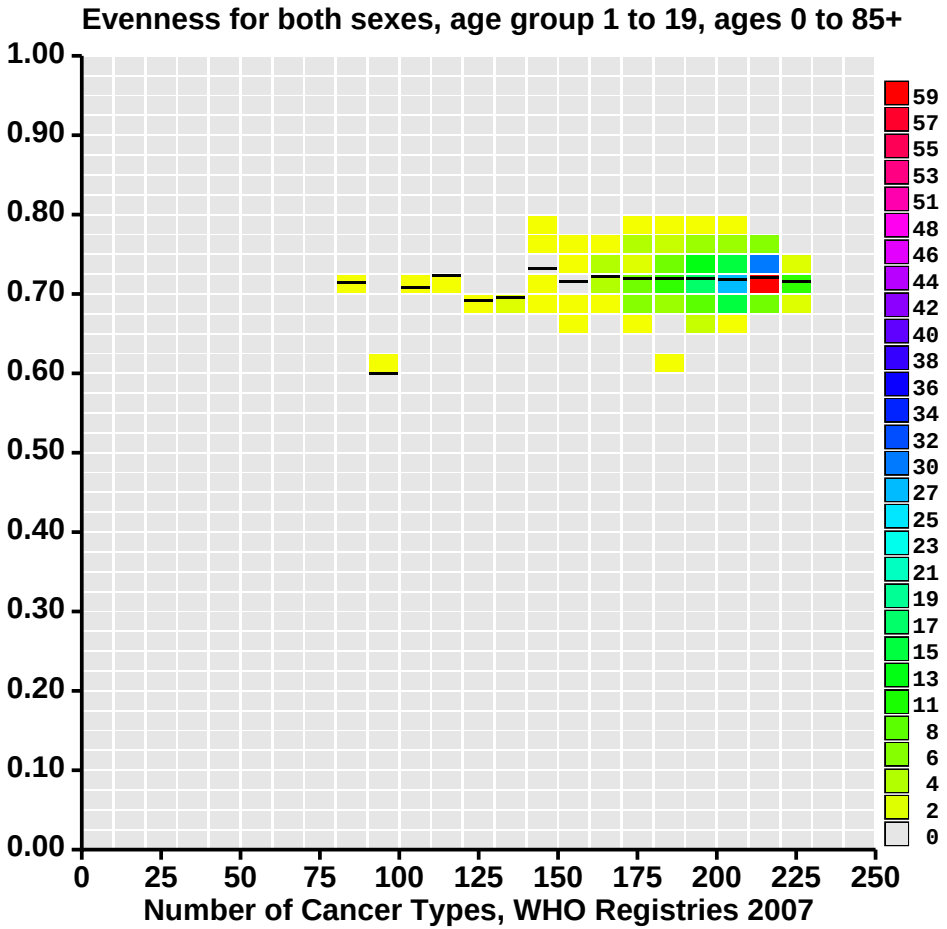
Site	Full title	Groupings used in tables	Short title used in tables
C00	Malignant neoplasm of lip	-	Lip
C01	Malignant neoplasm of base of tongue	C01-C02 are grouped	Tongue
C02	Malignant neoplasm of other and unspecified parts of tongue		
C03	Malignant neoplasm of gum	C03-C06 are grouped	Mouth
C04	Malignant neoplasm of floor of mouth		
C05	Malignant neoplasm of palate		
C06	Malignant neoplasm of other and unspecified parts of mouth		
C07	Malignant neoplasm of parotid gland	C07-C08 are grouped	
C08	Malignant neoplasm of other and unspecified major salivary glands		Salivary gland
C09	Malignant neoplasm of tonsil	-	Tonsil
C10	Malignant neoplasm of oropharynx	-	Other oropharynx
C11	Malignant neoplasm of nasopharynx	-	Nasopharynx
C12	Malignant neoplasm of pyriform sinus	C12-C13 are grouped	Hypopharynx
C13	Malignant neoplasm of hypopharynx		
C14	Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx	-	Pharynx unspecified
C15	Malignant neoplasm of oesphagus	-	Oesophagus
C16	Malignant neoplasm of stomach	-	Stomach
C17	Malignant neoplasm of small intestine	-	Small intestine
C18	Malignant neoplasm of colon	-	Colon
C19	Malignant neoplasm of rectosigmoid junction	C19-C20 are grouped	Rectum
C20	Malignant neoplasm of rectum		
C21	Malignant neoplasm of anus and anal canal	-	Anus
C22	Malignant neoplasm of liver and intrahepatic bile ducts	-	Liver
C23	Malignant neoplasm of gallbladder	C23-C24 are grouped	Gallbladder etc.
C24	Malignant neoplasm of other and unspecified parts of biliary tract		
C25	Malignant neoplasm of pancreas	-	Pancreas
C26	Malignant neoplasm of other and ill defined digestive organs	C26 is included in other and unspecified	

Cancer Incidence WHO data 1992

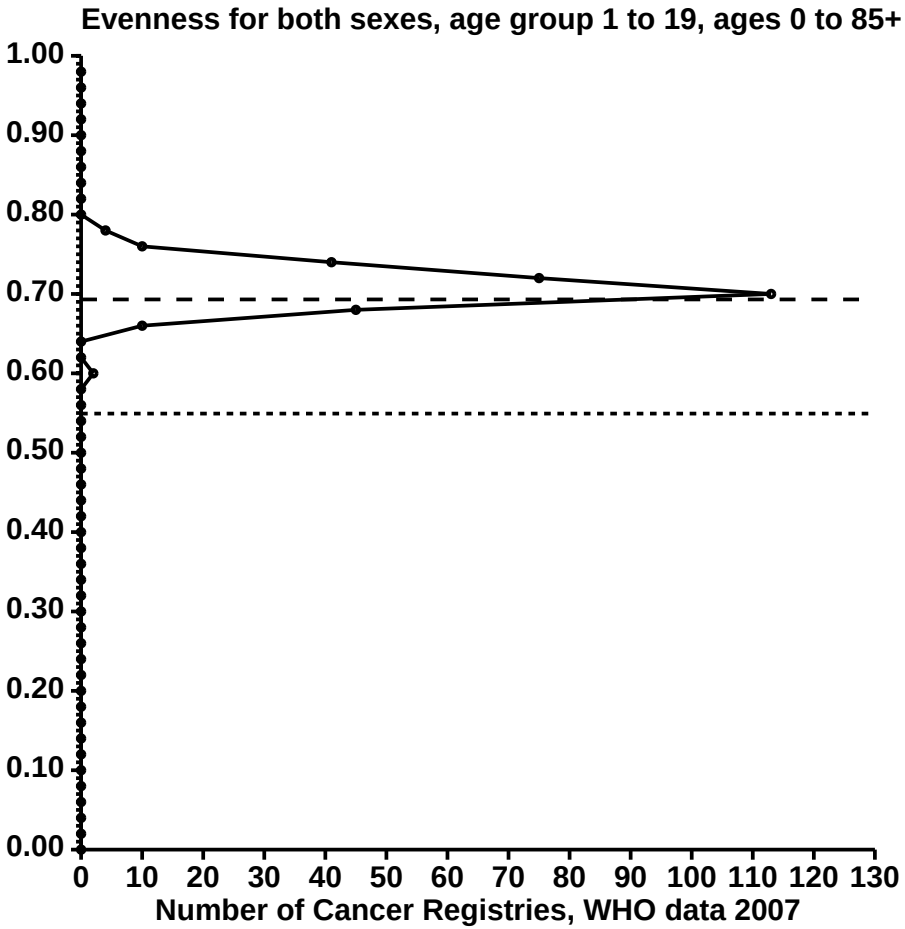


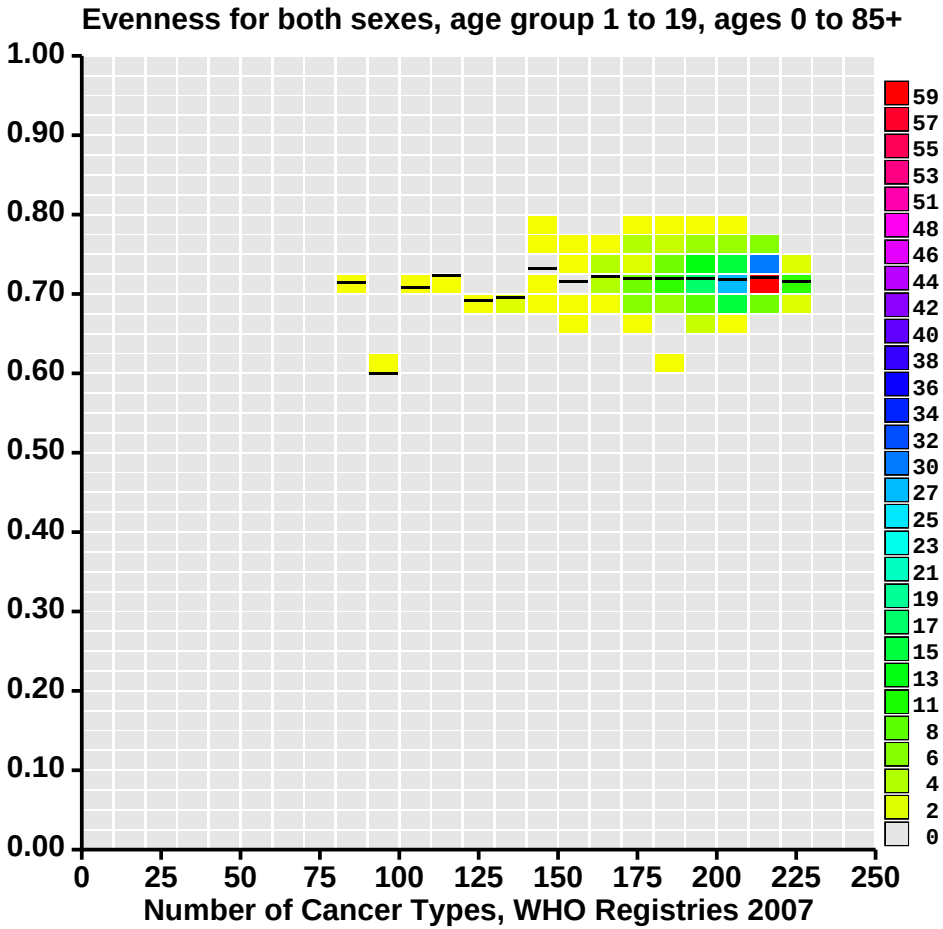
Cancer Incidence WHO data 2007





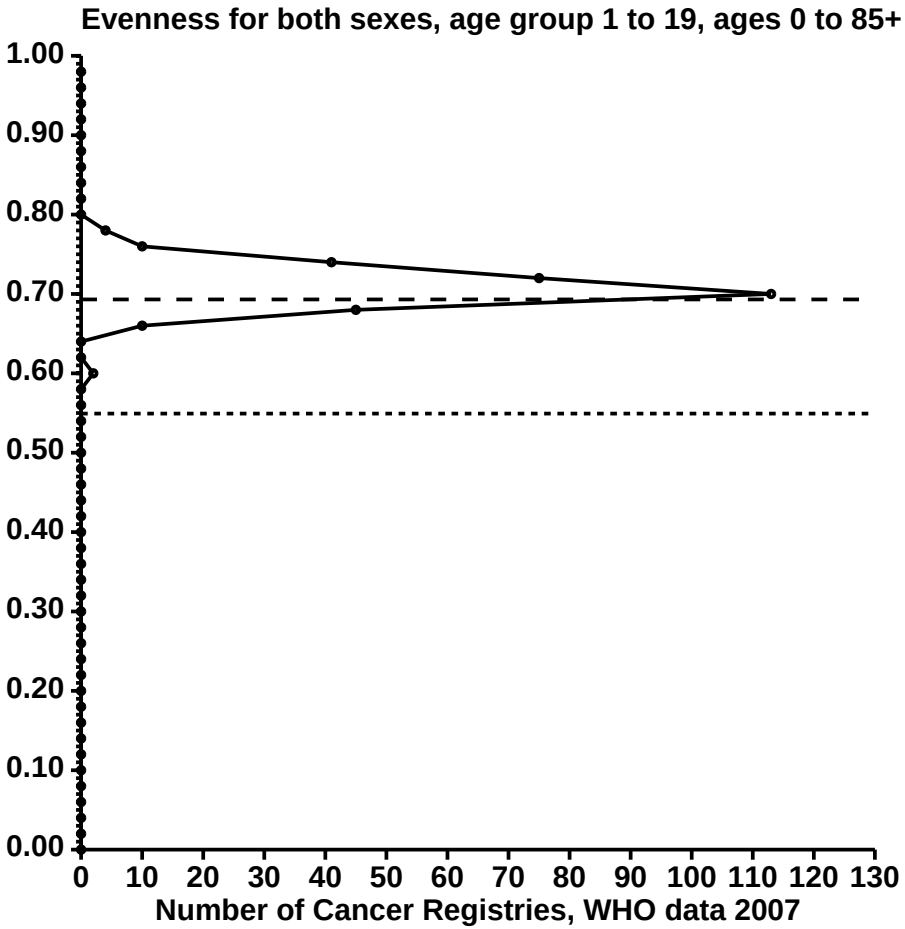
Cancer Incidence WHO data 2007

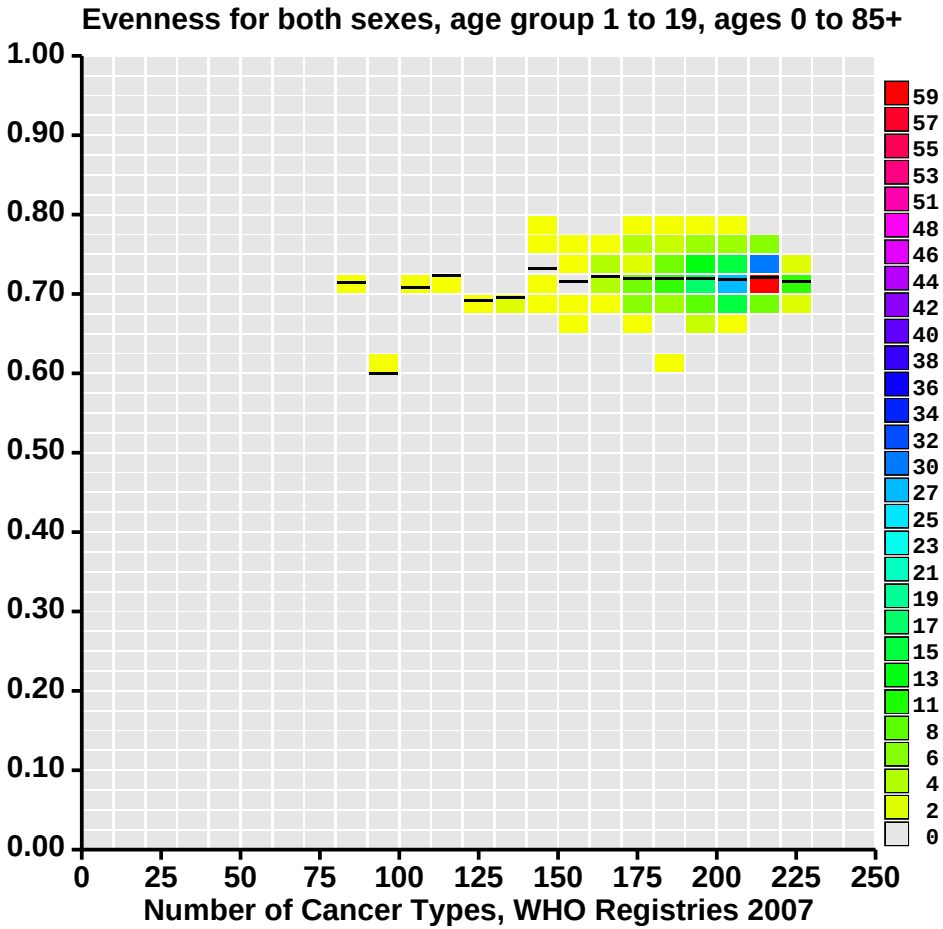




- Same results in 1992 and 2007: cancer type evenness is $\sim 70\%$

Cancer Incidence WHO data 2007





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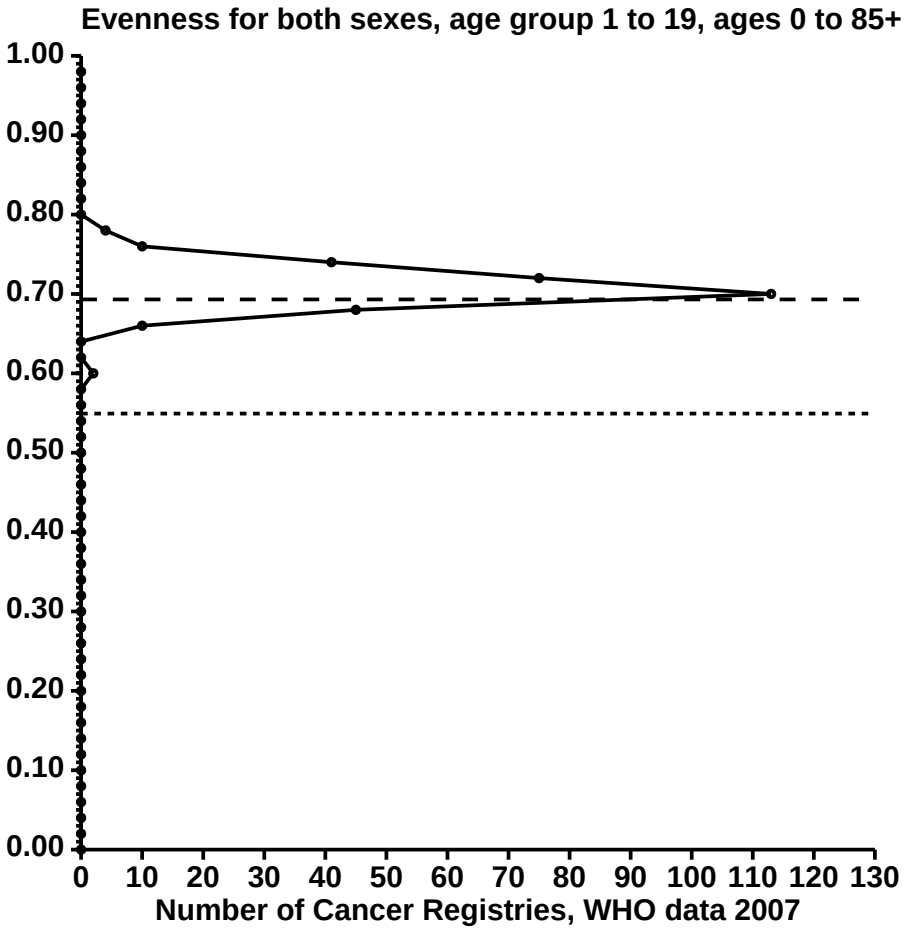
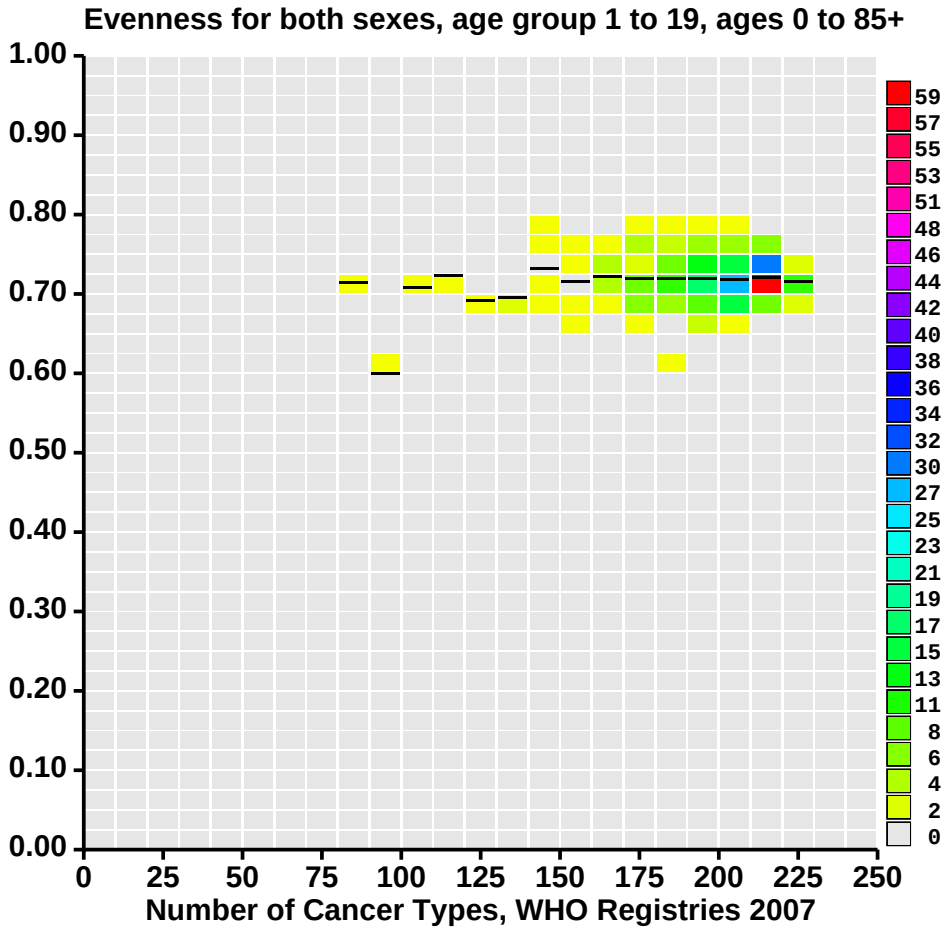
- **Hypothesis:**
  Cancer is a proxy for cell types, tissues or cell control systems

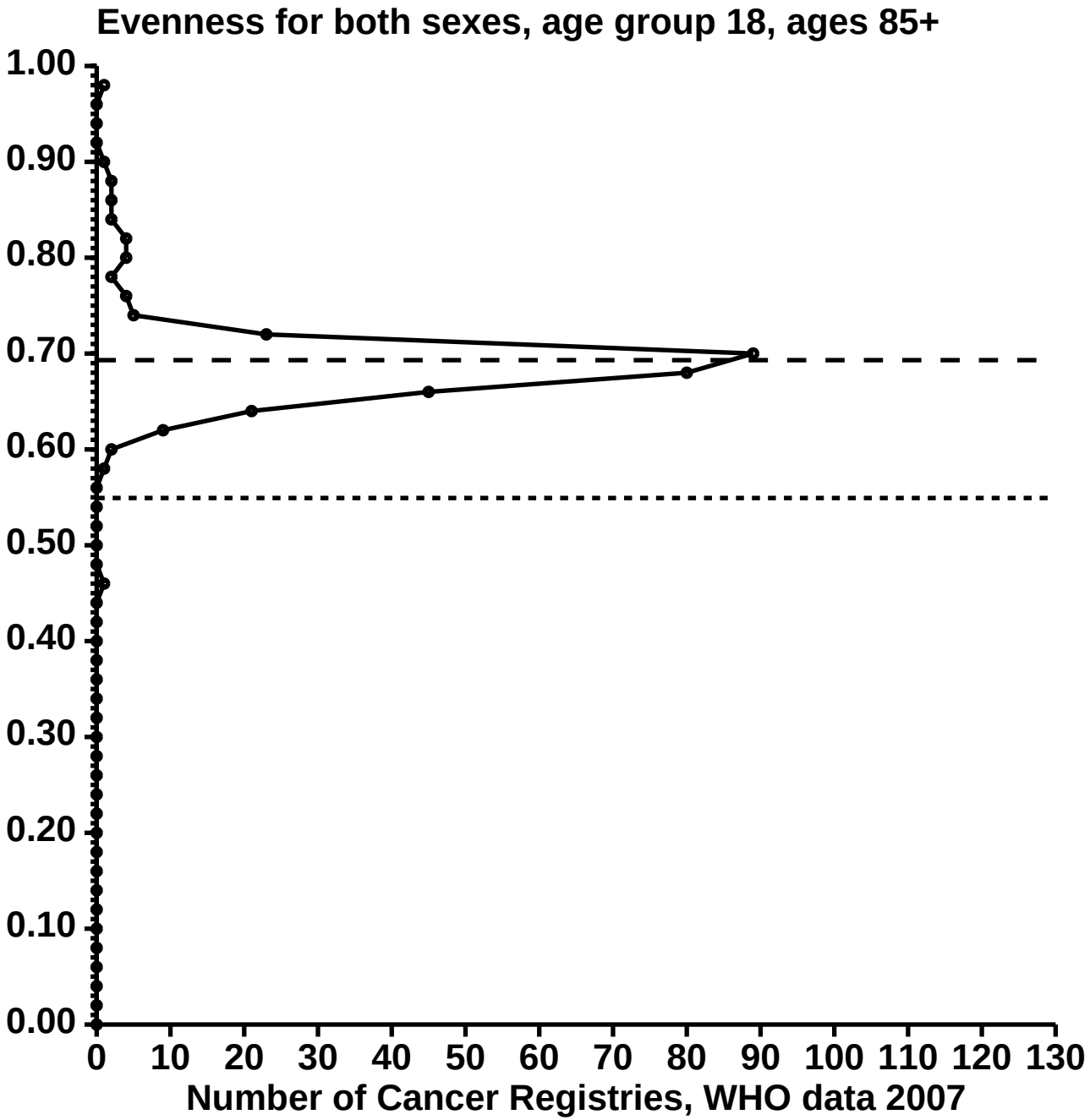
Cancer Incidence WHO data 2007



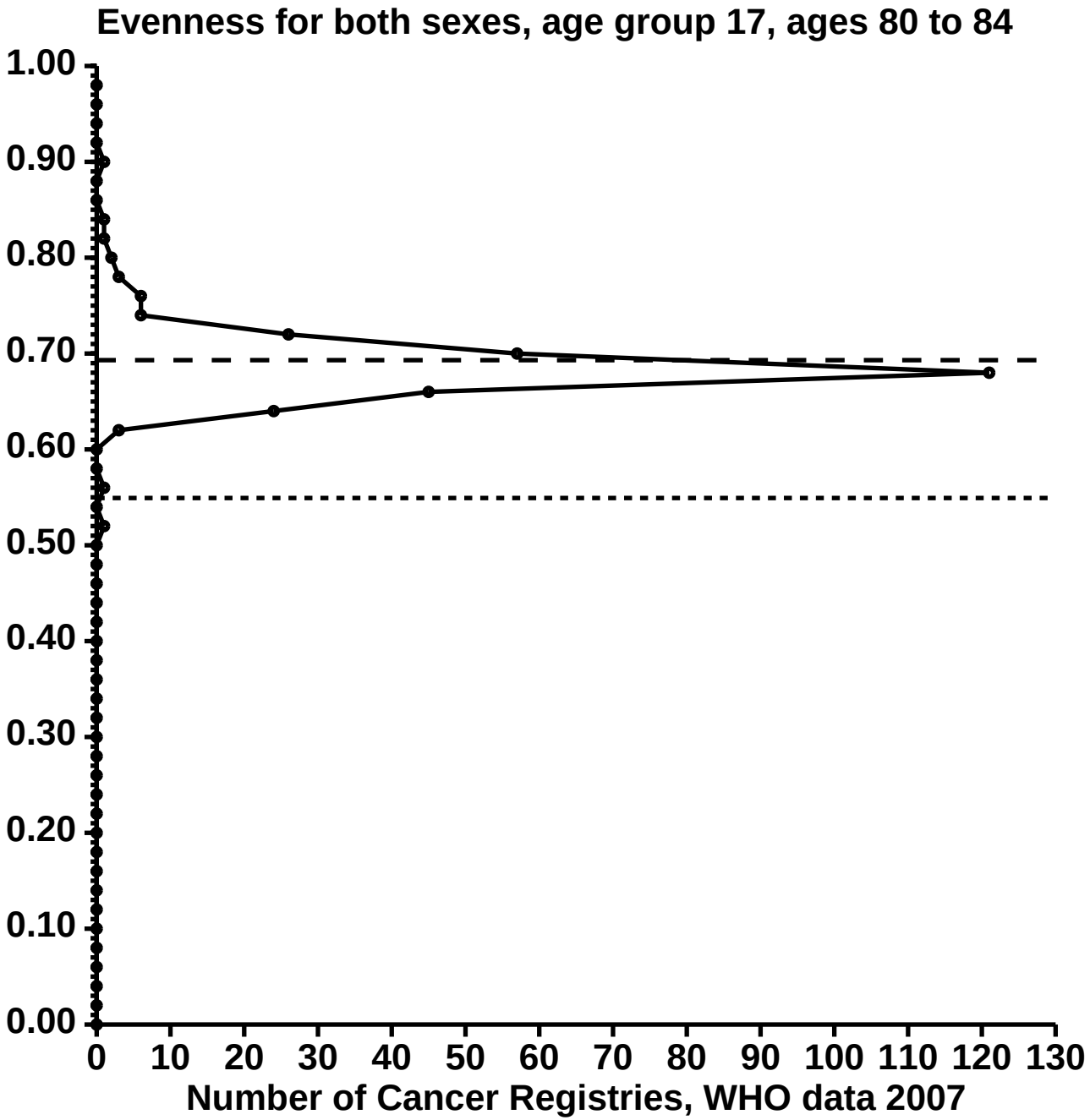


- Same results in 1992 and 2007: cancer type evenness is $\sim 70\%$
- **Hypothesis:**
  Cancer is a proxy for cell types, tissues or cell control systems
- Human development is a **Class 1 biological system!**

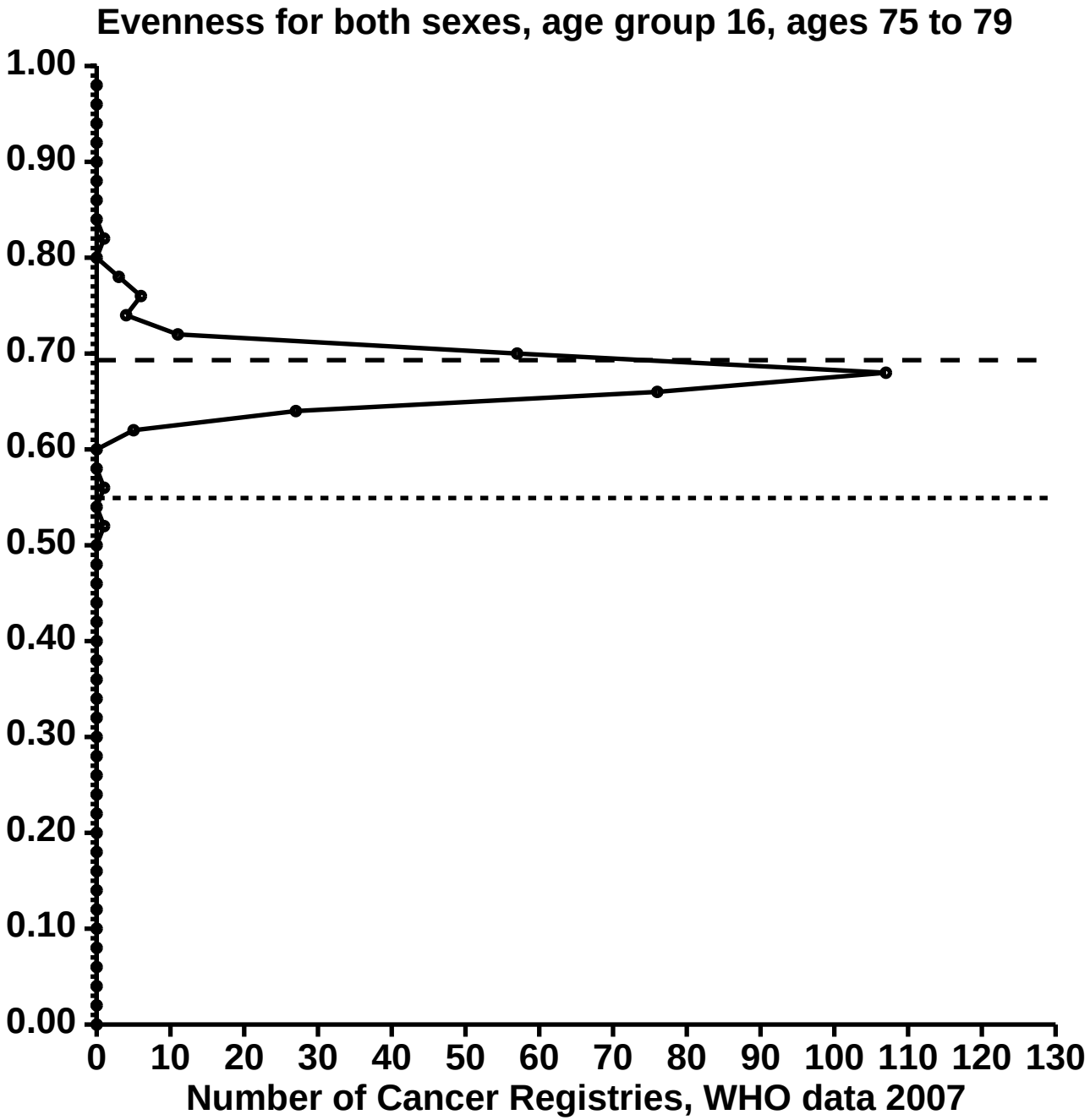
Cancer Incidence WHO data 2007



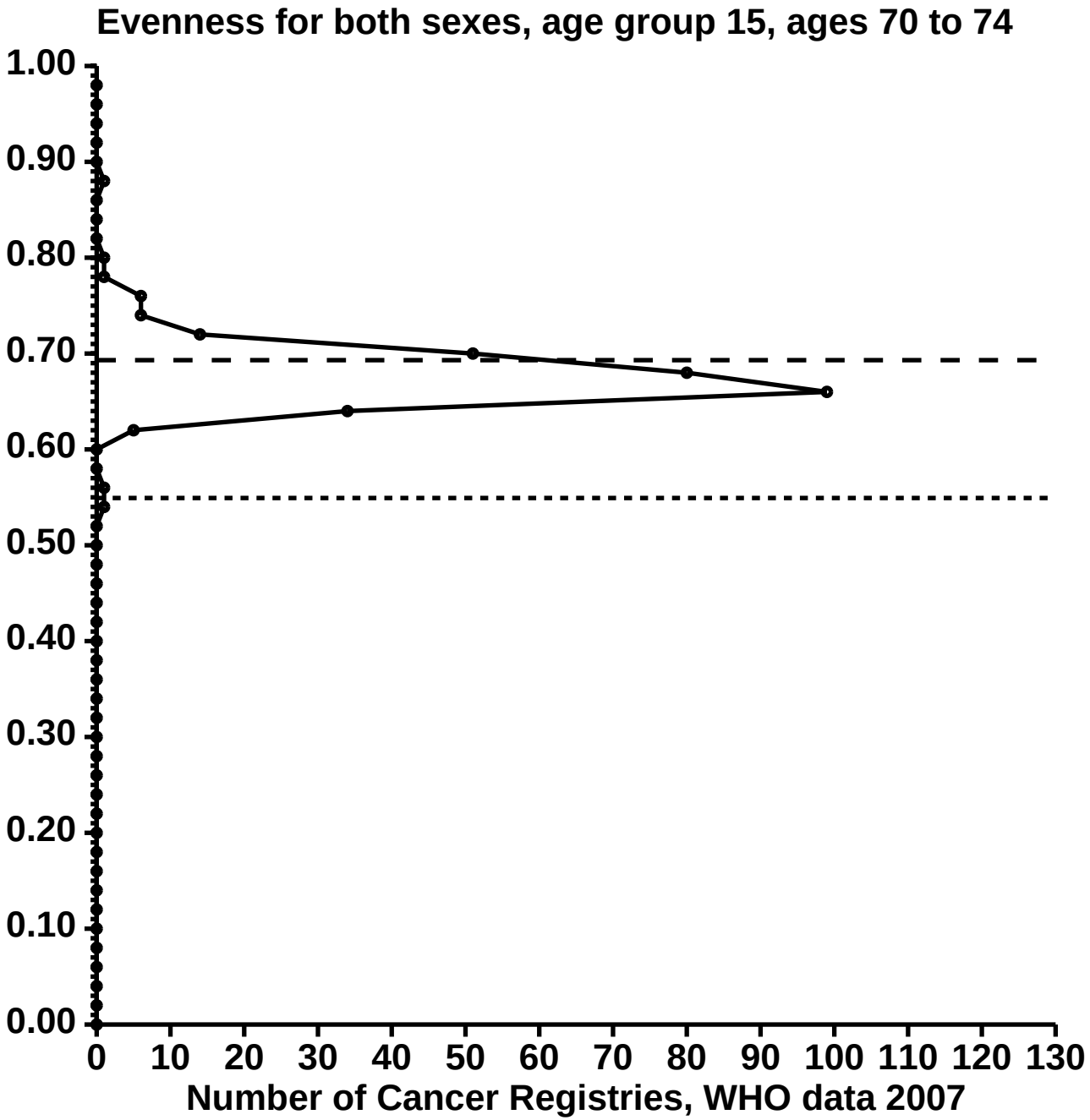
Cancer Incidence WHO data 2007



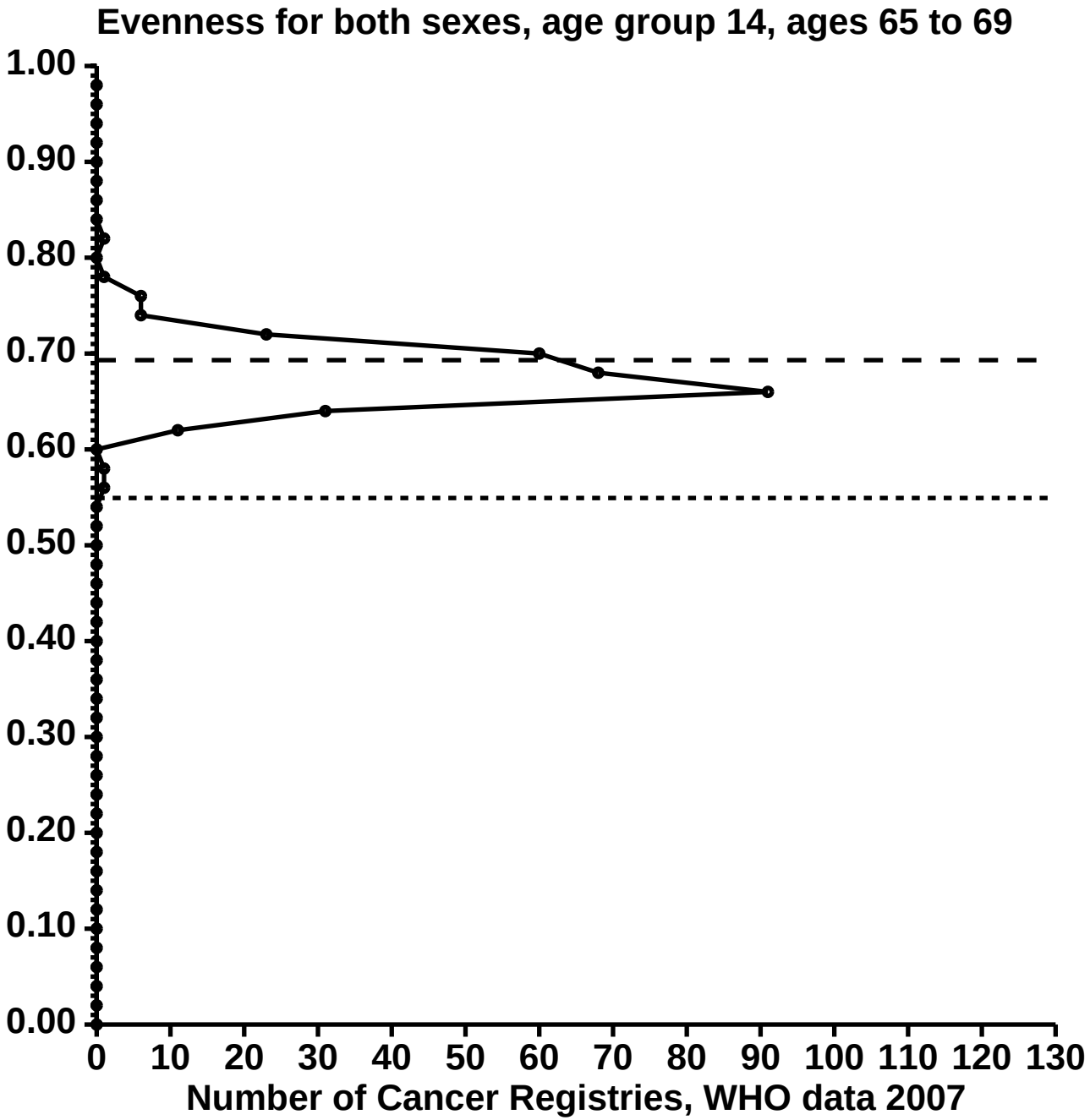
Cancer Incidence WHO data 2007



Cancer Incidence WHO data 2007



Cancer Incidence WHO data 2007



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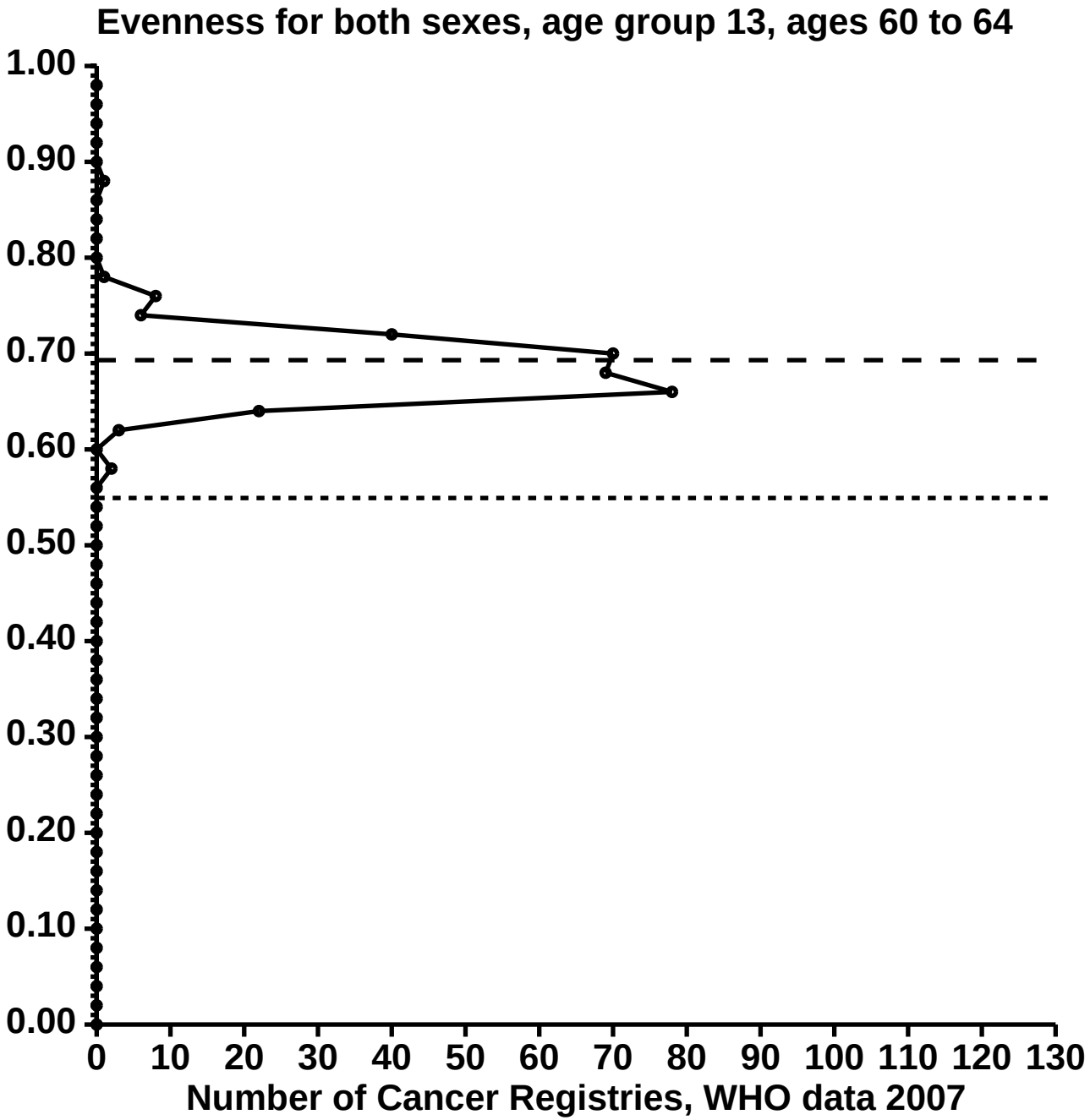

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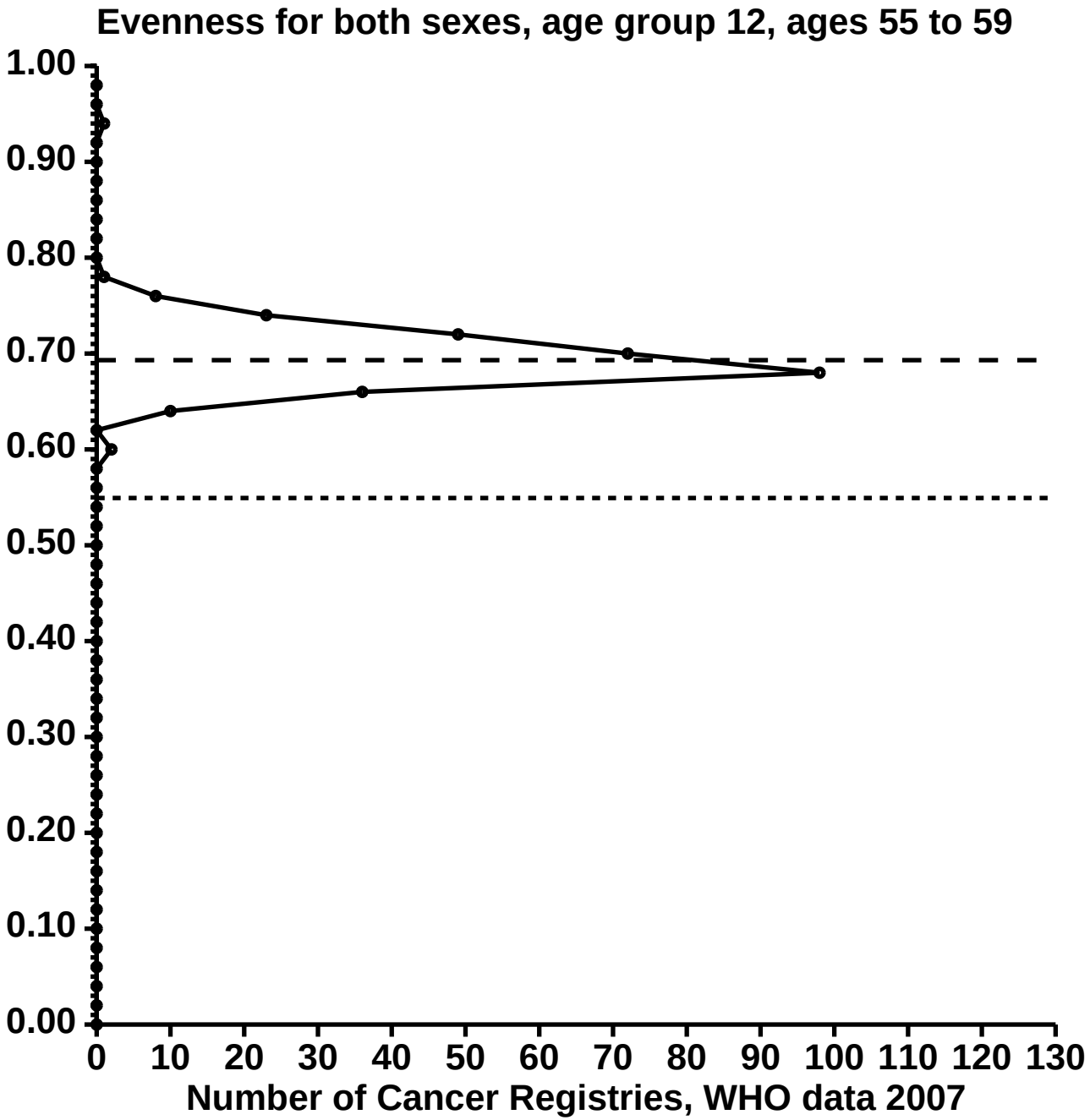
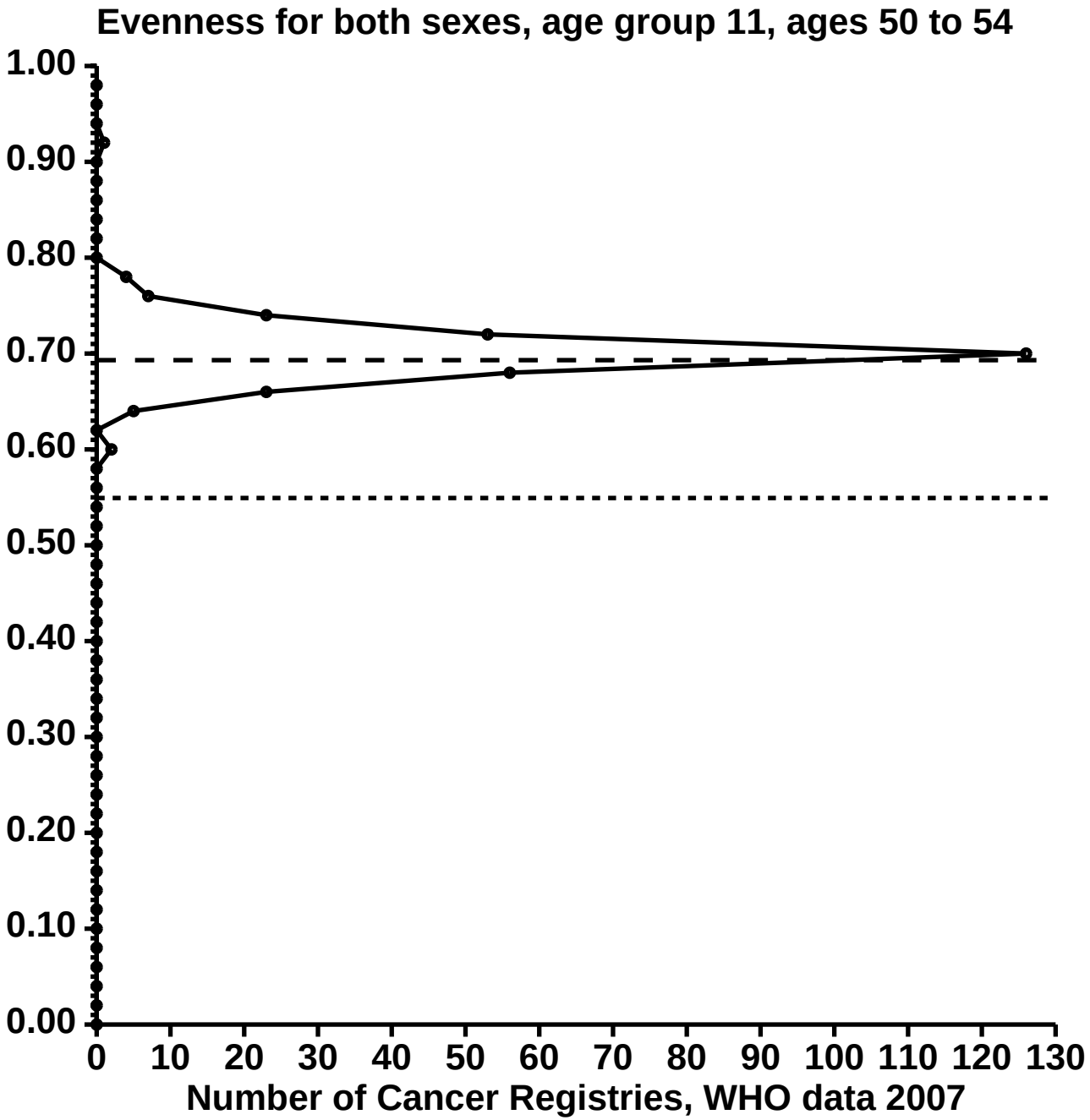


Cancer Incidence WHO data 2007



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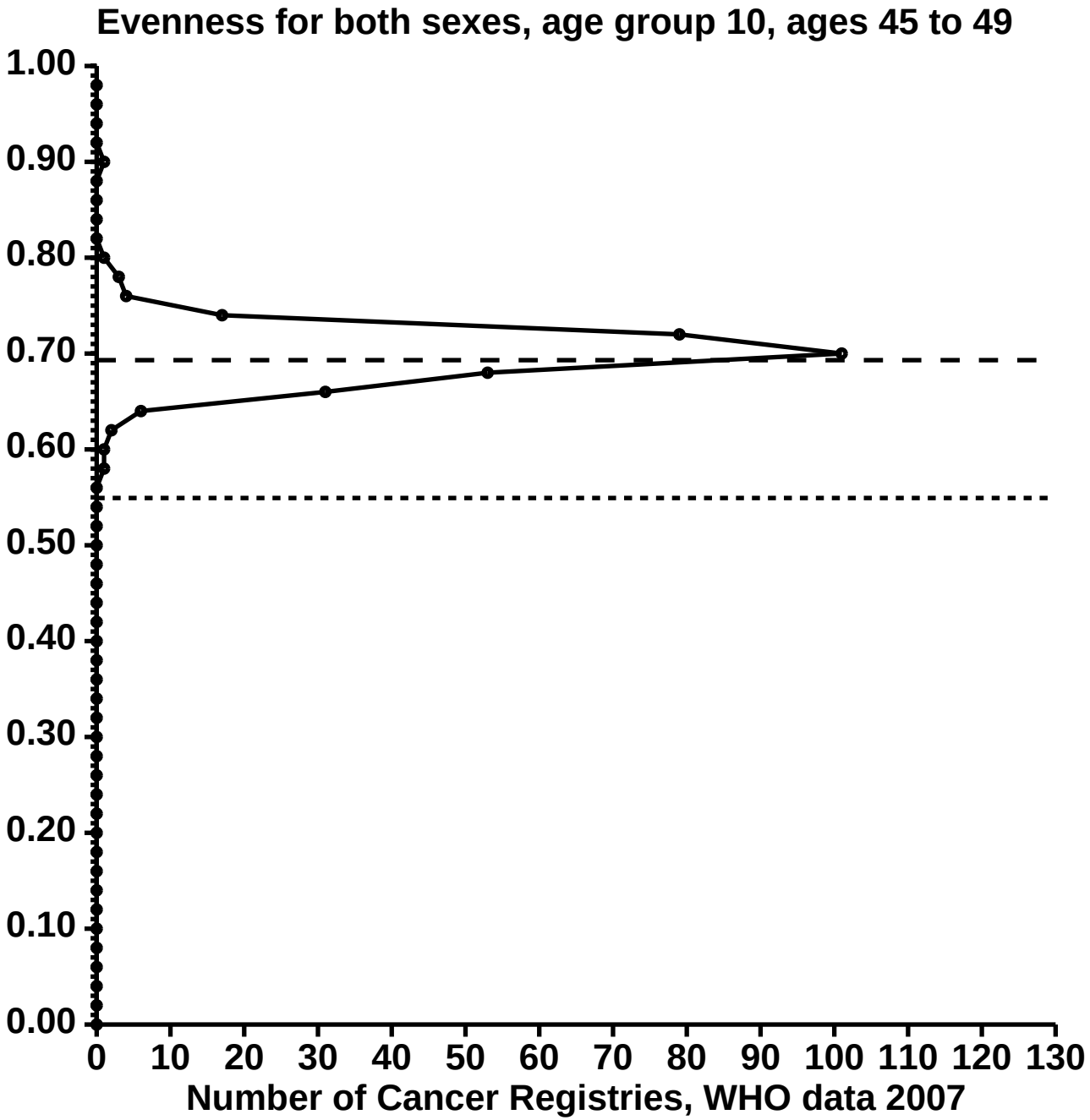

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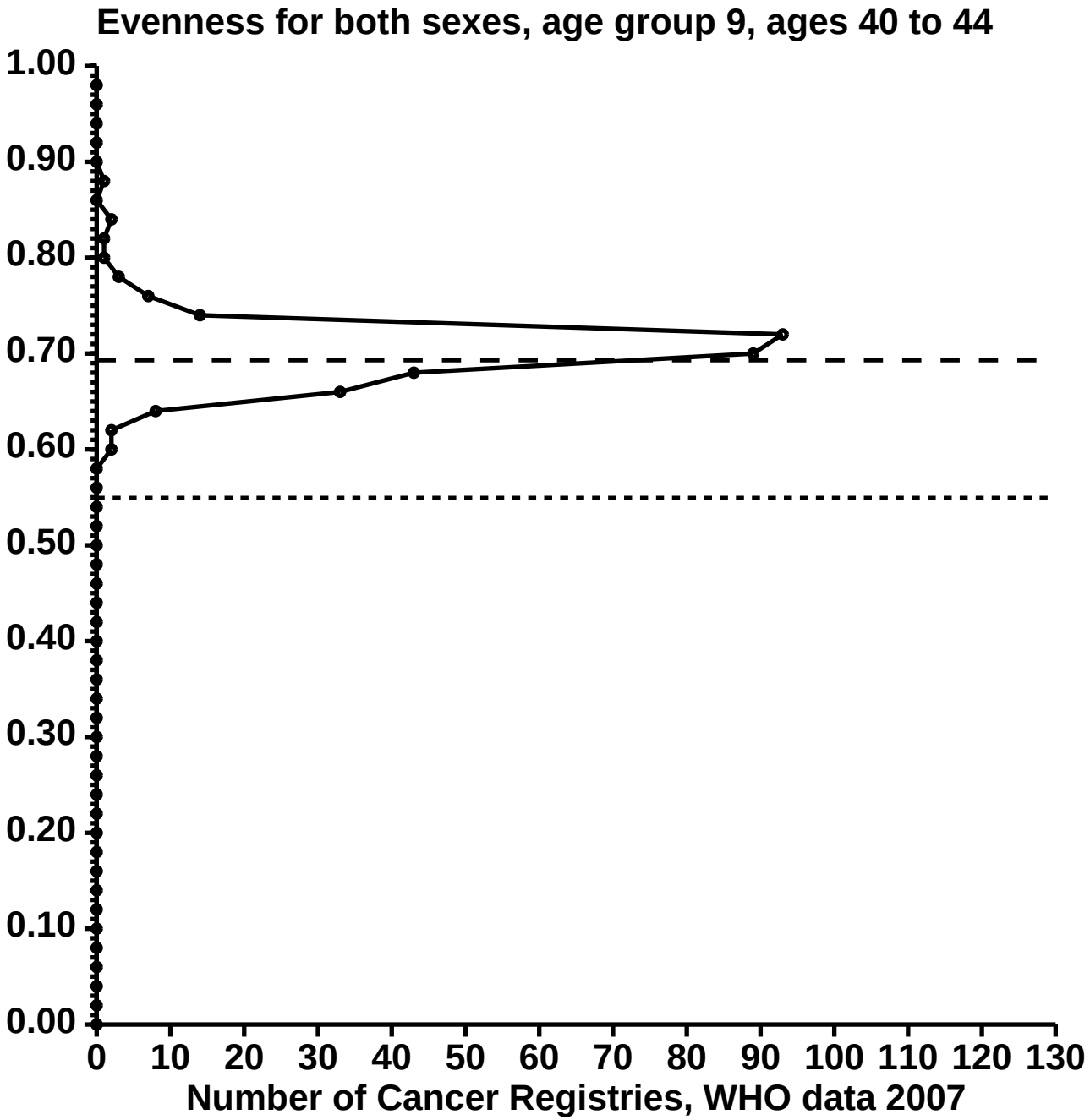

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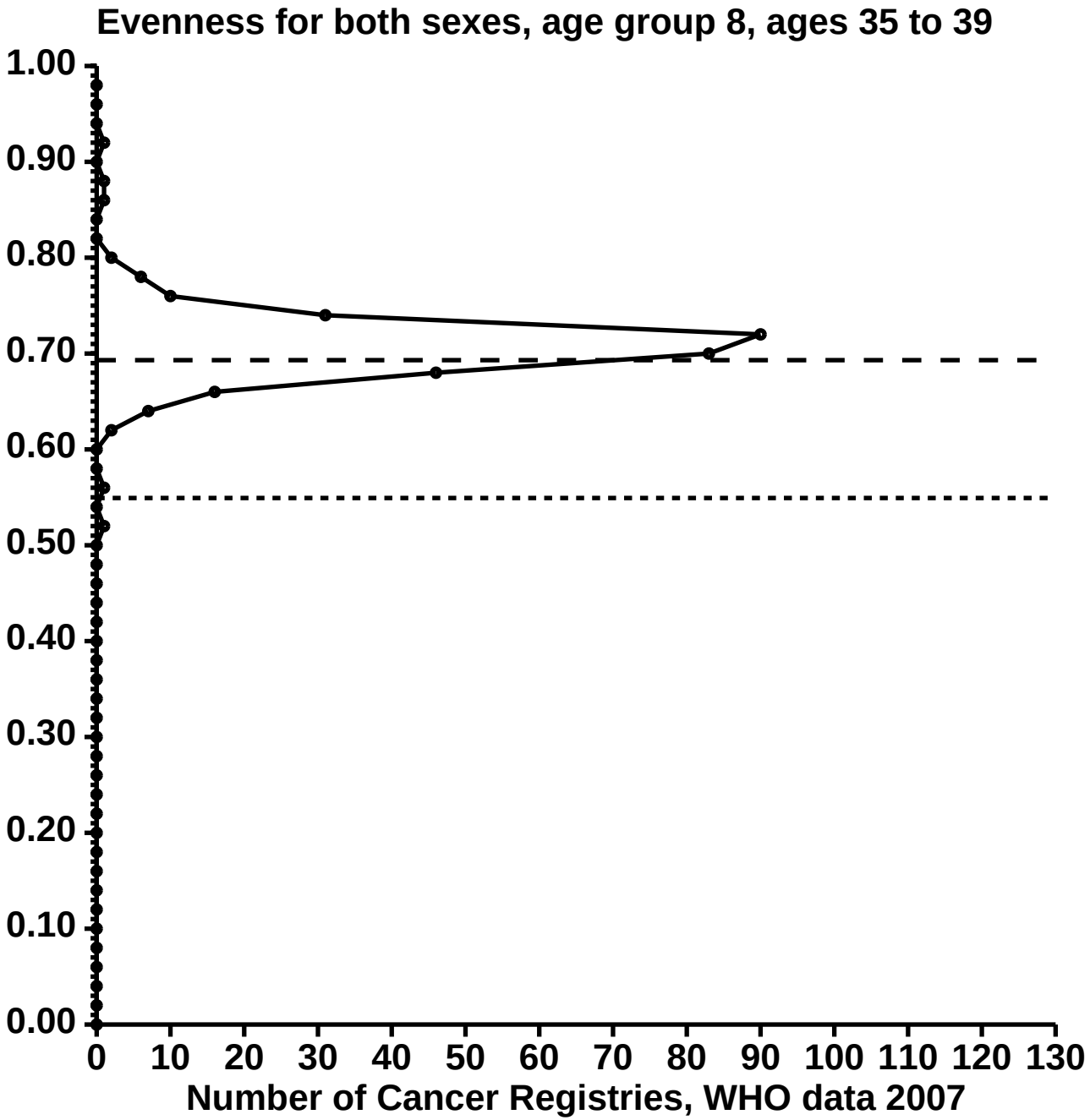

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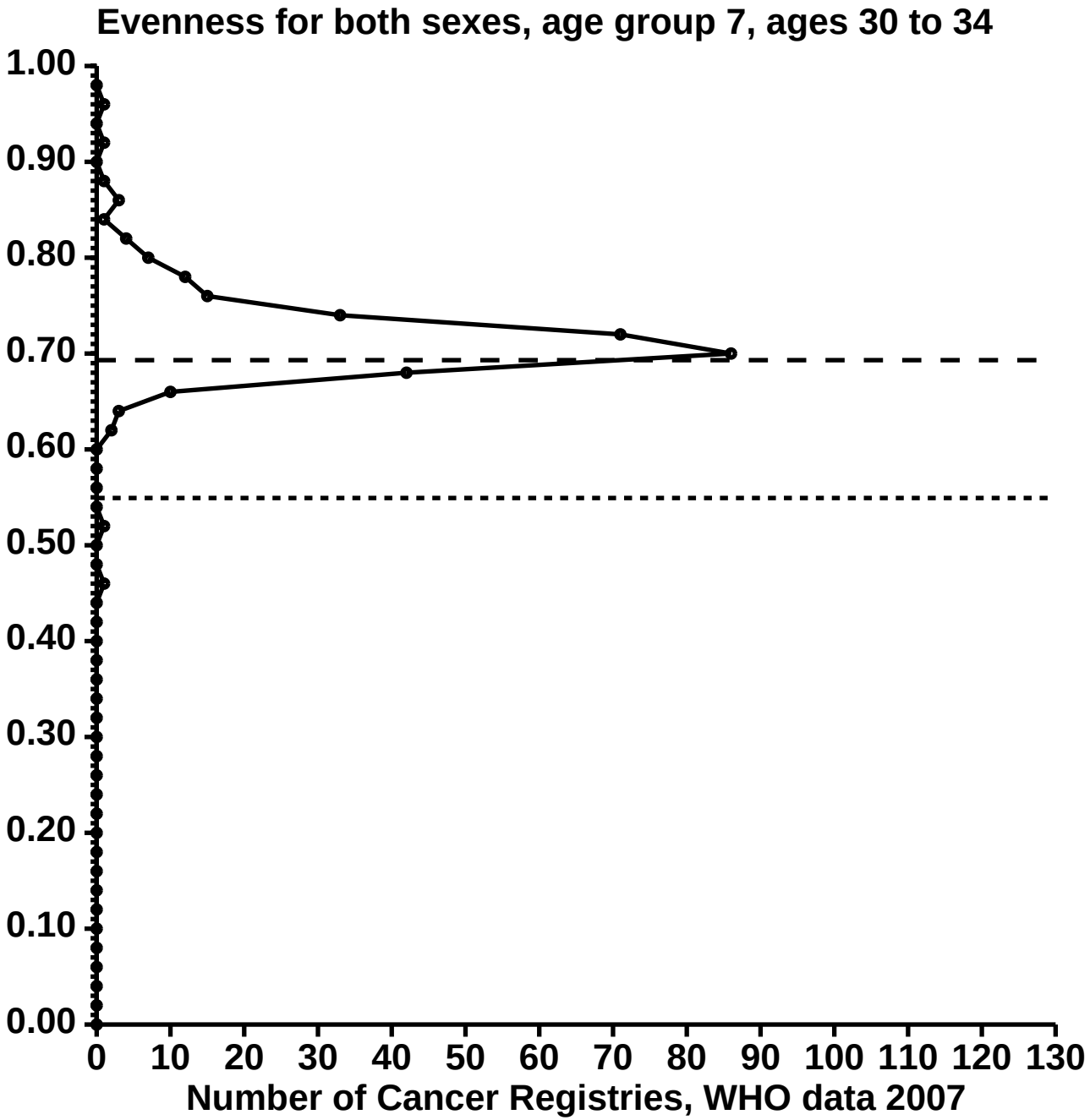

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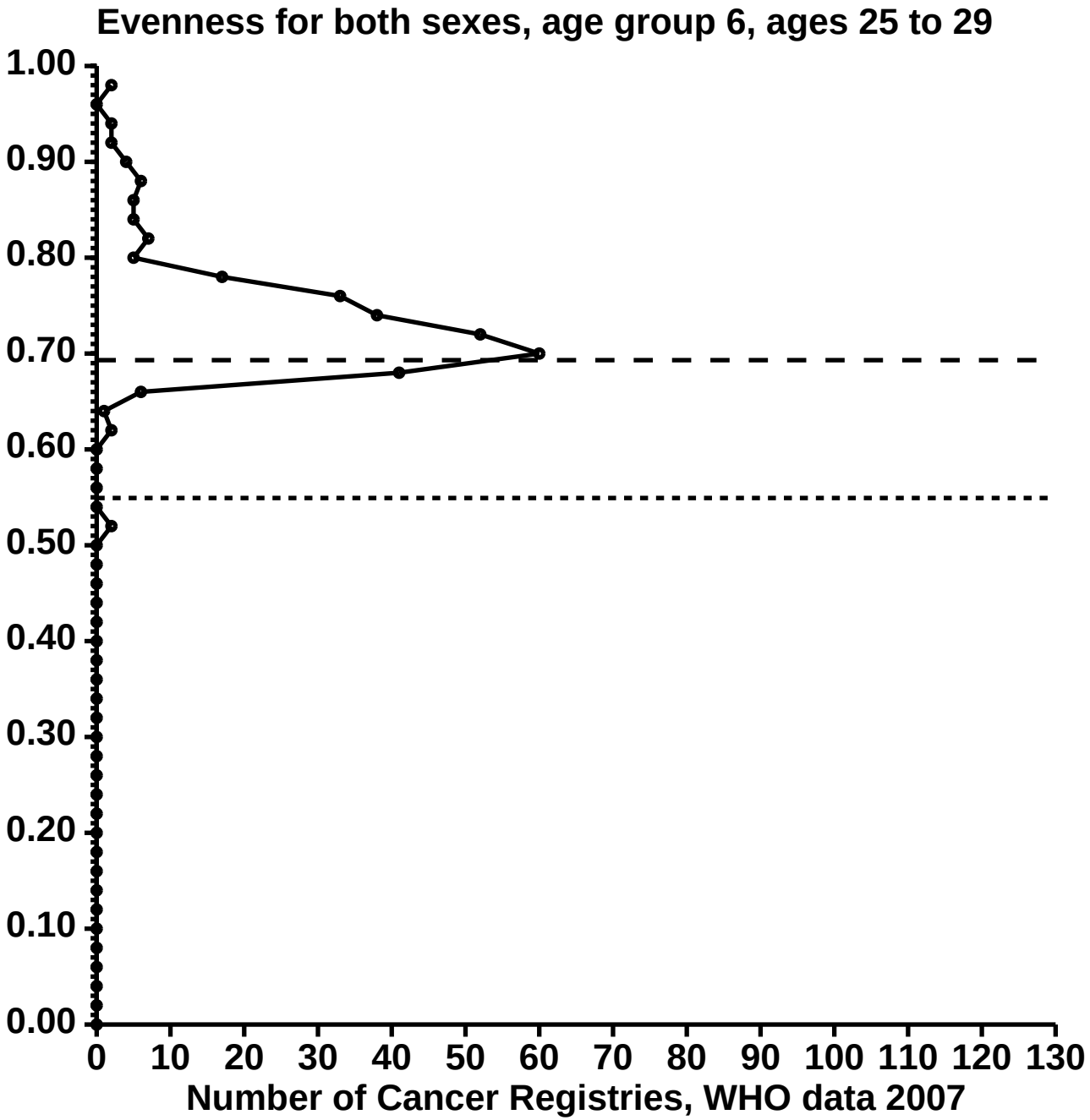

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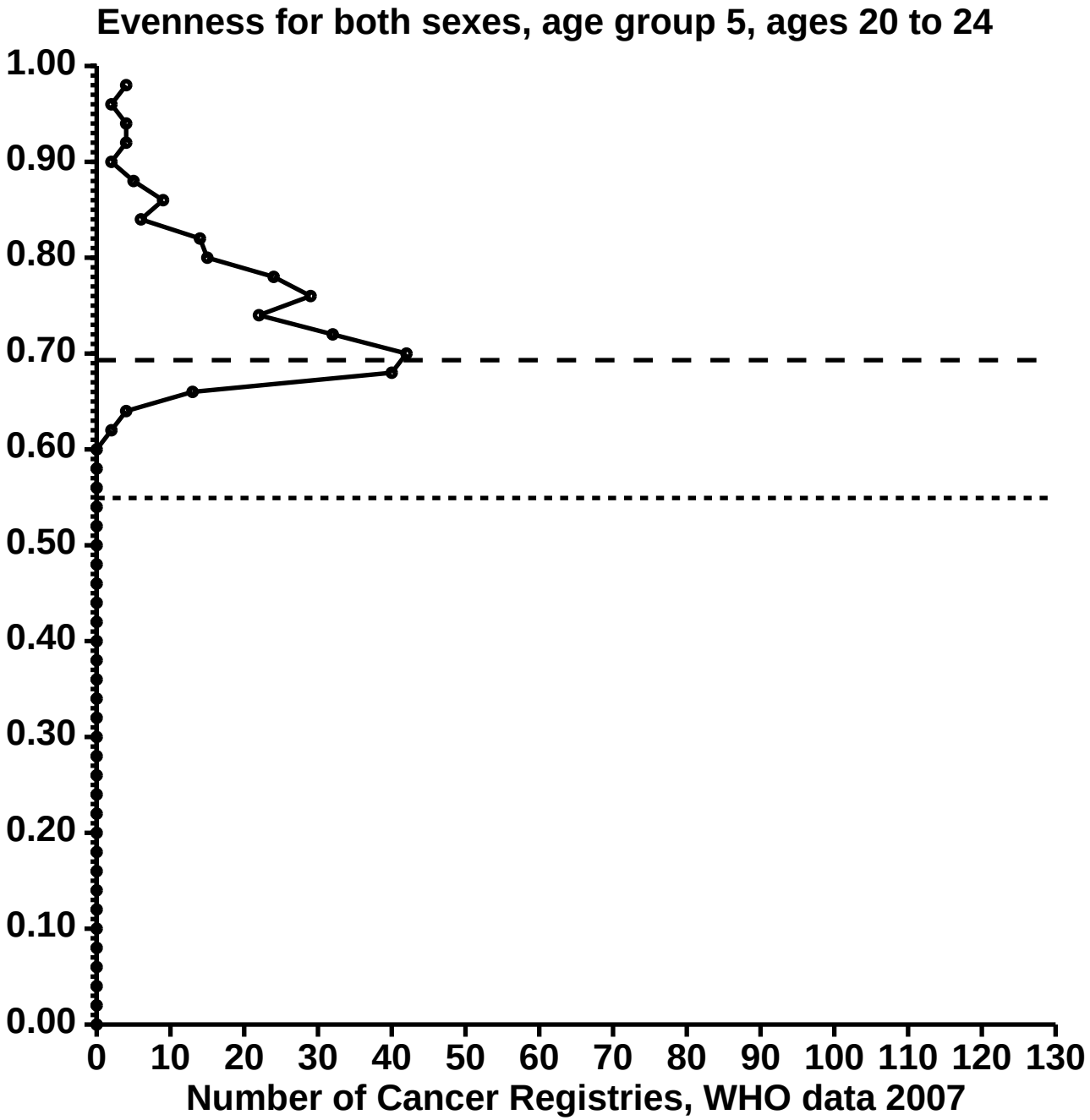

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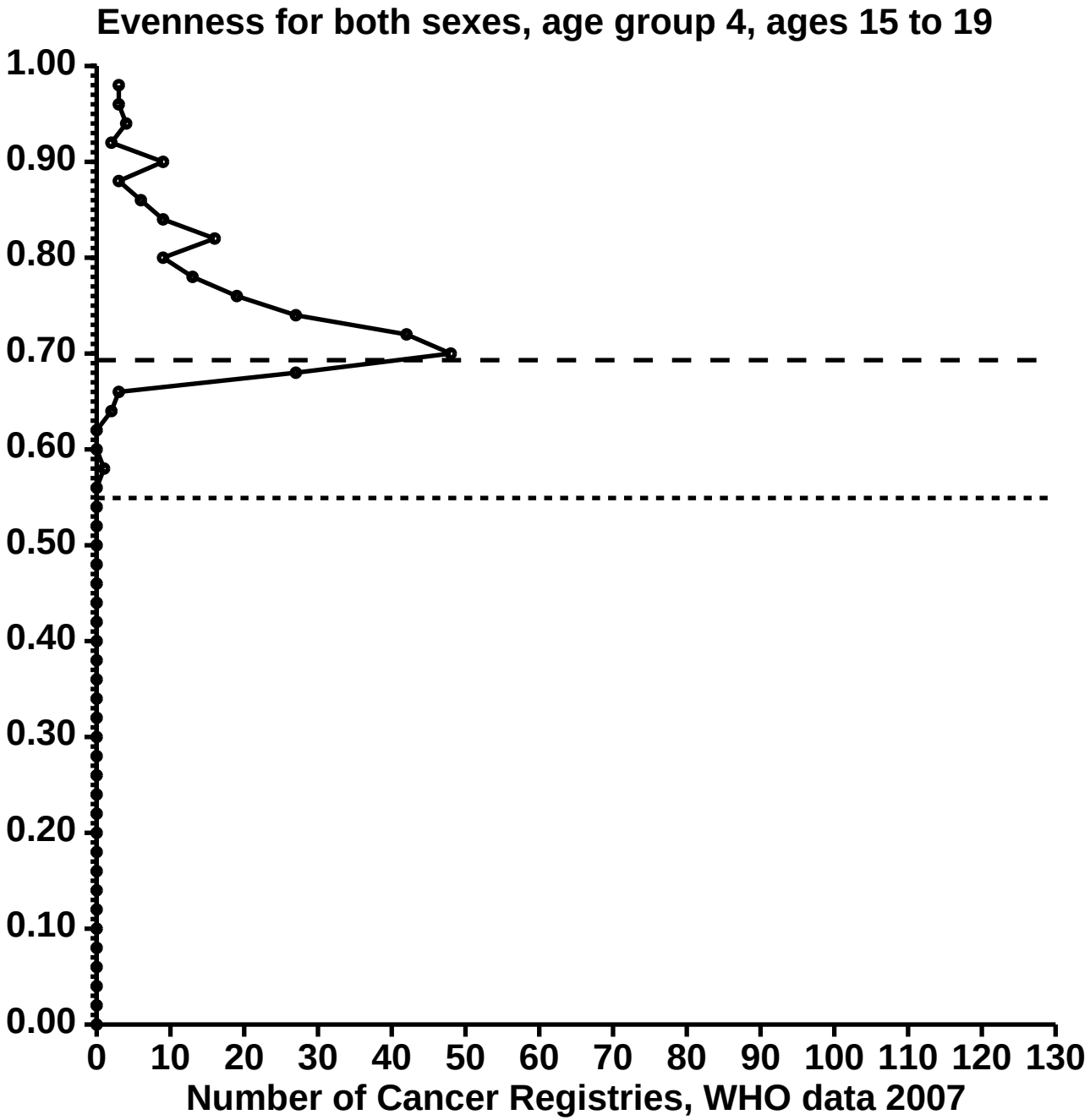

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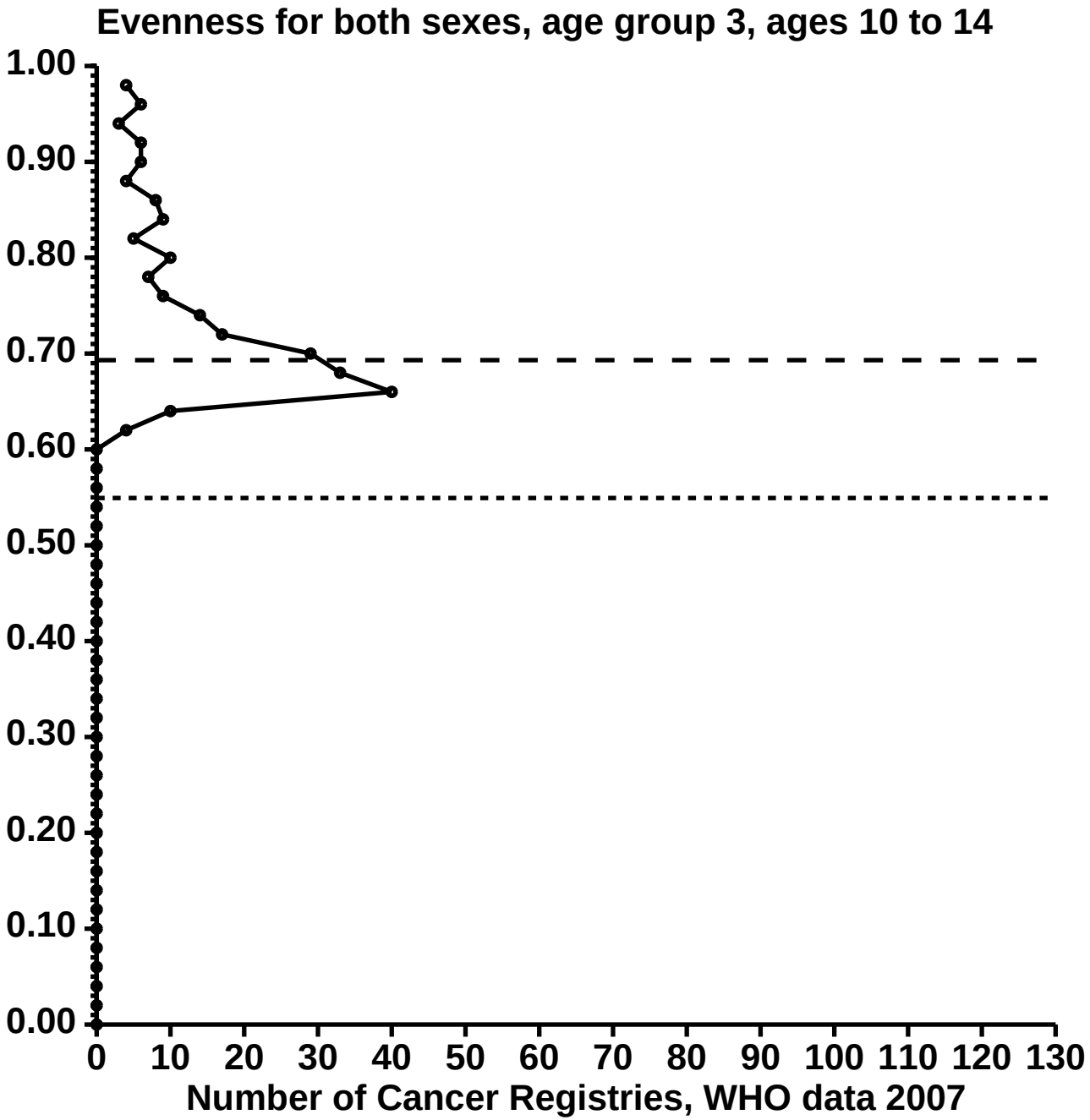

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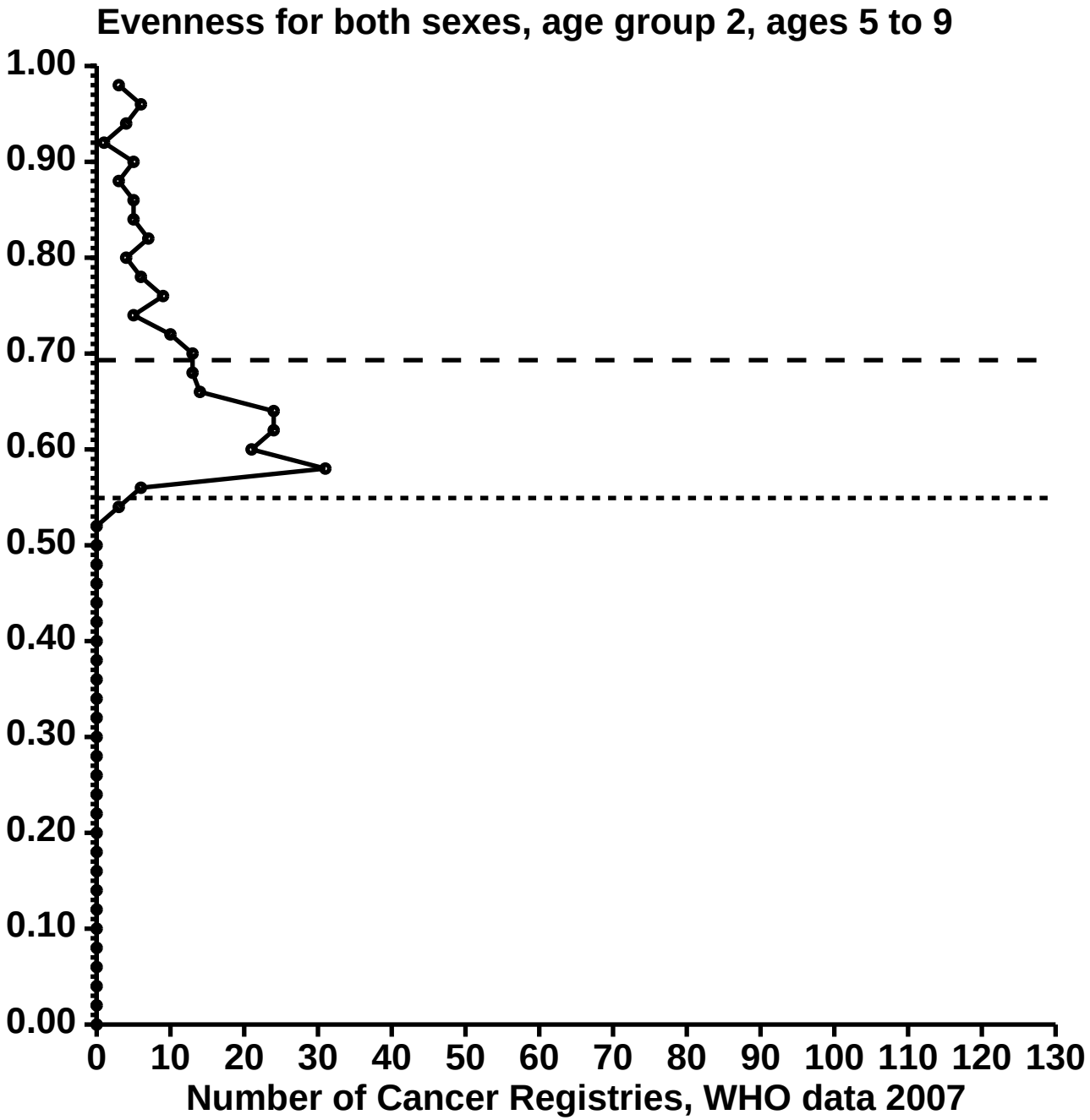

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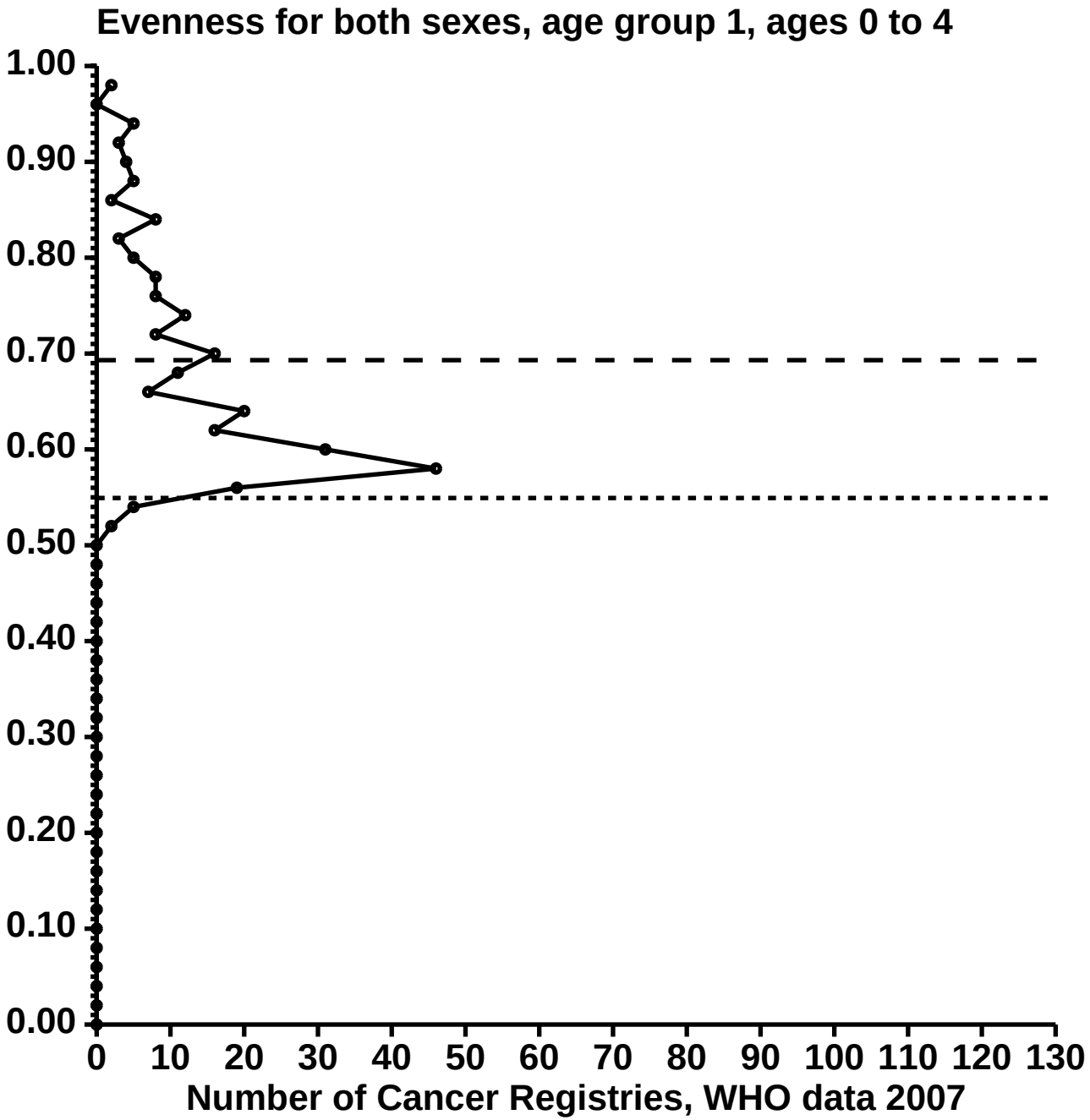
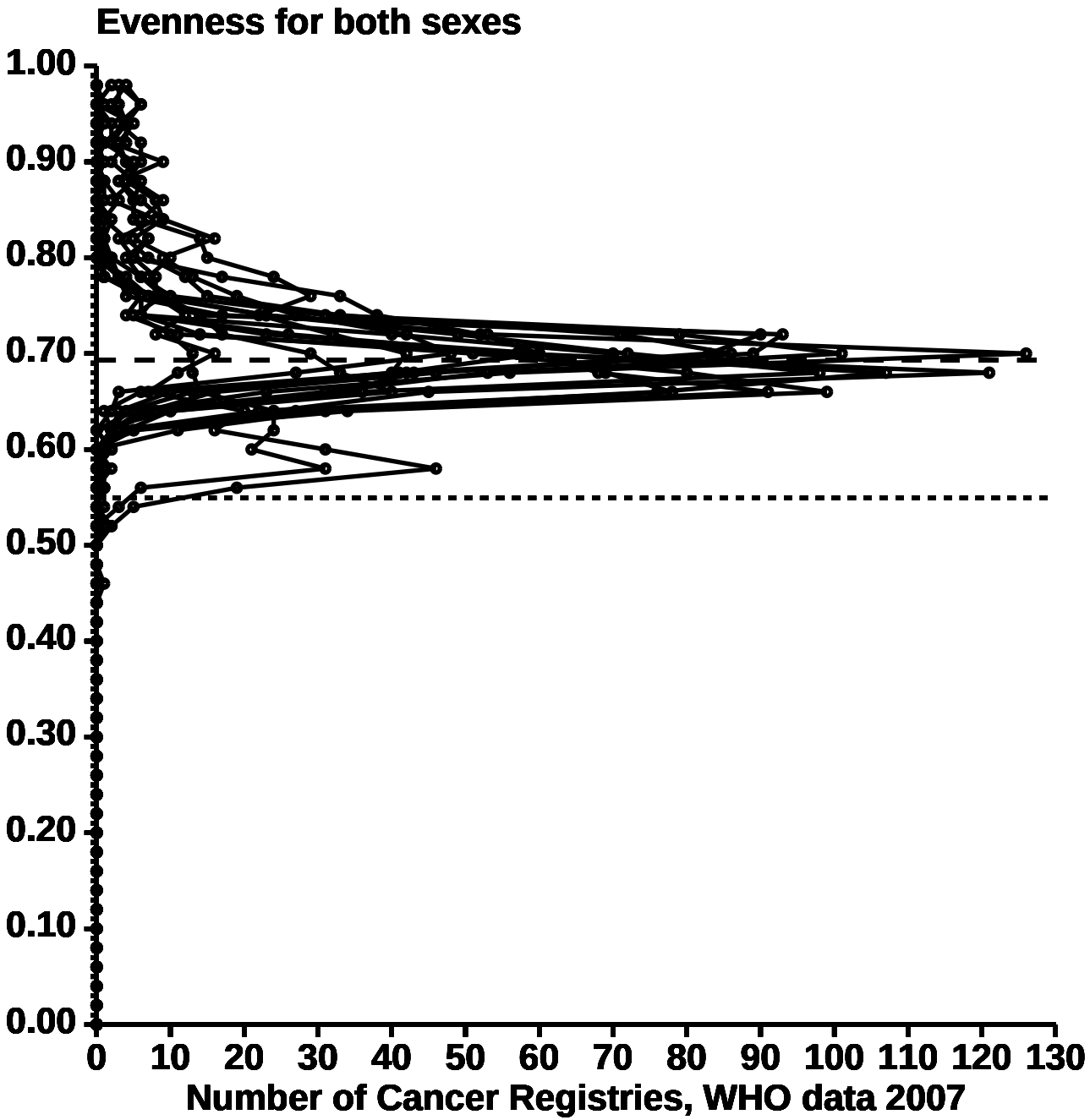


Cancer Incidence WHO data 2007



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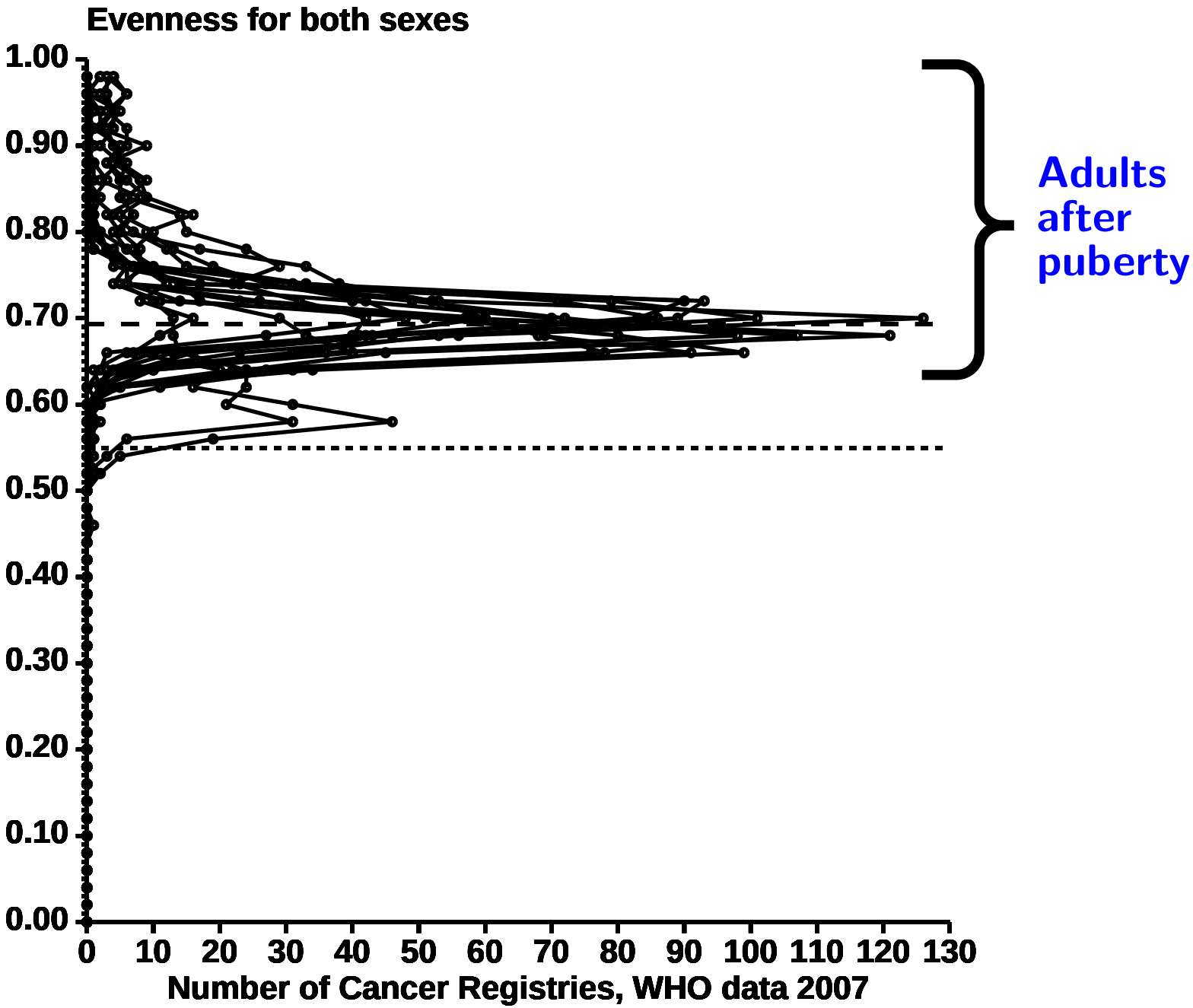

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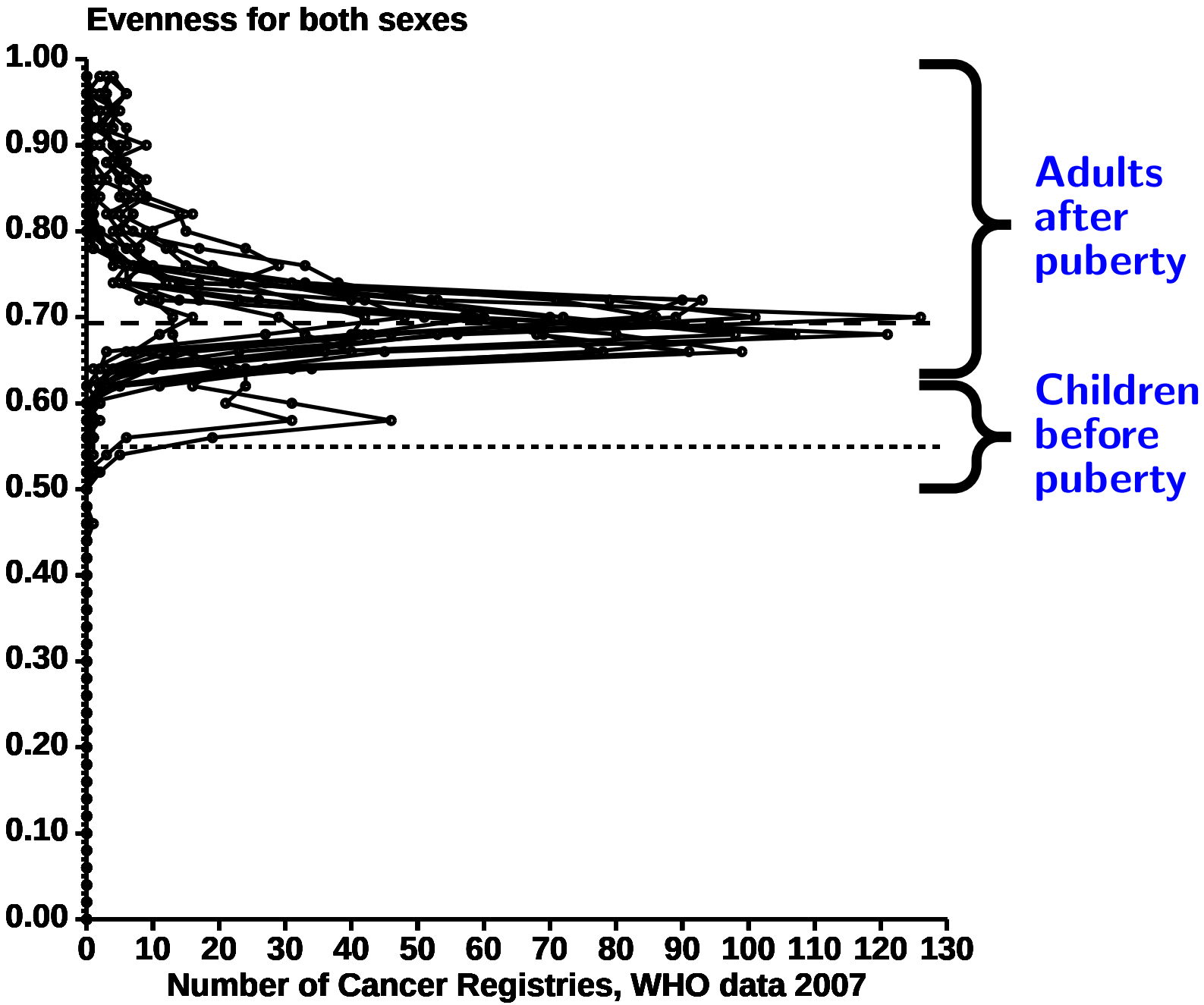

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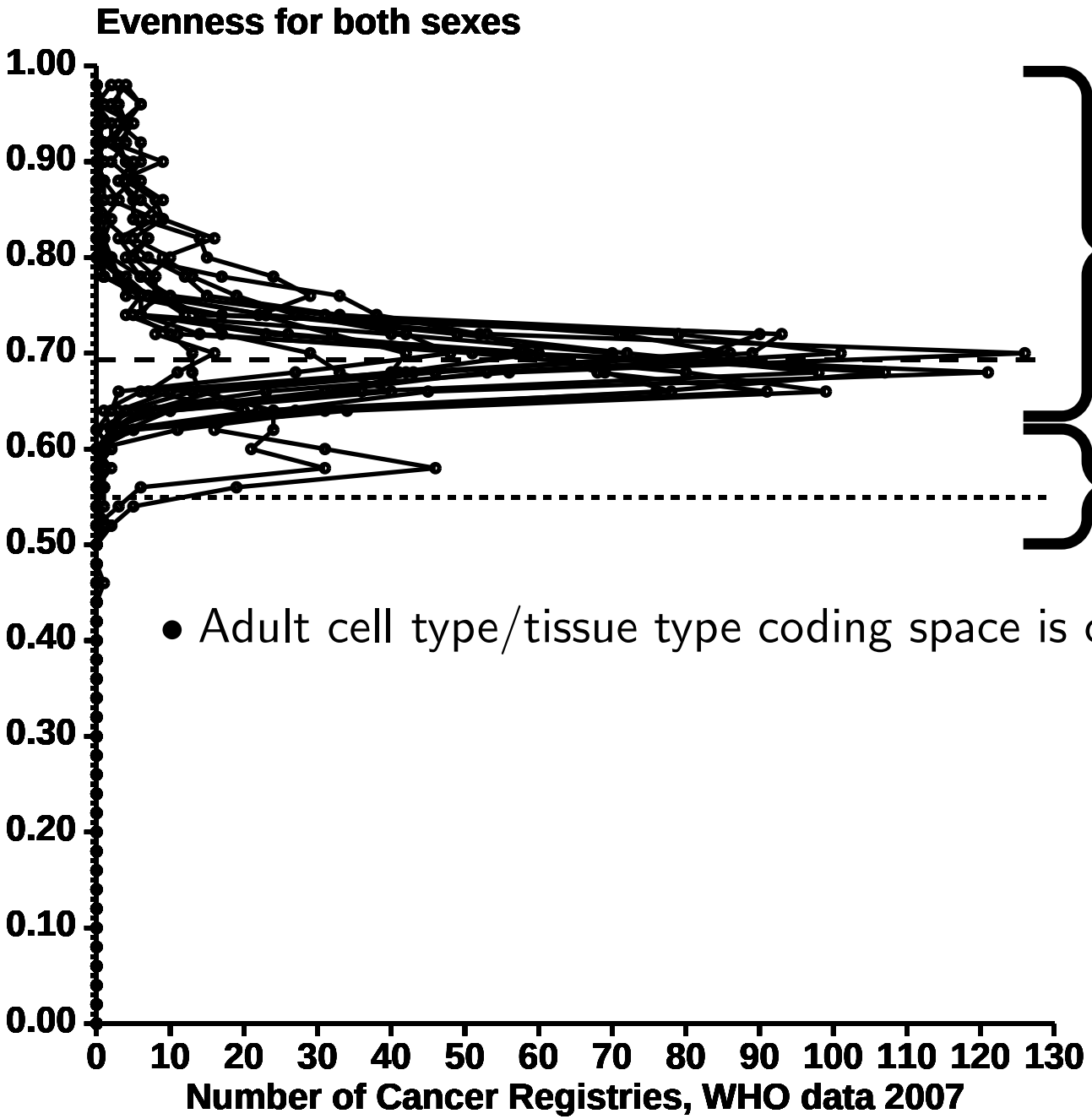
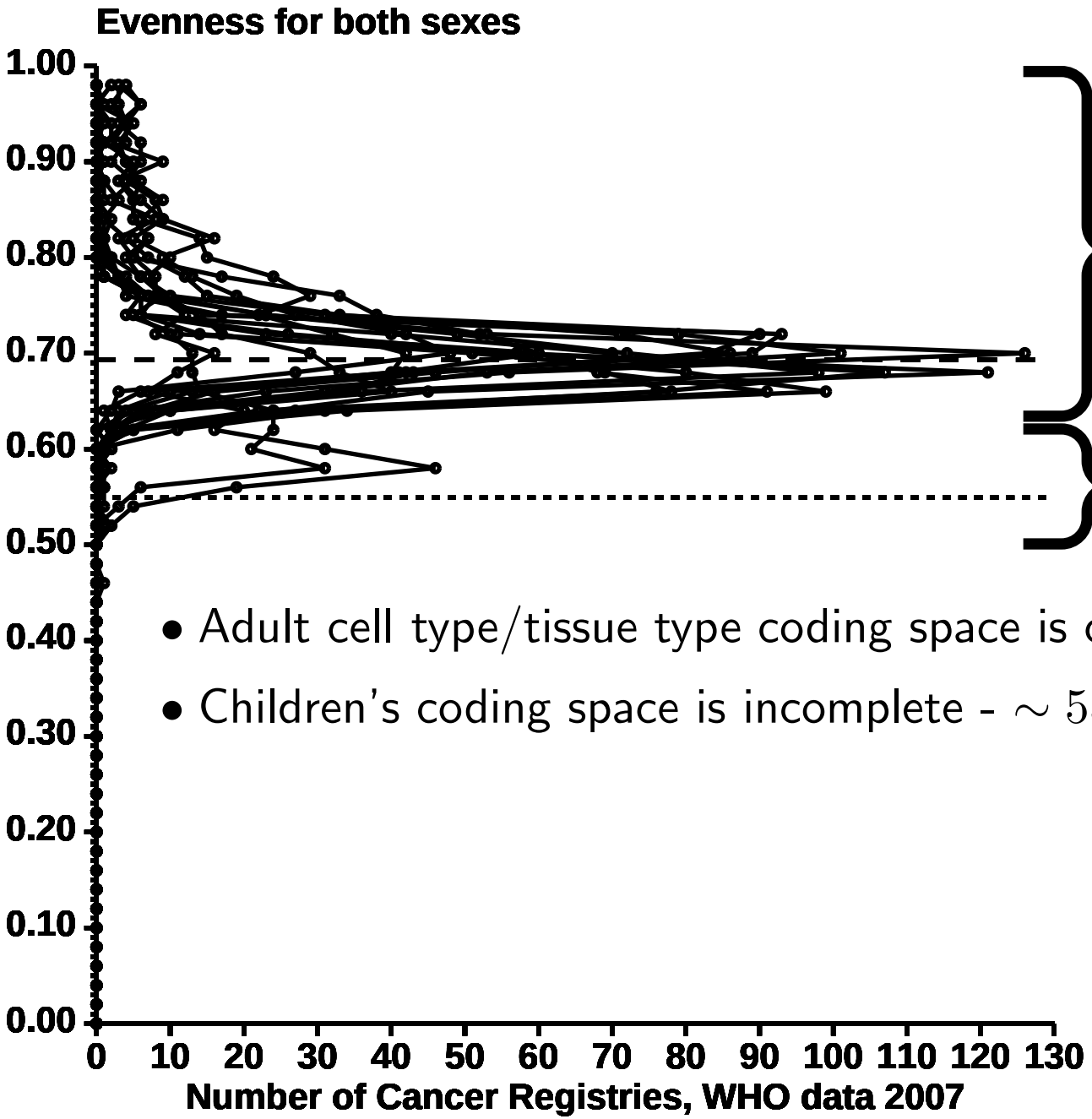


- Adult cell type/tissue type coding space is complete, $\sim 70\%$

Cancer Incidence WHO data 2007



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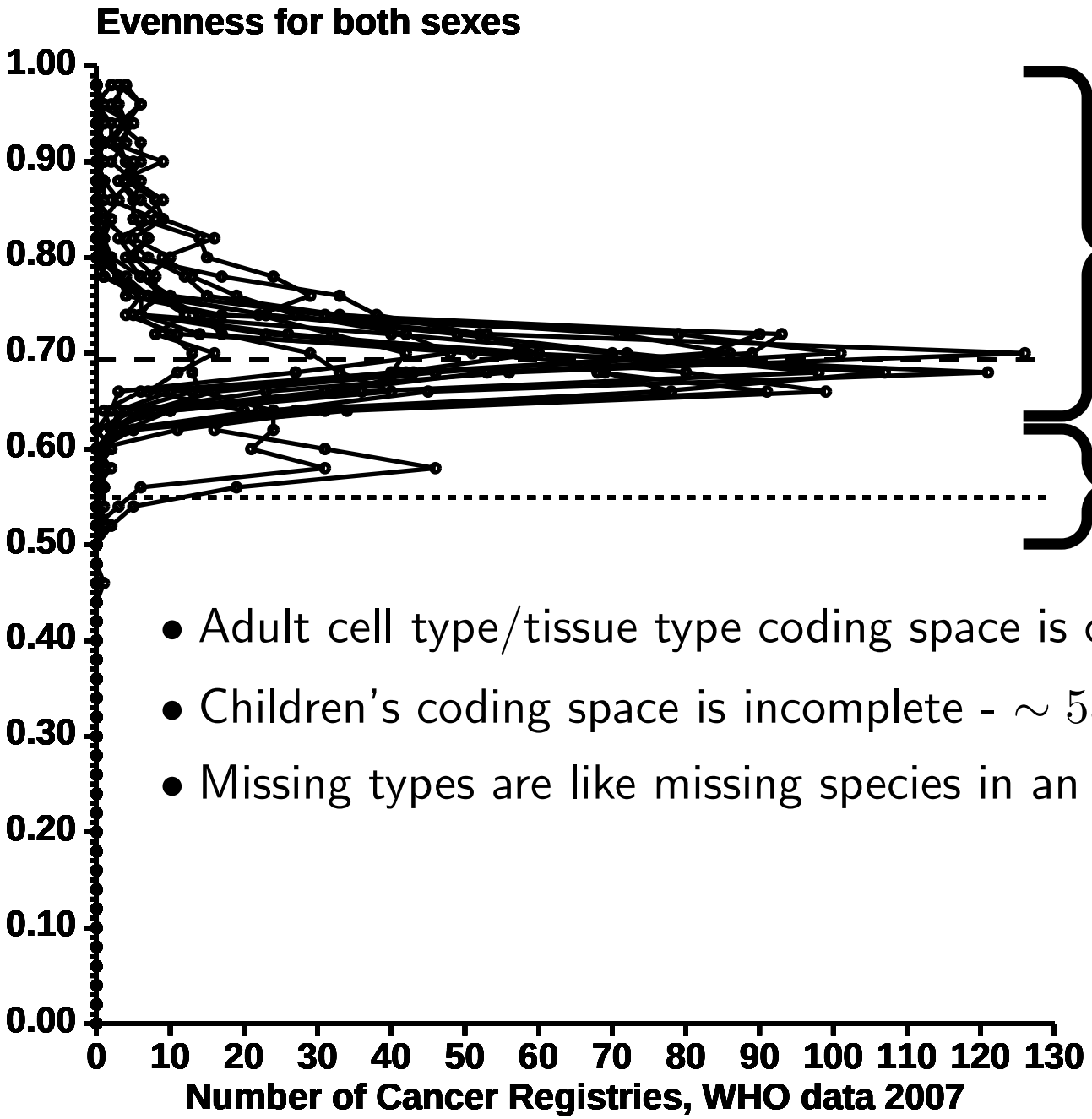
- Children's coding space is incomplete - $\sim 55\%$?

Cancer Incidence WHO data 2007



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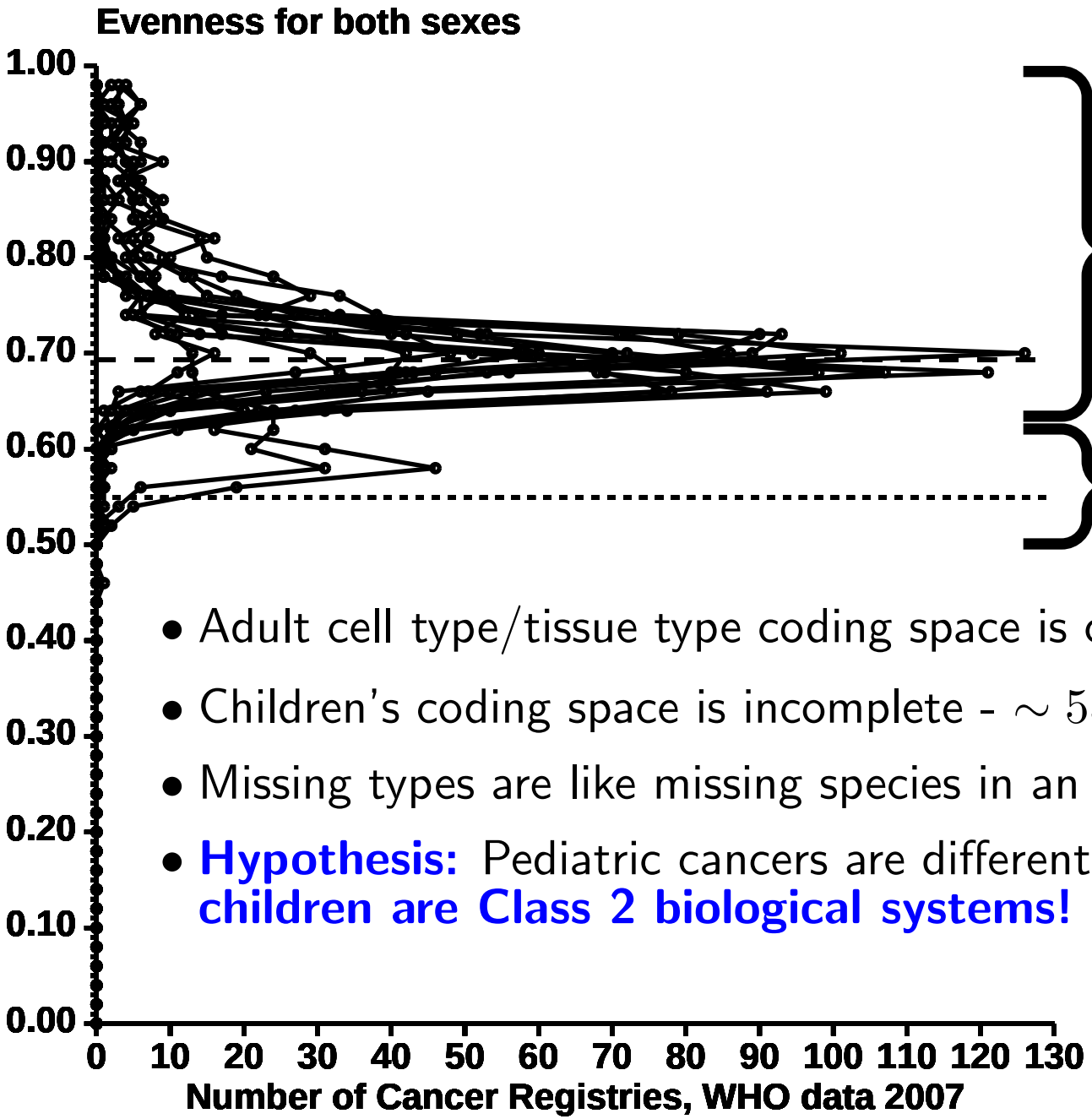
- Missing types are like missing species in an ecosystem?

Cancer Incidence WHO data 2007



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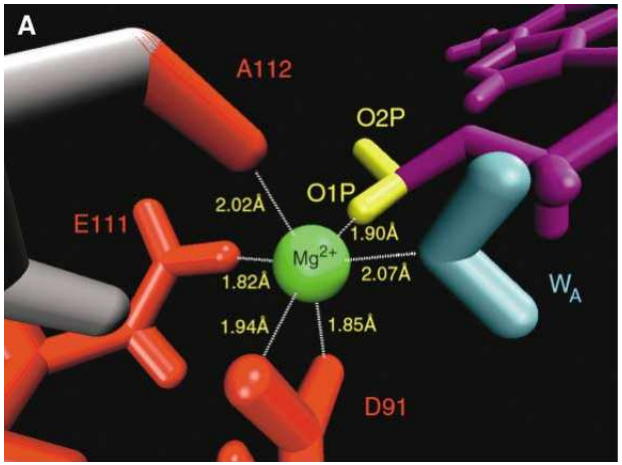
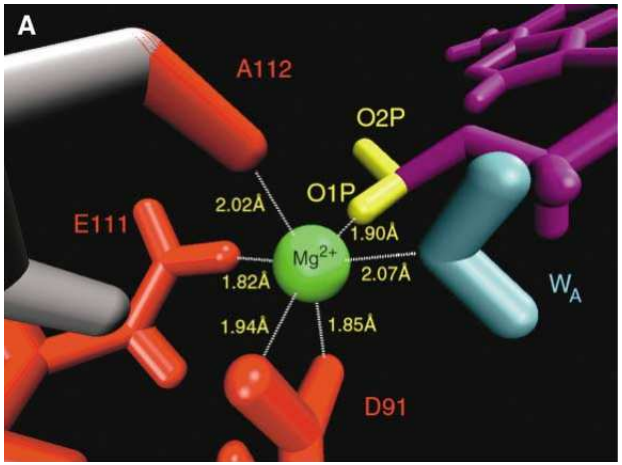
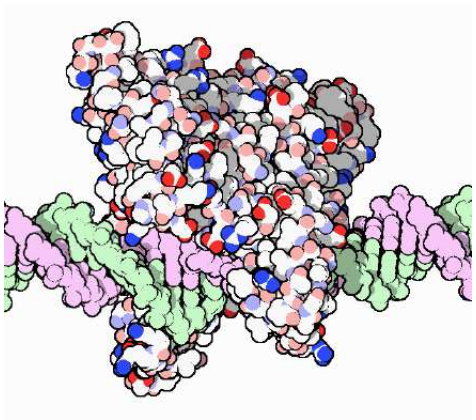
- **Hypothesis:** Pediatric cancers are different because **children are Class 2 biological systems!**

Conclusions

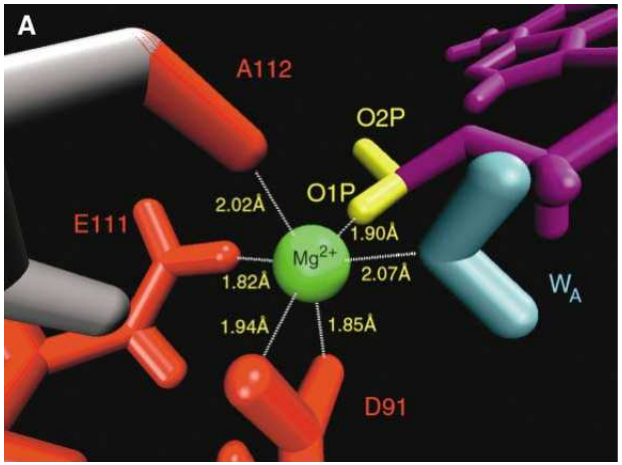


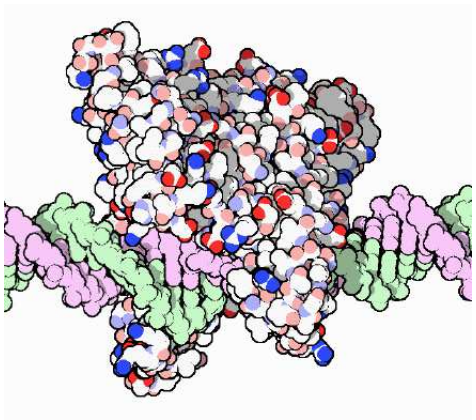
Conclusions

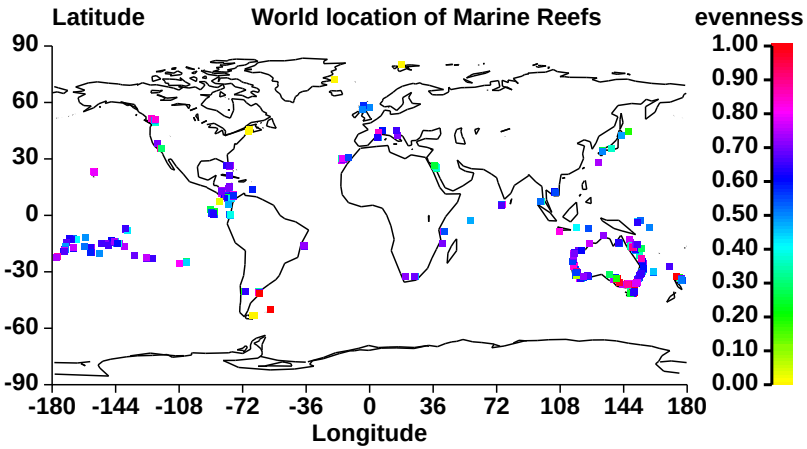




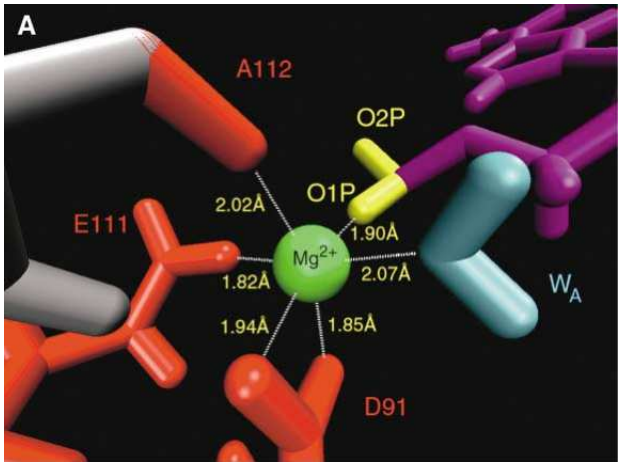
Conclusions

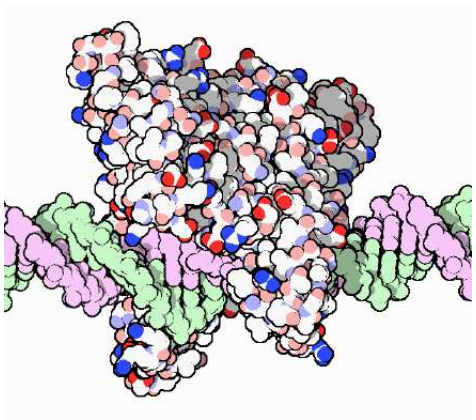


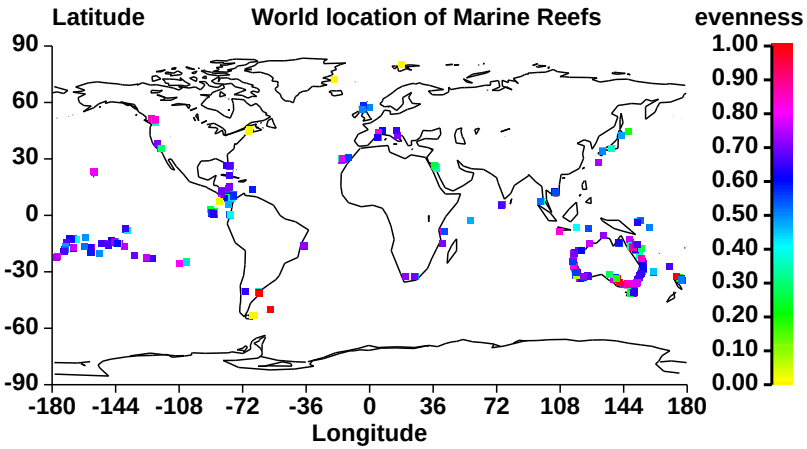




Conclusions

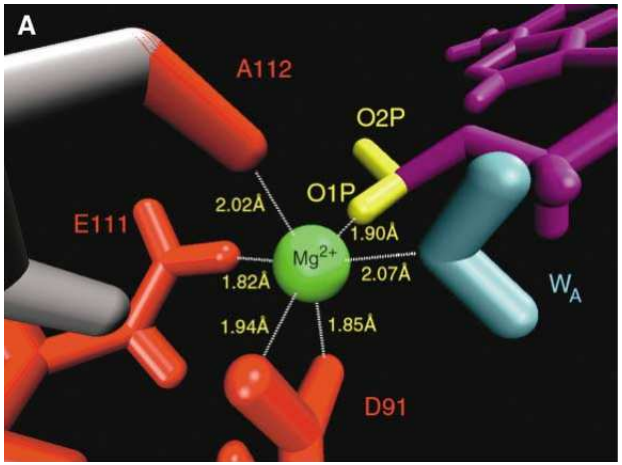


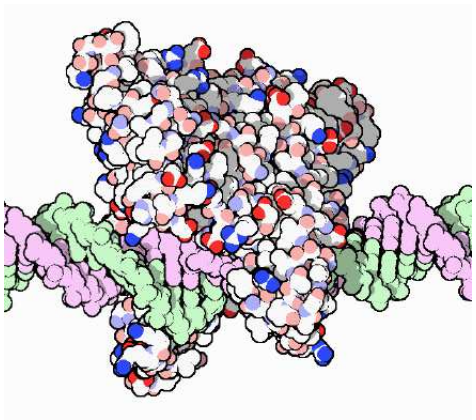


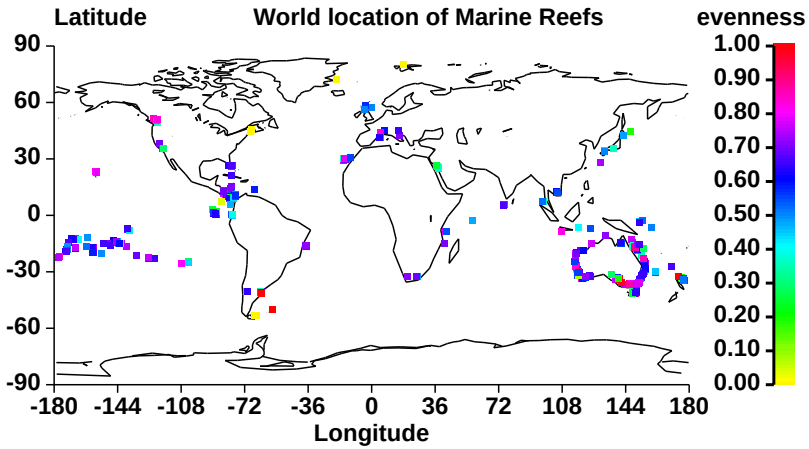


Three Principles of Biological States

Conclusions

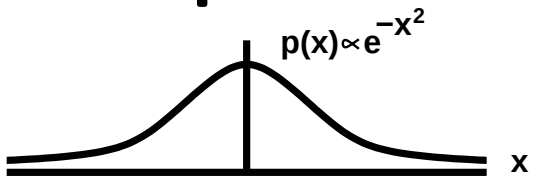




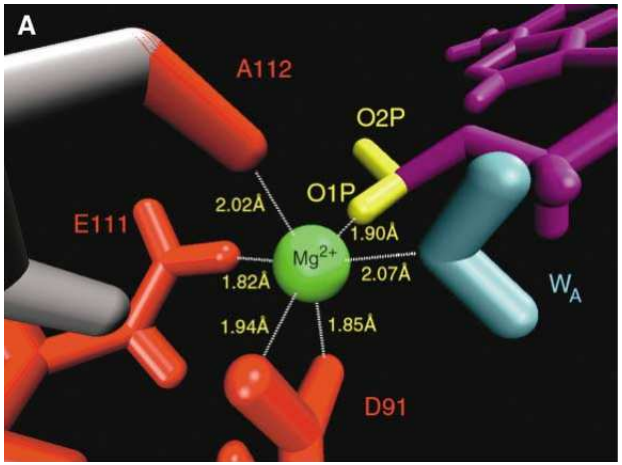


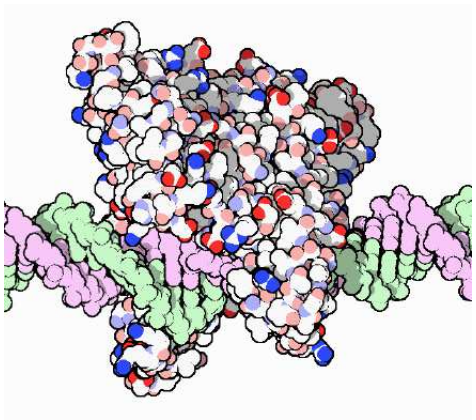
Three Principles of Biological States

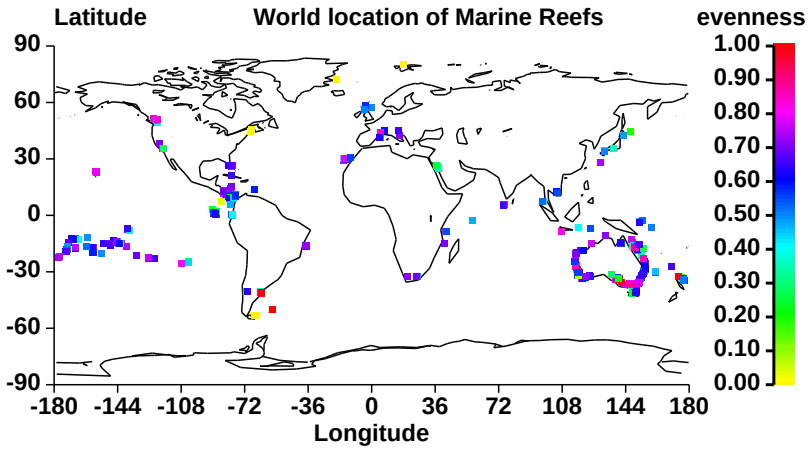
- Noise



Conclusions

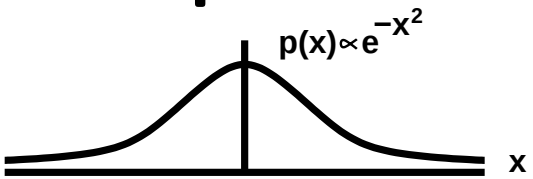




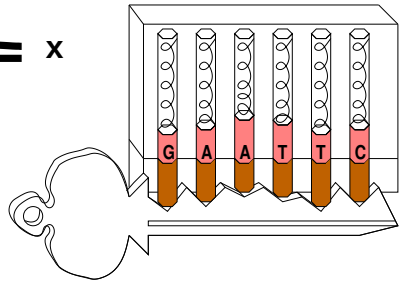


Three Principles of Biological States

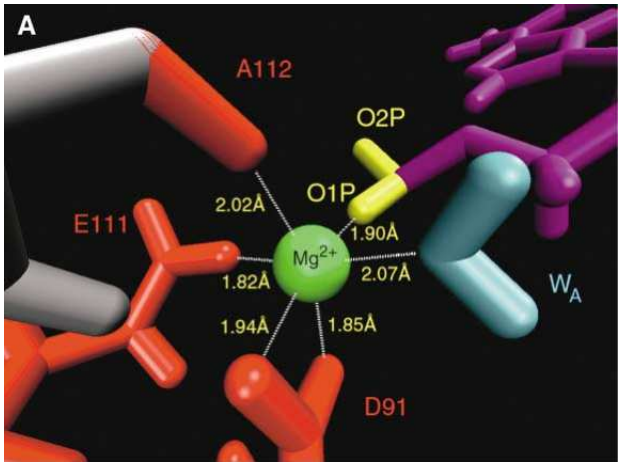
- Noise

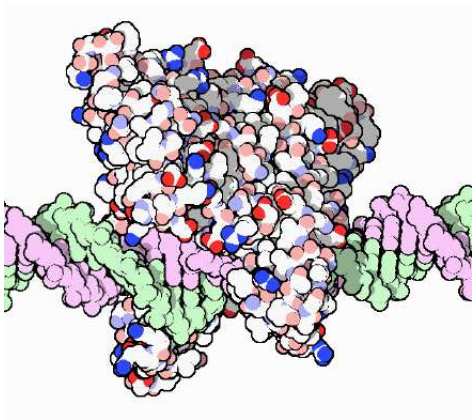


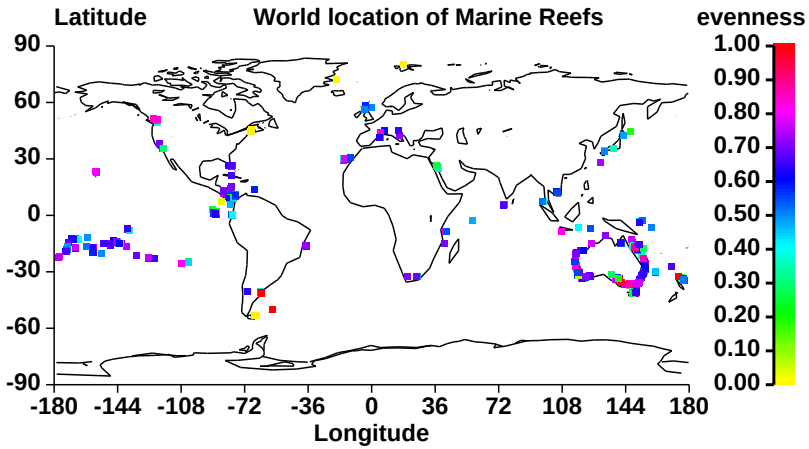
- High dimensionality



Conclusions

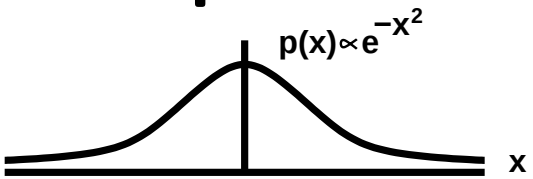




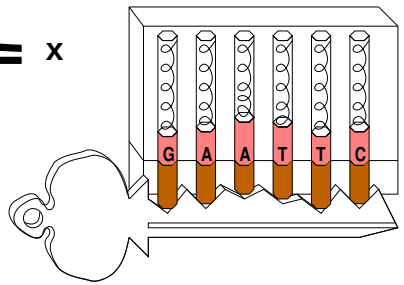


Three Principles of Biological States

- Noise



- High dimensionality



- Separation of states

These Principles imply that the isothermal efficiency will be: 0.69, 0.55, 0.46 . . .

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Version

version = 1.74 of ecologytalk.tex 2014 Oct 25