BIOINFORMATICS 1

or why biologists need computers

http://www.bioinformatics.uni-muenster.de/teaching/courses-2015/bioinf1/index.hbi

Prof. Dr. Wojciech Makałowski
Institute of Bioinformatics

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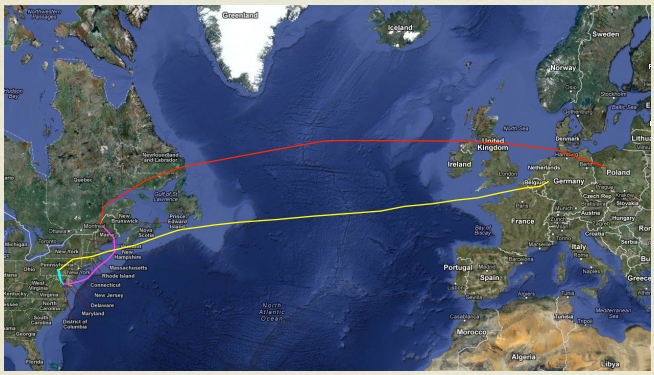
POZNAŃ -> MONTREAL ->BETHESDA -> STATE COLLEGE -> MÜNSTER



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TOPICS TO BE COVERED IN THIS COURSE

- Introduction to bioinformatics from the evolutionary perspective. [WM]
- Next Generation Sequencing. [WM]
- Sequence alignment and similarity search. [WM]
- Sequence assembly and gene prediction. [WM]
- Principles of heredity. Mutations, substitutions and polymorphisms. [CA]
- Distances and models. Synonymous and non-synonymous substitutions. Basics of the neutral theory. [CA]
- Phylogenetic inference. [CA]

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HANDS ON COMPUTER LAB

Computer Lab B, Schlossplatz 2b

- Nucleotide sequence analyses [November 10 - 12]
- Phylogenetic inference [December 8 - 10]
- Registration after November 1st at

http://bioinformatics.uni-muenster.de/teaching/register.pl

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CONTACT

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- Prof. Wojciech Makałowski wojmak@uni-muenster.de
- Norbert Grundmann ngrundma@uni-muenster.de (lab coordinator)
- http://www.bioinformatics.uni-muenster.de/teaching/courses-2013/bioinf1/index.hbi
- office hours - see the web site

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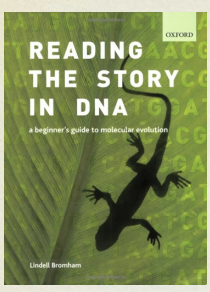
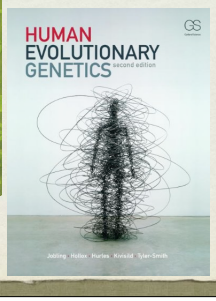
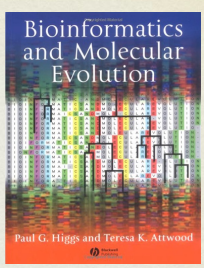
RECOMMENDED BOOKS







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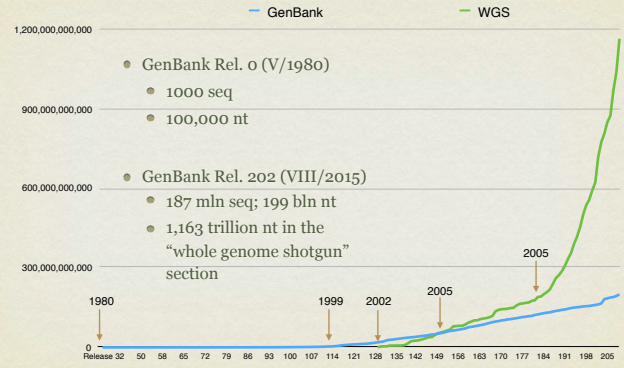
GROWTH OF BIOMEDICAL INFORMATION - GENBANK



- GenBank Rel. 0 (V/1980)
  - 1000 seq
  - 100,000 nt
- GenBank Rel. 202 (VIII/2015)
  - 187 mln seq; 199 bln nt
  - 1,163 trillion nt in the "whole genome shotgun" section

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TECHNOLOGY MEETS BIOLOGY

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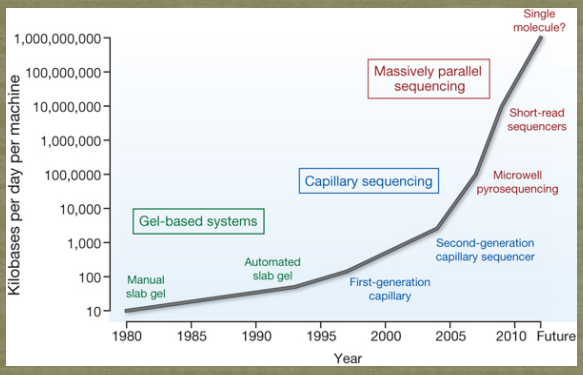
IMPROVING TECHNOLOGY



MR Stratton *et al. Nature* **458**, 719-724 (2009)

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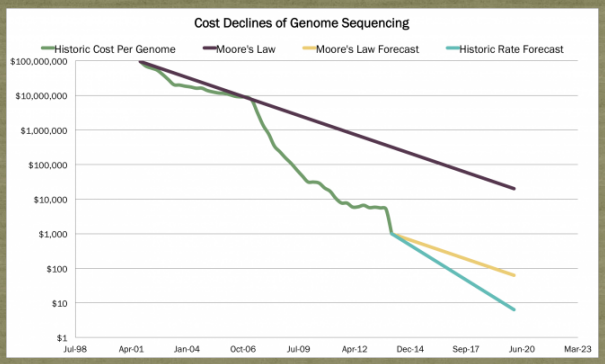
IMPROVING TECHNOLOGY



http://ark-invest.com/genomic-revolution/declining-costs-of-genome-sequencing

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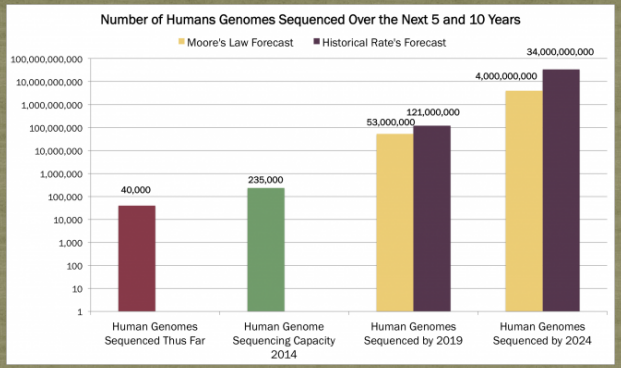
IMPROVING TECHNOLOGY



http://ark-invest.com/genomic-revolution/declining-costs-of-genome-sequencing

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GETTING SEQUENCES

TGCATCGATCGTAGCTAGCTAGCGCATGCTAGCTAGCTAGCTAGCTACGATGCATCG
TGCATCGATCGATGCATGCTAGCTAGCTAGCTAGCATGCTAGCTAGCTAGCTATTGG
CGCTAGCTAGCATGCATGCATGCATCGATGCATCGATTATAAGCGCGATGACGTCAG
CGCGCGCATTATGCCGCGGCATGCTGCGCACACACAGTACTATAGCATTAGTAAAAA
GGCCGCGTATATTTTACACGATAGTGCGGCGCGGCGCGTAGCTAGTGCTAGCTAGTC
TCCGGTTACACAGGTAGCTAGCTAGCTGCTAGCTAGCTGCTGCATGCATGCATTAGT
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AGCTCTCATCGCGCGGGGGGATGCTTAGCGTGGTGTGTGTGTGTGGTGTGTGTGGTC
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CGCTAGCTAGCATGCATGCATGCATCGATGCATCGATTATAAGCGCGATGACGTCAG
TCCGGTTACACAGGTAGCTAGCTAGCTGCTAGCTAGCTGCTGCATGCATGCATTAGT

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READING ≠ UNDERSTANDING

Carmina qui quondam studio florente peregi, flebilis heu maestos cogor inire modos.

Ecce mihi lacerae dictant scribenda Camenae et ueris elegi fletibus ora rigant.

Boethius, *Consolatio Philosophiae*

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READING ≠ UNDERSTANDING

We shall best understand the probable course of natural selection by taking the case of a country undergoing some physical change. If the country were open were open on its borders, new forms would certainly immigrate, and this also would bla, bla bla become extinct inhabitants.

Charles Darwin - *The Origin of Species*

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READING ≠ UNDERSTANDING

We shall best understand the probable course of [redacted] by taking the case of a country undergoing some physical change. If the country were open were open on its borders, new forms would certainly immigrate, and this also would bla, bla bla become extinct inhabitants.

Charles Darwin - *The Origin of Species*

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CHALLENGE: HOW FROM THIS...

TGCATCGATCGTAGCTAGCTAGCGCATGCTAGCTAGCTAGCTAGCTACGATGCATCG
TGCATCGATCGATGCATGCTAGCTAGCTAGCTAGCATGCTAGCTAGCTAGCTATTGG
CGCTAGCTAGCATGCATGCATGCATCGATGCATCGATTATAAGCGCGATGACGTCAG
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CGCTAGCTAGCATGCATGCATGCATCGATGCATCGATTATAAGCGCGATGACGTCAG
TCCGGTTACACAGGTAGCTAGCTAGCTGCTAGCTAGCTGCTGCATGCATGCATTAGT

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HOW TO SOLVE THE PROBLEM - A HUMAN OR A COMPUTER?

- very smart
- slow
- error prone
- doesn't like repetitive tasks

- not so smart (stupid)
- extremely fast
- very accurate
- doesn't understand human languages;

needs instruction provided in a special way

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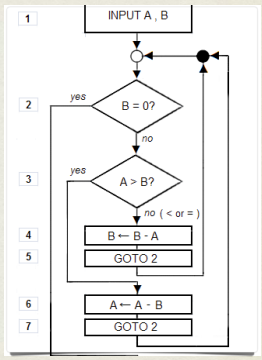
ALGORITHM

A step-by-step problem-solving procedure, especially an established, recursive computational procedure for solving a problem in a finite number of steps.



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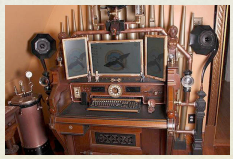
EXAMPLE TASK: PUT SHOES ON!

A human just understands an order and often executes it automatically even without thinking

A computer needs detailed instruction (an algorithm)



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PUT SHOES ON! INSTRUCTION FOR A COMPUTER

1. Find two the same shoes
2. Check if you have left and right shoe
3. Check if they are of the same size
4. Check if this is the right size
5. Put the left shoe on
6. Put the right shoe on
7. Tie the laces

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THE ORIGIN OF THE FIELD

Paulien Hogeweg coined the term *bioinformatica* to define "the study of informatic processes in biotic systems". Hesper B, Hogeweg P (1970) Bioinformatica: een werkconcept. Kameleon 1(6): 28–29. (In Dutch.) Leiden: Leidse Biologen Club.

... but its origin can be tracked back many decades earlier.

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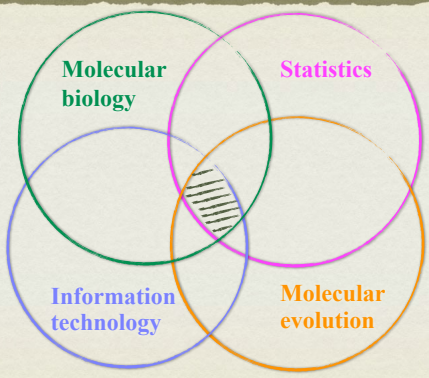
BIOINFORMATICS EMERGED AS AN INTERSECTION BETWEEN DIFFERENT DISCIPLINES



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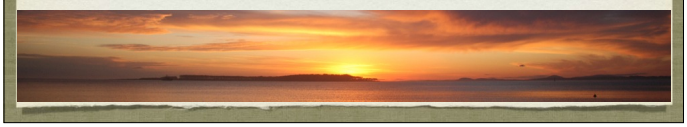
BIOINFORMATICS - DEFINITION

- Research, development, or application of computational tools and approaches for expanding the use of biological data, including those to acquire, store, organize, archive, analyze, or visualize such data.
- Its goal is to enable biological discovery based on existing information or in other words transform biological data into information and eventually into knowledge.



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ROLE OF BIOINFORMATICS IN MODERN BIOLOGY

- molecular biology
- molecular evolution
- genomics
- system biology
- protein engineering
- drug design
- personalized medicine
- biogeography

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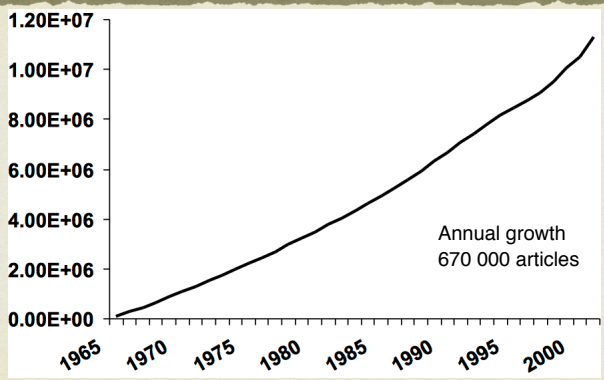
GROWTH OF BIOMEDICAL INFORMATION - MEDLINE



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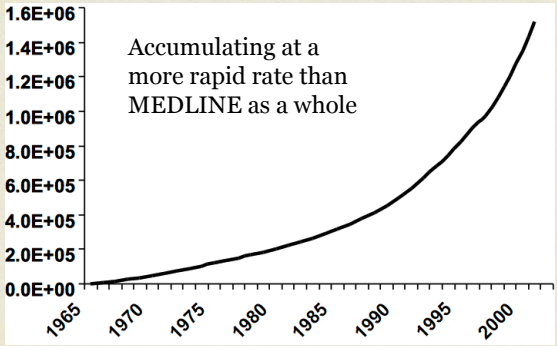
GROWTH OF BIOMEDICAL INFORMATION - SECTION G5 OF MEDLINE - MOL BIOL & GENETICS



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BIOLOGICAL DATABASES

- organized sets of large amount of data, usually coupled with a software that enables data search, information extraction, and data update
- databases should be characterized by
  - easy data access
  - the possibility to extract only the information that is desirable

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INFORMATION IN DATABASES

- Databases and resources may contain many different kinds of information. Each item of entry is typically called an entry. Regardless of the type of resource, each entry comprises two main parts, each broken into one or more fields
- Descriptive information - Annotation
  - Description
  - Literature references
- The raw data – sequence or observations
- The most valuable information is frequently the annotation with the raw data providing a scaffold to organize this curated information.

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HISTORICAL (?) LOOK AT DATABASES

- Early systems were file based
  - One entry - one file
  - Lookup based on computer system functions such as grep
- Drawbacks to file-based systems
  - Concurrency
  - No way to check consistency
    - Are values appropriate for fields?
    - Have you updated all necessary information?
  - Unable to limit queries to specific fields
  - Queries and especially updates may be slow and require special programming skills

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GENBANK RECORD

```
LOCUS       AF062069     3808 bp    mRNA            INV       02-MAR-2000
DEFINITION  Limulus polyphemus myosin III mRNA, complete cds.
ACCESSION   AF062069
VERSION     AF062069.2  GI:7144484
KEYWORDS    .
SOURCE      Atlantic horseshoe crab.
  ORGANISM  Limulus polyphemus
            Eukaryota; Metazoa; Arthropoda; Chelicerata; Merostomata;
            Xiphosura; Limulidae; Limulus.
REFERENCE   1  (bases 1 to 3808)
  AUTHORS   Battelle,B.-A., Andrews,A.W., Calman,B.G., Sellers,J.R.,
            Greenberg,R.M. and Smith,W.C.
  TITLE     A myosin III from Limulus eyes is a clock-regulated phosphoprotein
  JOURNAL   J. Neurosci. (1998) In press
REFERENCE   2  (bases 1 to 3808)
  AUTHORS   Battelle,B.-A., Andrews,A.W., Calman,B.G., Sellers,J.R.,
            Greenberg,R.M. and Smith,W.C.
  TITLE     Direct Submission
  JOURNAL   Submitted (29-APR-1998) Whitney Laboratory, University of Florida,
            9505 Ocean Shore Blvd., St. Augustine, FL 32086, USA
REFERENCE   3  (bases 1 to 3808)
  AUTHORS   Battelle,B.-A., Andrews,A.W., Calman,B.G., Sellers,J.R.,
            Greenberg,R.M. and Smith,W.C.
  TITLE     Direct Submission
  JOURNAL   Submitted (02-MAR-2000) Whitney Laboratory, University of Florida,
            9505 Ocean Shore Blvd., St. Augustine, FL 32086, USA
  REMARK    Sequence update by submitter
COMMENT     On Mar 2, 2000 this sequence version replaced gi:3132700.
```

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GENBANK RECORD

```
FEATURES             Location/Qualifiers
     source          1..3808
                     /organism="Limulus polyphemus"
                     /db_xref="taxon:6850"
                     /tissue_type="lateral eye"
     CDS             258..3302
                     /note="N-terminal protein kinase domain; C-terminal myosin
                     heavy chain head; substrate for PKA"
                     /codon_start=1
                     /product="myosin III"
                     /protein_id="AAC16332.2"
                     /db_xref="GI:7144485"
                     /translation="MEYKCISEHLPFETLPDPGDRFEVQELVGTGTYATVYSAIDKQA
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                     EFLEEGTAADLLATHRRFGIHLKEDLIALIIKEVVRAVQYLHENSIIHRDIRAANIMF
                     SKEGYVKLIDFGLSASVKNTNGKAQSSVGSPYWMAPEVISCDCLQEPYNYTCDVWSIG
                     ITAIELADTVPSLSDIHALRAMFRINRNPPPSVKRETRWSETLKDFISECLVKNPEYR
                     PCIQEIPQHPFLAQVEGKEDQLRSELVDILKKNPGEKLRNKPYNVTFFKNGHLKTISGQ
BASE COUNT     1201 a     689 c     782 g    1136 t
ORIGIN
        1 tcgacatctg tggtcgcttt ttttagtaat aaaaaattgt attatgacgt cctatctgtt
     3781 aagatacagt aactagggaa aaaaaaaa
//
```

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MODERN RESOURCES

- Relational Database Management Systems (RDBMS)
  - Introduced in the 1970s
  - Off-the-shelf software (commercial and open source)
    - Oracle, DB2, MySQL
  - High level declarative language - SQL
  - Concurrency
  - Transaction control
  - Consistency

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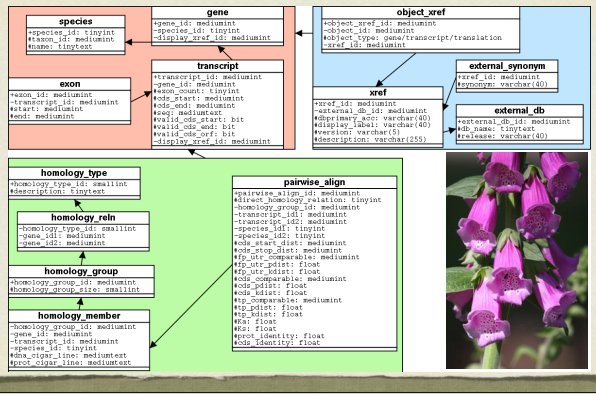
RELATIONAL DATABASES - AN EXAMPLE



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CRITICAL ISSUES FOR BIOLOGICAL DATABASES

- Annotation
  - Correctness
  - Consistency
  - Quality
- Archival Quality
- Updates
  - Raw data
  - Annotation

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CRITICAL ISSUES ANNOTATION

- Correctness – many genes are annotated primarily based on sequence comparisons. Annotation is copied from a similar sequence to a novel sequence. This may cause some problems
  - Comparison may have been done when the data were less complete
  - If sequence is incorrectly annotated, this error propagates through the database

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CRITICAL ISSUES ANNOTATION QUALITY

- Who supplies the annotation? An expert, or a non-expert at the database
- Many databases have defined groups of "experts" to help annotated genes or gene families, but there is no peer-review of information in databases
- What is the vocabulary?

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CRITICAL ISSUES ARCHIVAL QUALITY

- Databases have been torn between trying to be archival – to simply report information as experts publish it (*primary databases*), or curated – to provide the best editorially reviewed data on a topic (*secondary DB*).
- Can the same entry be recovered later?
  - Accession numbers are more stable than entry or locus names
  - Many databases do not note that there have been changes to the data! What you retrieve today may be different than yesterday

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CRITICAL ISSUES UPDATES

- How often are updates done? Major databases take direct submissions.
- Generally, only the original submitter can change an entry, even if you can prove it is wrong. This is tied to the question of archival versus curated.
- How is annotation updated as more knowledge is available? Who decides?

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SECONDARY (SPECIALIZED) DATABASES

- Boom of biological databases
- Every year first issue of *Nucleic Acids Research* dedicated to biological databases
  - http://nar.oxfordjournals.org/content/43/D1.toc
  - this year's database issue includes 1509 databases
  - the first collection published in 1993 contained description of 24 databases

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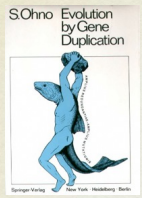
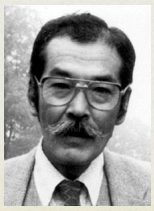
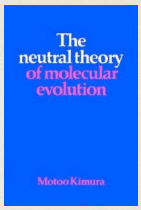
EVOLUTIONARY BASIS OF BIOINFORMATICS







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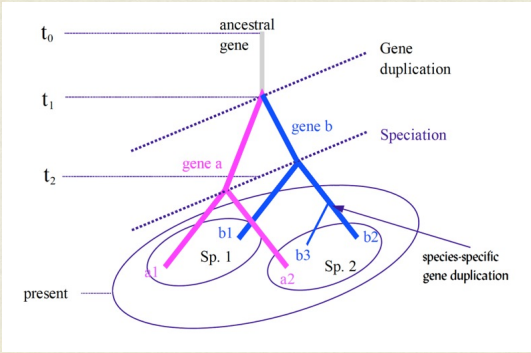
EVOLUTIONARY BASIS OF BIOINFORMATICS



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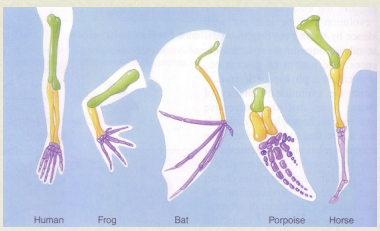
HOMOLOGS



Two anatomical structures or behavioral traits within different organisms which originated from a structure or trait of their common ancestral organism. The structures or traits in their current forms may not necessarily perform the same functions in each organism, nor perform the functions it did in the common ancestor. An example: the wing of a bat, the fin of a whale and the arm of a man are homologous structures.

http://www.everythingbio.com/glos/definition.php?ID=3385

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HOMOLOGS AT THE MOLECULAR LEVEL

```
cow      ATG---ACTAACATTCGAAAGTCCCACCCACTAATAAAAATTGTAAAC
sheep    ATG---ATCAACATCCGAAAAACCCACCCACTAATAAAAATTGTAAAC
goat     ATG---ACCAACATCCGAAAGACCCACCCATTAATAAAAATTGTAAAC
horse    ATG---ACAAACATCCGGAAATCTCACCCACTAATTAAAATCATCAAT
donkey   ATG---ACAAACATCCGAAAATCCCACCCGCTAATTAAAATCATCAAT
ostrich  ATGGCCCCCAACATTCGAAAATCGCACCCCCTGCTCAAAATTATCAAC
emu      ATGGCCCCTAACATCCGAAAATCCCACCCTCTACTCAAAATCATCAAC
turkey   ATGGCACCCAATATCCGAAAATCACACCCCCTATTAAAAACAATCAAC
```

Two sequences that share common ancestry. Significant sequence similarity usually suggests homology, however sequence similarity may occur also by chance and some homologous sequences may diverge beyond detectable similarity.

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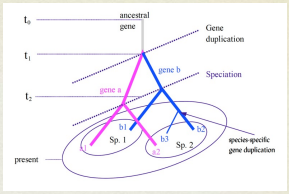
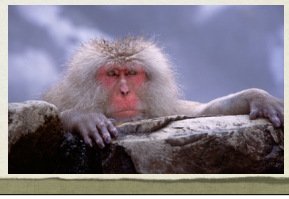
HOMOLOGS: ORTHOLOGS AND PARALOGS

ORTHOLOGS. Genes or sequences that result from a speciation event followed by a sequence divergence. Such genes may not exist side by side in the same genome. The last common ancestor of two orthologous sequences existed just before speciation event.





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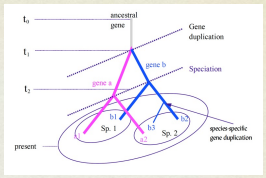
HOMOLOGS: ORTHOLOGS AND PARALOGS

PARALOGS. Genes or sequences that resulted from duplication of genetic material followed by a sequence divergence. Such genes may descend and diverge while existing side by side in the same genome. If speciation occurs after gene duplication, then two paralogous genes may exist in two different genomes. The last common ancestor of two paralogous sequences existed just before duplication event.



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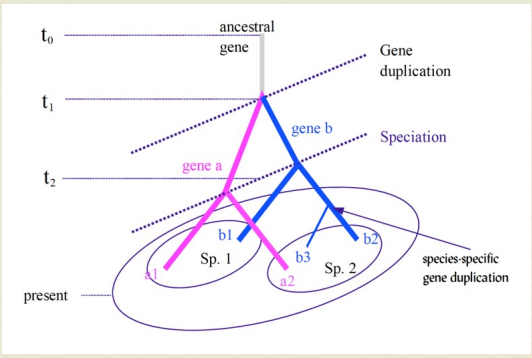
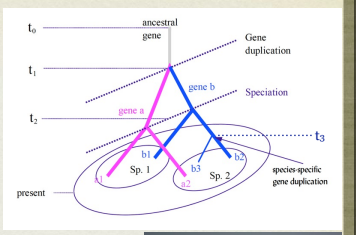
EVOLUTIONARY BASIS OF BIOINFORMATICS

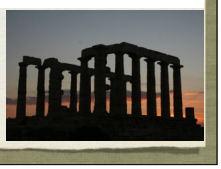


51

HOMOLOGS: ORTHOLOGS AND PARALOGS

Compared Genes	Relation	Time of last comm. ancestor	Evolutionary event at the time of last common ancestor	Presence in the same species
A - B	paralogy	t_1	gene duplication	yes
A1 - A2	orthology	t_2	speciation	no
A1 - B1	paralogy	t_1	gene duplication	yes
A1 - B2	paralogy	t_1	gene duplication	no
A1 - B3	paralogy	t_1	gene duplication	no
A2 - A1	orthology	t_2	speciation	no
A2 - B1	paralogy	t_1	gene duplication	no
A2 - B2	paralogy	t_1	gene duplication	yes
A2 - B3	paralogy	t_1	gene duplication	yes
B1 - A1	paralogy	t_1	gene duplication	yes
B1 - A2	paralogy	t_1	gene duplication	no
B1 - B2	orthology	t_2	speciation	no
B1 - B3	orthology	t_2	speciation	no
B2 - A1	paralogy	t_1	gene duplication	no
B2 - A2	paralogy	t_1	gene duplication	yes
B2 - B1	orthology	t_2	speciation	no
B2 - B3	paralogy	t_3	gene duplication	yes
B3 - A1	paralogy	t_1	gene duplication	yes
B3 - A2	paralogy	t_1	gene duplication	no
B3 - B1	orthology	t_2	speciation	no
B3 - B2	paralogy	t_3	gene duplication	yes





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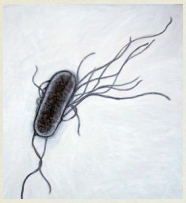
COMPARATIVE GENOMICS



What is true for *E. coli* is also true for elephant.
J. Monod, c. 1961

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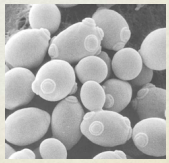
COMPARATIVE GENOMICS



What is true for yeast is also true for human.
D. Botstein, 1988

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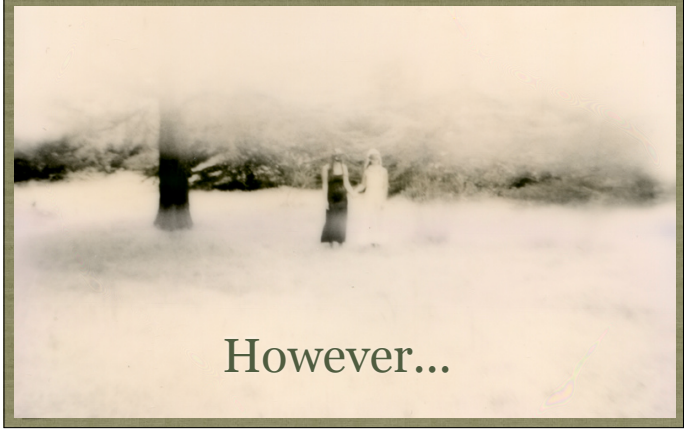
COMPARATIVE GENOMICS



However…

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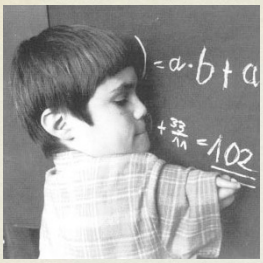
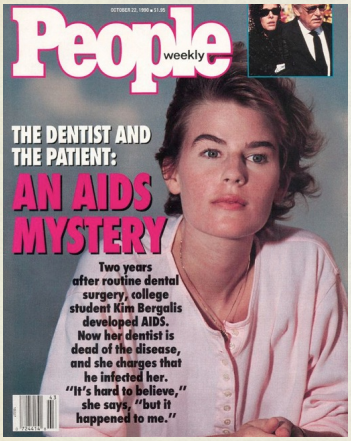
COMPARATIVE GENOMICS



15 000 victims of thalidomide

What is true for mouse is not necessarily true for human…

56



Did the Florida Dentist infect his patients with HIV?

Kimberly Bergalis

(1968-1991)

David J. Acer

(1940-1990)

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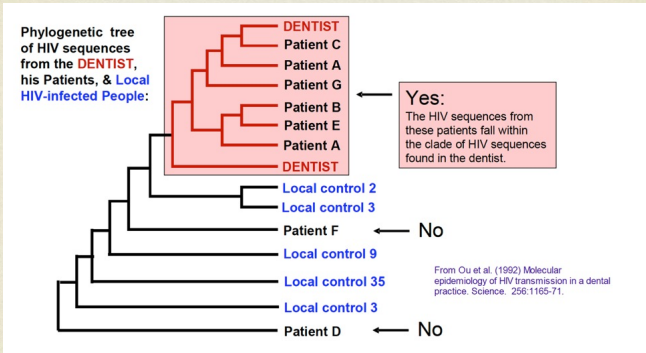
DID THE FLORIDA DENTIST INFECT HIS PATIENTS WITH HIV?



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THE MYSTERY OF THE CHILEAN BLOB

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THE MYSTERY OF THE CHILEAN BLOB

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>Chilean_Blob
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GTTGAGGAGGACTAAACCAGACTCAACTCCGAAAAATTA
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TATTTATCCAAAACTCAACCACAACCACACTATCTCTGT
CCCAGACATGAAACAAAACACCCATTACCACAACCCTTA
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TCTCGGGCTTTATCCCCAAATGAATAATTATTCAAGAAC
TAACAAAAAACGAAACCCTCATCATACCAACCTTCATAG
CCACCACAGCATTACTCAACCTCTACTTCTATATACGCC
TCACCTACTCAACAGCACTAACCCTATTCCCCTCCACAA
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AG
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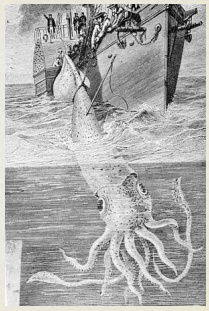

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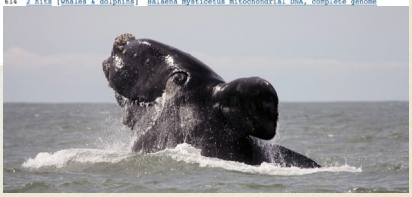
THE MYSTERY OF THE CHILEAN BLOB

Lineage Report

```
Cetacea [whales & dolphins]
- Odontoceti [whales & dolphins]
. - Physeteridae [whales & dolphins]
. . - Physeter catodon ---------- 1085  3 hits [whales & dolphins]  Physeter catodon NADH dehydrogenase subunit 2 (nad2) gene,
. . - Kogia breviceps ----------- 638   1 hit  [whales & dolphins]  Kogia breviceps complete mitochondrial genome
. . Orcaella brevirostris ------- 593   1 hit  [whales & dolphins]  Orcaella brevirostris isolate 97 mitochondrion, complete ge
. . Grampus griseus ------------- 593   1 hit  [whales & dolphins]  Grampus griseus mitochondrion, complete genome
. . Feresa attenuata ------------ 592   2 hits [whales & dolphins]  Feresa attenuata isolate 21 mitochondrion, complete genome
. . Tursiops truncatus (bottle-nosed dolphin) ... 592   1 hit  [whales & dolphins]  Tursiops truncatus mitochondrion, complete genome
. . Globicephala melas ---------- 586   3 hits [whales & dolphins]  Globicephala melas isolate Glomel042 mitochondrion, partial
. . Peponocephala electra ------- 580   2 hits [whales & dolphins]  Peponocephala electra isolate 96 mitochondrion, complete ge
. . Globicephala macrorhynchus -- 580   4 hits [whales & dolphins]  Globicephala macrorhynchus isolate Glomac65 mitochondrion,
. . Pseudorca crassidens -------- 577   3 hits [whales & dolphins]  Pseudorca crassidens mitochondrion, complete genome
. . Orcinus orca (Orca) --------- 569  34 hits [whales & dolphins]  Orcinus orca isolate ENFPGXJ mitochondrion, complete genome
. . Sotalia fluviatilis --------- 569   2 hits [whales & dolphins]  Sotalia fluviatilis haplotype 19 NADH dehydrogenase subunit
. . Platanista minor ------------ 569   1 hit  [whales & dolphins]  Platanista minor complete mitochondrial genome
. . Steno bredanensis ----------- 566   2 hits [whales & dolphins]  Steno bredanensis isolate Stebre09 mitochondrion, partial g
. Megaptera novaeangliae -------- 636   5 hits [whales & dolphins]  Megaptera novaeangliae voucher GOM9049 NADH dehydrogenase s
. Balaenoptera bonaerensis ------ 630   1 hit  [whales & dolphins]  Balaenoptera bonaerensis mitochondrial DNA, complete genome
. Eubalaena japonica ------------ 619   1 hit  [whales & dolphins]  Eubalaena japonica mitochondrial DNA, complete genome
. Balaenoptera brydei ----------- 614   2 hits [whales & dolphins]  Balaenoptera brydei mitochondrial DNA, complete genome, iso
. Balaena mysticetus (Greenland right whale) .... 614   2 hits [whales & dolphins]  Balaena mysticetus mitochondrial DNA, complete genome
. Balaenoptera musculus ---------
. Balaenoptera edeni ------------
. Balaenoptera omurai -----------
. Eschrichtius robustus (California gray whale) .
. Balaenoptera borealis ---------
. Caperea marginata -------------
. Balaenoptera physalus (finback whale) ........
```



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THE MYSTERY OF THE CHILEAN BLOB

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>emb|AJ277029.2| Physeter macrocephalus mitochondrial genome
Length=16428

 Score = 1074 bits (581),  Expect = 0.0
 Identities = 585/587 (99%), Gaps = 0/587 (0%)
 Strand=Plus/Plus

Query  1     TAATACTAACTATATCCCTACTCTCCATTCTCATCGGGGGTTGAGGAGGACTAAACCAGA  60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  4400  TAATACTAACTATATCCCTACTCTCCATTCTCATCGGGGGTTGAGGAGGACTAAACCAGA  4459

Query  61    CTCAACTCCCGAAAAATTATAGCTTACTCATCAATCGCCCACATAGGATGAATAACCACAA  120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  4460  CTCAACTCCCGAAAAATTATAGCTTACTCATCAATCGCCCACATAGGATGAATAACCACAA  4519

Query  121   TCCTACCCTACAATACAACCATAACCCTACTAAACCTACTAATCTATGTCACAATAACCT  180
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Sbjct  4520  TCCTACCCTACAATACAACCATAACCCTACTAAACCTACTAATCTATGTCACAATAACCT  4579

Query  181   TCACCATATTCATACTATTTATCCAAAACTCAACCACAACCACACTATCTCTGTCCCAGA  240
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Sbjct  4580  TCACCATATTCACACTATTTATCCAAAACTCAACCACAACCACACTATCTCTGTCCCAGA  4639

Query  241   CATGAAACAAAACACCCATTACCACAACCCTTACCATACTTACCCTACTTTCCATAGGGG  300
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Sbjct  4640  CATGAAACAAAACACCCATTACCACAACCCTTACCATACTTACCCTACTTTCCATAGGGG  4699

Query  301   GCCTCCCACCACTCTCCGGGCTTTATCCCCAAATGAATAATTATTCAAGAACTAACAAAAA  360
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Sbjct  4700  GCCTCCCACCACTCTCCGGGCTTTATCCCCAAATGAATAATTATTCAAGAACTAACAAAAA  4759

Query  361   ACGAAACCCTCATCATACCAACCTTCATAGCCACACCAGCATTACTCAACCTCTACTTCT  420
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Sbjct  4760  ACGAAGCCCTCATCATACCAACCTTCATAGCCACACCAGCATTACTCAACCTCTACTTCT  4819

Query  421   ATATACGCCTCACCTACTCAACAGCACTAACCCTATTCCCCTCCACAAATAACATAAAAA  480
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Query  481   TAAAATGACAATTCTACCCCACAAAACGAATAACCCTCCTGCCAACAGCAATTGTAATAT  540
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Sbjct  4880  TAAAATGACAATTCTACCCCACAAAACGAATAACCCTCCTGCCAACAGCAATTGTAATAT  4939

Query  541   CAACAATACTCCTACCCCTTACACCAATACTCTCCACCCTATTATAG  587
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Sbjct  4940  CAACAATACTCCTACCCCTTACACCAATACTCTCCACCCTATTATAG  4986
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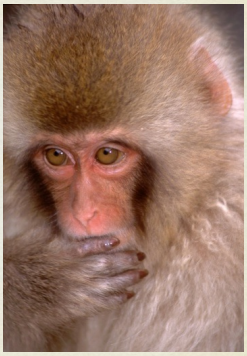
BIOINFORMATICS CREED

- Remember about biology
- Do not trust the data
- Use comparative approach
- Use statistics
- Know the limits
- Remember about biology!!!



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