BINF630/BIOL580 Bioinformatics Methods

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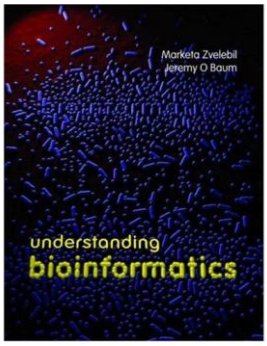
Recommended book



Marketa J Zvelebil,
Jeremy O Baum

UNDERSTANDING BIOINFORMATICS

New York: Garland Science, 2008.

Bioinformatics

Bioinformatics is a field that deals with biological information, data, and knowledge, and their storage, retrieval, management, and optimal use for problem solving and decision making.

NIH working definition of bioinformatics and computational biology (July 2000)

The NIH Biomedical Information Science and Technology Initiative Consortium agreed on the following definitions of bioinformatics and computational biology recognizing that no definition could completely eliminate overlap with other activities or preclude variations in interpretation by different individuals and organizations.

Bioinformatics: Research, development, or application of computational tools and approaches for expanding the use of biological, medical, behavioral or health data, including those to acquire, store, organize, archive, analyze, or visualize such data.

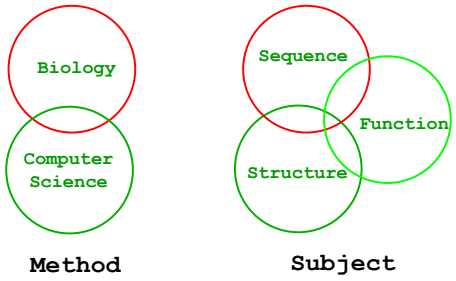
Computational Biology: The development and application of data-analytical and theoretical methods, mathematical modeling and computational simulation techniques to the study of biological, behavioral, and social systems.

COMPUTATIONAL BIOLOGY
COMPUTATIONAL STRUCTURAL BIOLOGY
COMPUTATIONAL MOLECULAR BIOLOGY
BIOINFORMATICS
GENOMICS
STRUCTURAL GENOMICS
PROTEOMICS
…
…

Omics sciences

Connectomics
Cytomics
Epigenomics
Exposomics
Exomics
Genomics
Glycomics
Interferomics
Interactomics
Ionomics
Kinomics
Lipidomics
Mechanomics
Metabolomics
Metagenomics
Metallomics
ORFeomics
Organomics
Pharmacogenomics
Phenomics
Physiomics
Proteomics
Regulomics
Secretomics
Speecheomics
Transcriptomics

Bioinformatics



Informatics

in•for•mat•ics (in′fər mat′iks) *n.* (*used with a sing. v.*) the study of information processing; computer science. [trans. of Russ informátika (1966); see INFORMATION, -ICS]

Random House Unabridged Dictionary

Information

General	Information theory
knowledge or intelligence communicated, received or gained	indication of the number of possible choices

```
Th_ qui_k br_wn _ox ju_ps ov__ th_ laz_ d_g
Ae_h uz_ ko_ wm so_g oqr_it ypu_vn tr_e oj_
```

Information

```
Th_ qui_k br_wn _ox ju_ps ov__ th_ laz_ d_g
Ae_h uz_ ko_ wm so_g oqr_it ypu_vn tr_e oj_
```

```
The quick brown fox jumps over the lazy dog
Aedh uzh kox wm sobg oqrfit ypulvn tree ojc
```

Information and uncertainty

Information is a decrease in uncertainty

$$\log_2(M) = -\log_2(M^{-1}) = -\log_2(P)$$

Shannon's formula for uncertainty

$$H = -\sum_{i=1}^{M} P_i \log_2 P_i$$

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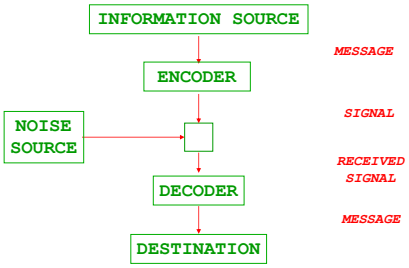
Communication

Fundamental problem of communication:

reproducing at one point either exactly or approximately a message selected at another point

The Mathematical Theory of Communication
Claude Shannon and Warren Weaver

Communication system



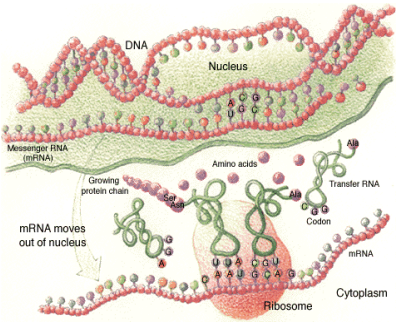
Adopted from C.E. Shannon, ***The Mathematical Theory of Communication***, 1949

Communication system duality

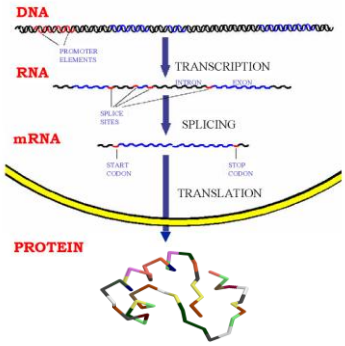
"This duality can be pursued further and is related to the duality between past and future and the notions of control and knowledge. Thus we may have knowledge of the past but cannot control it; we may control the future but have no knowledge of it."

C. E. Shannon (1959)

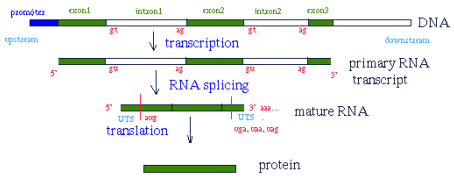
Cell Informatics



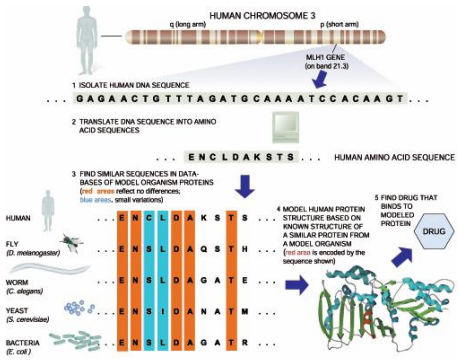
Cell Informatics



Cell Informatics

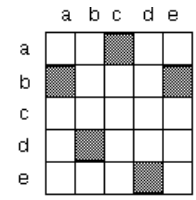


Sequence – structure – function



Luscombe *et al.*, 2001

Error correcting codes



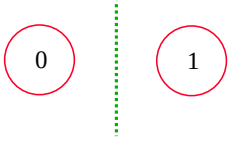
Code words ac, ba, be, db, ed in the permutation space of [a..e]x[a..e]

Hamming metric

The sum of bit changes necessary to move from one point in the permutation space to another point in the permutation space

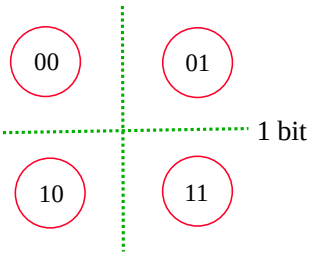
0000 and 0111 are separated by Hamming distance of 3:
0000 - 0001 - 0011 - 0111

Information Theory

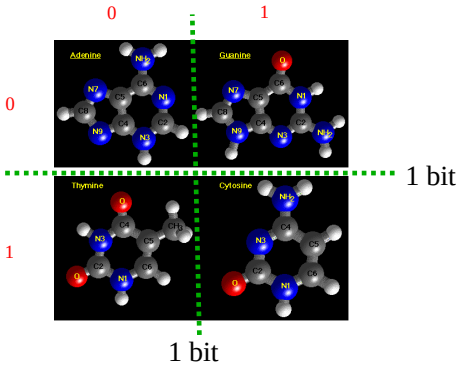


1 bit

Information Theory



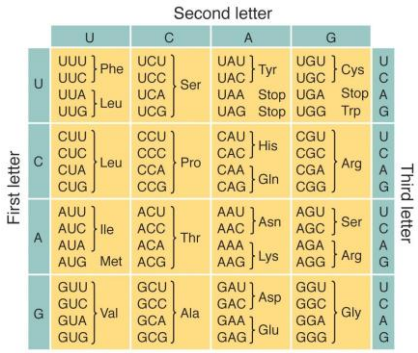
Nucleotide permutation space



Standard genetic code

TTT	F Phe	TCT	S Ser	TAT	Y Tyr	TGT	C Cys
TTC	F Phe	TCC	S Ser	TAC	Y Tyr	TGC	C Cys
TTA	L Leu	TCA	S Ser	TAA	* **Ter**	TGA	* **Ter**
TTG	L **Leu**	TCG	S Ser	TAG	* **Ter**	TGG	W Trp
CTT	L Leu	CCT	P Pro	CAT	H His	CGT	R Arg
CTC	L Leu	CCC	P Pro	CAC	H His	CGC	R Arg
CTA	L Leu	CCA	P Pro	CAA	Q Gln	CGA	R Arg
CTG	L **Leu**	CCG	P Pro	CAG	Q Gln	CGG	R Arg
ATT	I Ile	ACT	T Thr	AAT	N Asn	AGT	S Ser
ATC	I Ile	ACC	T Thr	AAC	N Asn	AGC	S Ser
ATA	I Ile	ACA	T Thr	AAA	K Lys	AGA	R Arg
ATG	M **Met**	ACG	T Thr	AAG	K Lys	AGG	R Arg
GTT	V Val	GCT	A Ala	GAT	D Asp	GGT	G Gly
GTC	V Val	GCC	A Ala	GAC	D Asp	GGC	G Gly
GTA	V Val	GCA	A Ala	GAA	E Glu	GGA	G Gly
GTG	V Val	GCG	A Ala	GAG	E Glu	GGG	G Gly

Standard genetic code



Griffiths *et al.*, 2004

Differences from the Standard Code

Vertebrate Mitochondrial Code

```
AGA   Ter *   Arg R
AGG   Ter *   Arg R
AUA   Met M   Ile I
UGA   Trp W   Ter *
```

Yeast Mitochondrial Code

```
AUA   Met M    Ile I
CUU   Thr T    Leu L
CUC   Thr T    Leu L
CUA   Thr T    Leu L
CUG   Thr T    Leu L
UGA   Trp W    Ter *
CGA   absent   Arg R
CGC   absent   Arg R
```

Noise Sources

- Vector sequences
- Heterologous sequences
- Rearranged & deleted sequences
- Repetitive element contamination
- Sequencing errors / Natural polymorphisms
- Frameshift errors

Standard genetic code

```
  AAs = FFLLSSSSYY**CC*WLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG
Starts = ---M---------------M---------------M----------------------------
 Base1 = TTTTTTTTTTTTTTTTCCCCCCCCCCCCCCCCAAAAAAAAAAAAAAAAGGGGGGGGGGGGGGGG
 Base2 = TTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGGTTTTCCCCAAAAGGGG
 Base3 = TCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAG
```

Frameshift Errors

```
ATGAAATTTGGAAACTTCCTTCTCACTTATCAGCCACCTGAGCTATCTCAGACCGAAGTGATGAAGCGATTGGTTAATCT
  5'3'Frame1 MKFGNFLLTYQPPELSQTEVMKRLVN
  5'3'Frame2 -NLETSFSLISHLSYLRPK--SDWLI
  5'3'Frame3 EIWKLPSHLSAT-AISDRSDEAIG-S
  3'5'Frame1 RLTNRFITSV-DSSGG--VRRKFPNF
  3'5'Frame2 D-PIASSLRSEIAQVADK-EGSFQIS
  3'5'Frame3 INQSLHHFGLR-LRWLISEKEVSKFH
```

Comparative Sequence Sizes

Yeast chromosome 3	350,000
Escherichia coli (bacterium) genome	4,600,000
Largest yeast chromosome now mapped	5,800,000
Entire yeast genome	15,000,000
Smallest human chromosome (Y)	50,000,000
Largest human chromosome (1)	250,000,000
Entire human genome	3,000,000,000