Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

Mathematical Modeling and Biology

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March 10, 2016

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What is modeling?

Mathematical modeling is

- to translate nature into mathematics

What is modeling?

Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

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Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

Mathematical modeling is

- to translate nature into mathematics
- to be logically consistent
- to fit the past and to predict future

What is modeling?

Mathematical modeling is

- to translate nature into mathematics
- to be logically consistent
- to fit the past and to predict future
- to fail against the test of time, i.e. to give way to better models

Human history has two periods – before and after calculus (1686/1687)

- Issac Newton (1642-1727) is the founding father of mathematical modeling

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Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

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- Calculus is the principle language of nature

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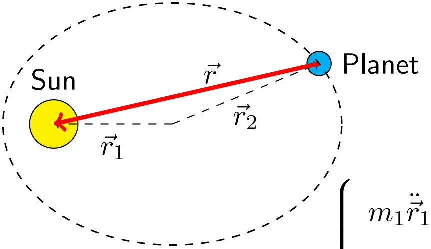
- Calculus is the principle language of nature
- This century is the century of mathematical biology, which is to translate Charles Darwin's (1809-1882) theory into mathematics

Model as approximation – Newton's planetary motion



$$\begin{cases} m_1\ddot{\vec{r}}_1 & = & -Gm_1m_2\dfrac{\vec{r}_1-\vec{r}_2}{\|\vec{r}_1-\vec{r}_2\|^3} \\ m_2\ddot{\vec{r}}_2 & = & -Gm_1m_2\dfrac{\vec{r}_2-\vec{r}_1}{\|\vec{r}_2-\vec{r}_1\|^3} \\ \vec{r} & = & \vec{r}_1-\vec{r}_2 \end{cases}$$

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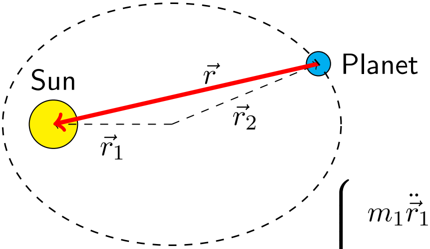


$$\begin{cases} m_1\ddot{\vec{r}}_1 = -Gm_1m_2\dfrac{\vec{r}_1-\vec{r}_2}{\|\vec{r}_1-\vec{r}_2\|^3} \\ m_2\ddot{\vec{r}}_2 = -Gm_1m_2\dfrac{\vec{r}_2-\vec{r}_1}{\|\vec{r}_2-\vec{r}_1\|^3} \\ \vec{r} = \vec{r}_1-\vec{r}_2 \end{cases}$$

- A few calculus maneuvers lead to

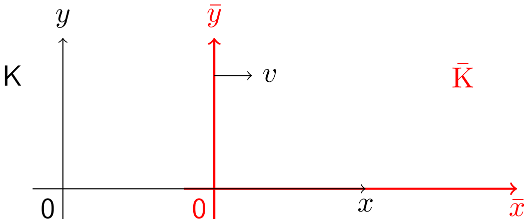
$$r(\theta) = \frac{\rho}{1+\epsilon\cos\theta}$$

with the eccentricity $0 \le \epsilon < 1$ for elliptic orbits

Special Relativity – Einstein's model of space and time

One Assumption:

The speed of light is constant for every stationary observer



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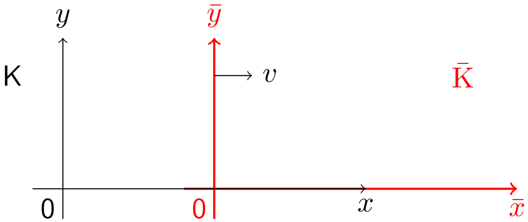

- A few calculus maneuvers lead to $E = mc^2$, and more

Special Relativity — Einstein's model of space and time

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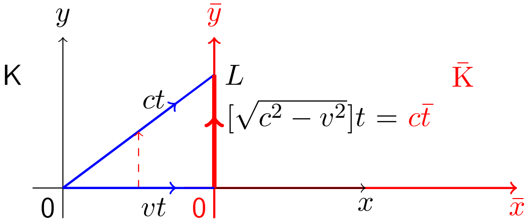

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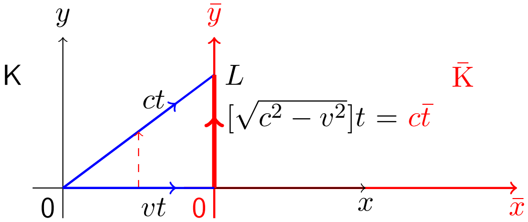
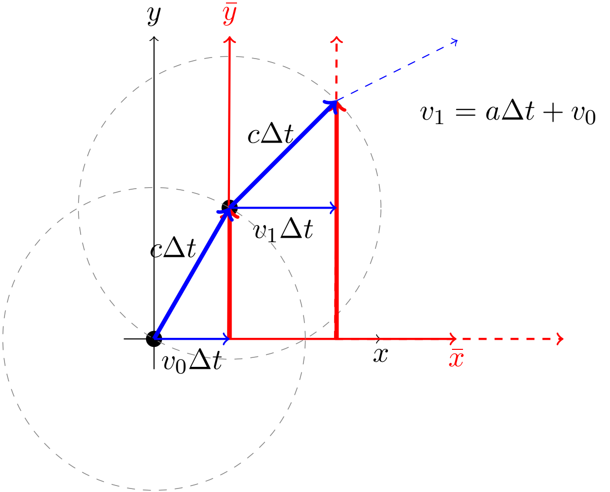


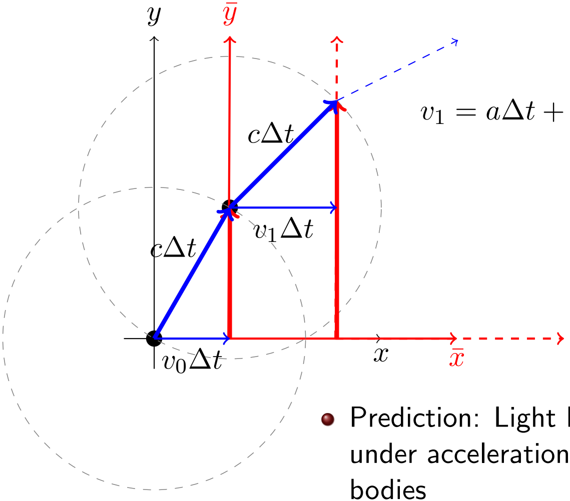
- Prediction: Time dilation for K-frame observer

$$t = \frac{L}{c\sqrt{1-(v/c)^2}} > \frac{L}{c} = \bar{t}$$

General Relativity — Model of space and time in acceleration



General Relativity — Model of space and time in acceleration



$v_1 = a\Delta t + v_0$

- Prediction: Light beam bends under acceleration or near massive bodies

Mathematical model need not be mathematical

Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

- Gregor Johann Mendel (1822-1884) found the first mathematical model in biology, leading to the discovery of gene

	Parent Genotype					
Offspring Genotype	$m_{rr} \times f_{rr}$	$m_{rD} \times f_{rD}$	$m_{DD} \times f_{DD}$	$m_{rr} \times f_{rD}$ or $m_{rD} \times f_{rr}$	$m_{rr} \times f_{DD}$ or $m_{DD} \times f_{rr}$	$m_{rD} \times f_{DD}$ or $m_{DD} \times f_{rD}$
z'_{rr}	1	1/4	0	1/2	0	0
z'_{rD}	0	1/2	0	1/2	1	1/2
z'_{DD}	0	1/4	1	0	0	1/2

One More Example: Structure of DNA by modeling

Mathematical Modeling and Biology

Bo Deng

Introduction

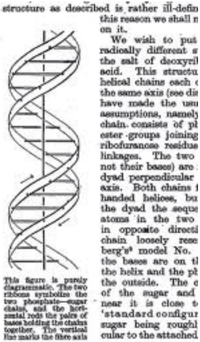
Examples of Models

Consistency

Model Test

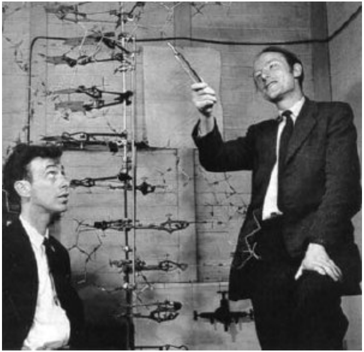
Mathematical Biology

Conclusion



structure as described is rather ill-defin
this reason we shall n
on it.
We wish to put
radically different s
the salt of deoxyril
acid. This structu
helical chains each c
the same axis (see di
have made the usu
assumptions, namely
chain consists of ph
ester groups joining
ribofuranose residue
linkages. The two
not their bases) are
dyad perpendicular
axis. Both chains f
handed helices, bu
the dyad the seque
atoms in the two
in opposite directi
chain loosely rese
berg's[a] model No.
the bases are on tl
the helix and the ph
the outside. The c
of the sugar and
near it is close t
'standard configur
sugar being roughl
cular to the attached

This figure is purely diagrammatic. The two ribbons symbolize the two phosphate—sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis



- Rosalind Franklin and Maurice Wilkins had the data, but James D. Watson and Francis Crick had the frame of mind to model the data (1953)

Another More – Predation in Ecology

The mathematical model was discovered by Crawford Stanley (Buzz) Holling (1930-) in 1959

- T_d — average time a predator takes to discover a prey

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- $T_{d,k} = T_d + T_k$ — average time a predator takes to discovery and kill a prey

Another More – Predation in Ecology

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- T_d — average time a predator takes to discover a prey
- T_k — average time a predator takes to kill a prey
- $T_{d,k} = T_d + T_k$ — average time a predator takes to discovery and kill a prey
- $R_d = \dfrac{1}{T_d}$ — rate of discovery, i.e. number of preys a predator would find in a unit time
- $R_k = \dfrac{1}{T_k}$ — rate of killing, i.e. number of preys a predator would kill in a unit time
- $R_{d,k} = \dfrac{1}{T_{d,k}} = \dfrac{1}{T_d + T_k}$ — rate of discovery and killing

Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

Model of Predation in Ecology

- And Holling's predation function form:

$$R_{d,k} = \frac{1}{T_d + T_k} = \frac{1/T_d}{1 + T_k(1/T_d)} = \frac{R_d}{1 + T_k R_d}$$

Model of Predation in Ecology

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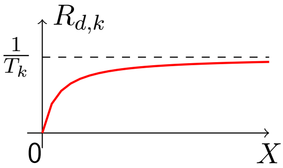
$$R_{d,k} = \frac{1}{T_d + T_k} = \frac{1/T_d}{1 + T_k(1/T_d)} = \frac{R_d}{1 + T_k R_d}$$

- Prediction: Assume the discovery rate is proportional to the prey population X, $R_d = aX$. Then the Holling Type II predation rate must saturate as $X \to \infty$

$$\lim_{X\to\infty} R_{d,k} = \lim_{X\to\infty} \frac{aX}{1 + T_k aX} = \frac{1}{T_k}$$



Consistency

- Not every piece of mathematics can be a physical law or model. Logical consistency is the first and necessary constraint

Time Invariance Principle (TIP)

A model must has the same functional form for every time independent observation

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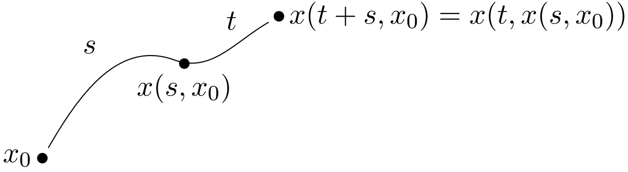
Time Invariance Principle (TIP)

A model must has the same functional form for every time independent observation

- Newtonian mechanics is TIP-consistent:



Special Relativity is self-consistent

Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

- Let P be a point, having $K = (x, y, z, t)$ coordinate in the K-frame and $\bar{K} = (\bar{x}, \bar{y}, \bar{z}, \bar{t})$ coordinate in the $\bar{K}$-frame. Then they are exchangeable via a linear transformation depending the speed v:

$$\bar{K} = KL(v)$$

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$$\bar{K} = KL(v)$$

- Let $\tilde{K} = (\tilde{x}, \tilde{y}, \tilde{z}, \tilde{t})$ be the coordinate of the same point in a $\tilde{K}$-frame moving at speed u with respect to the $\bar{K}$-frame. Then we have

$$\tilde{K} = \bar{K}L(u) = KL(v)L(u) = KL(w) \text{ with } w = \frac{u+v}{1+\frac{uv}{c^2}}$$

Special Relativity is self-consistent

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$$\tilde{K} = \bar{K}L(u) = KL(v)L(u) = KL(w) \text{ with } w = \frac{u+v}{1+\frac{uv}{c^2}}$$

- The operation $u \oplus v = \dfrac{u+v}{1+\frac{uv}{c^2}}$ for elements $u, v \in (-c, c)$ defines a commutative group

Holling's predation model is consistent

- T_c — average time to consume a prey

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- T_c — average time to consume a prey
- $T_{d,k,c} = T_d + T_k + T_c$ — average time to discover, kill, and consume a prey

Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

- T_c — average time to consume a prey
- $T_{d,k,c} = T_d + T_k + T_c$ — average time to discover, kill, and consume a prey
- Then the rate of predation is self-consistent:

$$R_{d,k,c} = \frac{1}{T_{d,k,c}} = \frac{1}{T_d + T_k + T_c}$$

$$= \frac{R_{d,k}}{1 + T_c R_{d,k}} = \frac{R_d}{1 + (T_k + T_c) R_d}$$

Pay the TIP, or else

- All differential equation models are TIP-consistent

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- Most mapping models in ecology are TIP-inconsistent

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- Example: Logistic map

$$x_{n+1} = Q_\lambda(x_n) = \lambda x_n(1 - x_n)$$

cannot be a model for which n represents time

Pay the TIP, or else

Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

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cannot be a model for which n represents time

- The time $n+2$ observation yields a different functional form:

$$x_{n+2} = Q_\lambda(x_{n+1}) = Q_\lambda(Q_\lambda(x_n)) \neq Q_\mu(x_n)$$

for any value μ. Strike one on the logistic map

Model Test – Finding the Best Fit

Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

- $\bar{x}_1, \dots, \bar{x}_n$ — Observed states at time $t_1, \dots, t_n$ for a natural process which are modeled by competing models $y(t; y_0, p)$ and $z(t; z_0, q)$, respectively, with parameter p, q, and initial state y_0, z_0

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- $\bar{x}_1, \dots, \bar{x}_n$ — Observed states at time $t_1, \dots, t_n$ for a natural process which are modeled by competing models $y(t; y_0, p)$ and $z(t; z_0, q)$, respectively, with parameter p, q, and initial state y_0, z_0

- Model selection criterion: All else being equal whichever has a smaller error is the benchmark model by default:

$$E_y = \min_{(y_0,p)} \sum_{i=1}^{n} [y(t_i; y_0, p) - \bar{x}_i]^2$$

$$E_z = \min_{(z_0,q)} \sum_{i=1}^{n} [z(t_i; z_0, q) - \bar{x}_i]^2$$

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Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

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- A parameter value is only meaningful to its model, and it can only be derived by best-fitting the observed data to the model

Model Test – Fit the past, predict the future

- Edmond Halley (1656-1742) used Newtonian mechanics to predict the 1758 return of Halley's Comet, giving the comet its name

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Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

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- Gregor Mendel's Laws of Inheritance (1866) was rediscovered in 1900, ushering in the science of modern genetics
- Holling's model of predation is ubiquitous in theoretical ecology

Example: One Life Rule

Every organism lives only once and must die in any finite time in the presence of infinite population density

Mathematical Modeling and Biology

Bo Deng

Introduction
Examples of Models
Consistency
Model Test
Mathematical Biology
Conclusion

Example: One Life Rule

Every organism lives only once and must die in any finite time in the presence of infinite population density

- In math translation: Let x_t be the population at time t. Then the per-capita change must satisfy

$$\frac{x_t - x_0}{x_0} = \frac{x_t}{x_0} - 1 \geq -1$$

Mathematical Modeling and Biology
Bo Deng
Introduction
Examples of Models
Consistency
Model Test
Mathematical Biology
Conclusion

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- Lead to

$$\text{One Life Rule} \iff \lim_{x_0 \to \infty} \frac{x_t - x_0}{x_0} = -1$$

and to the logistic equation

$$\dot{x}(t) = rx(t)[1 - x(t)/K]$$

with $x(t) = x_t$, r the max per-capita growth rate, and K the carrying capacity

Footnote: model or no model, generalization or relativism is often the problem

- Strike two on the logistic map $x_1 = \lambda x_0(1 - x_0)$:

$$\lim_{x_0 \to \infty} \frac{x_1 - x_0}{x_0} = \lim_{x_0 \to \infty} [\lambda(1 - x_0) - 1] = -\infty \neq -1$$

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- While the logistic equation, $x'(t) = rx(t)(1 - x(t)/K)$, dogged another consistency bullet

$$\lim_{x_0\to\infty} \frac{x(t; x_0) - x_0}{x_0} = \lim_{x_0\to\infty} \left[\frac{K}{x_0 + (K - x_0)e^{-rt}} - 1\right] = -1$$

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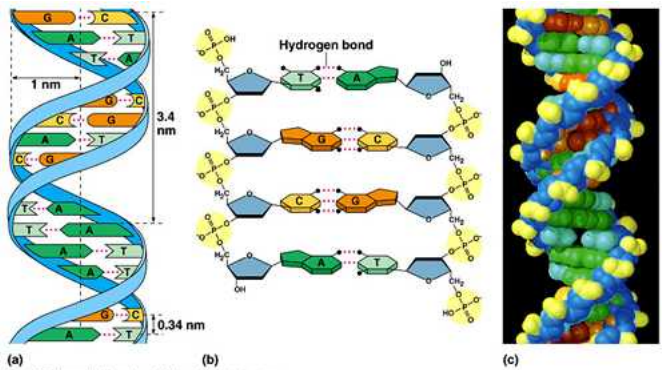
- There should be no different versions of the same reality, but refined approximations

One More Example: Why DNA is coded in 4 bases?



Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

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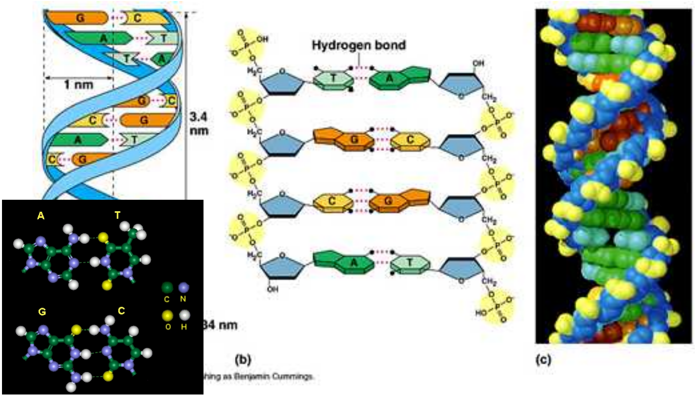

- The AT pair has one weak O-H bond but the GC pair has two O-H bonds. Hence, the GC pair takes longer to complete binding than the AT pair does

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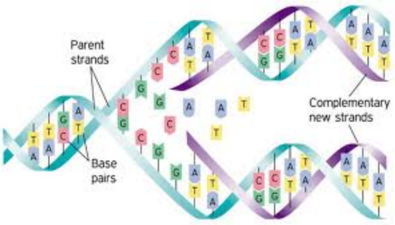

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Mathematical Modeling and Biology

Bo Deng

Introduction

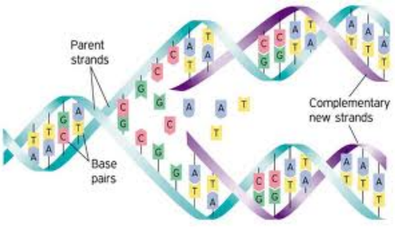
Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion



- Start with a conceptual model: DNA replication is a communication channel

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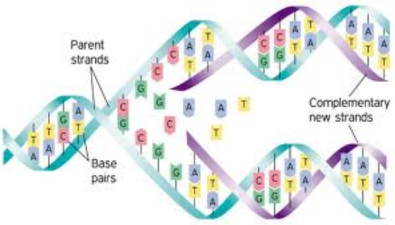

- Start with a conceptual model: DNA replication is a communication channel
- Every communication is characterized by the transmission data rate in bits per second, i.e. the information entropy per second

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Introduction
Examples of Models
Consistency
Model Test
Mathematical Biology
Conclusion

- For $2n$ paired bases, the replication rate is

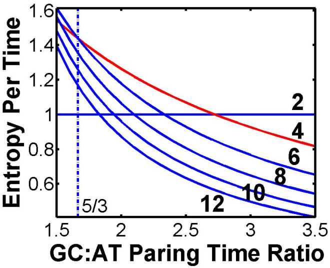
$$R_{2n} = \frac{\log_2(2n)}{\frac{\tau_{12}+\tau_{34}+\cdots+\tau_{(2n-1)(2n)}}{n}} \text{ in bits per time}$$

One More Example: Why DNA is coded in 4 bases?

- For $2n$ paired bases, the replication rate is

$$R_{2n} = \frac{\log_2(2n)}{\frac{\tau_{12}+\tau_{34}+\cdots+\tau_{(2n-1)(2n)}}{n}} \text{ in bits per time}$$

- If $\frac{5}{3} \le \frac{\tau_{GC}}{\tau_{AT}} \le 2.7$, then: $\max_n R_{2n} = R_4$



Mathematical Modeling and Biology

Bo Deng

Introduction

Examples of Models

Consistency

Model Test

Mathematical Biology

Conclusion

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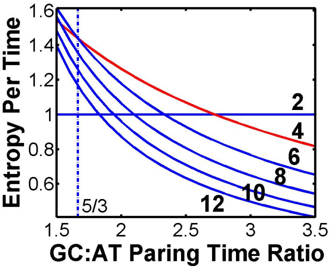

- Punch Line: Life is a reality show on your DNA channel

Closing Comments

- Mathematics is driven by open problems, but science is driven by existing solutions
- Mathematical modeling is to find the equation to which nature fits as a solution
- Mathematics is to create more hays but modeling is to find the needle in haystack
- Mathematical biology is not to solve mathematical problems of models but to find mathematical models for biological problems
- Training to be a mathematical modeler does need to solve mathematical problems of reasonable models.

Mathematical modeling is to construct the picture so that the consequence of the picture is the picture of the consequence.

– Anonymous or by Heinrich Hertz (1857-1894)