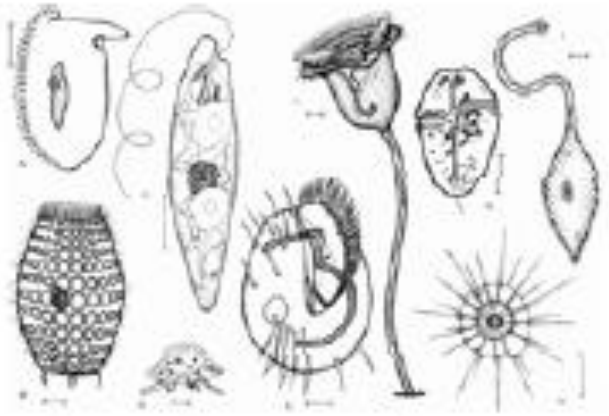
Basic Biological Crash Course

A “small” part of biology

[tolweb.org/tree/phylogeny.html]

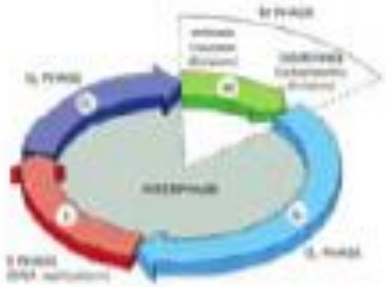
There's a long way from single *cells* to complex organisms, but *cells* are the building blocks of more complicated beings and therefore are worth studying.

Besides, *cells* are difficult to understand already. And they can be very complex as well!

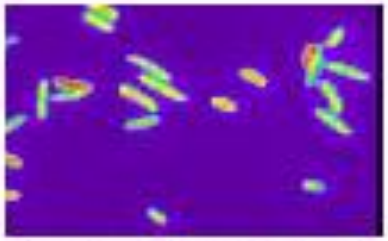


[this and other images were taken from Alberts *et al*, Molecular Biology of the Cell - 3rd ed]

What do cells do?



grow and divide



store information

form part of bigger organisms

move around

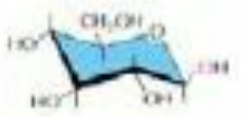
interact with the environment

and so on…

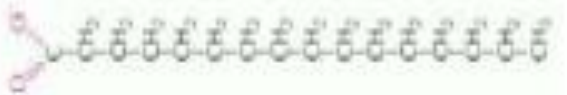
What's in a cell?

4 basic types of small organic molecules

- sugars ——— energy sources, food

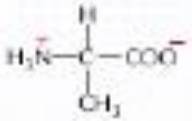


- fatty acids ——— membranes



- nucleotides ——— subunits of nucleic acids (*DNA*, *RNA*); can also act as energy carriers (ATP)

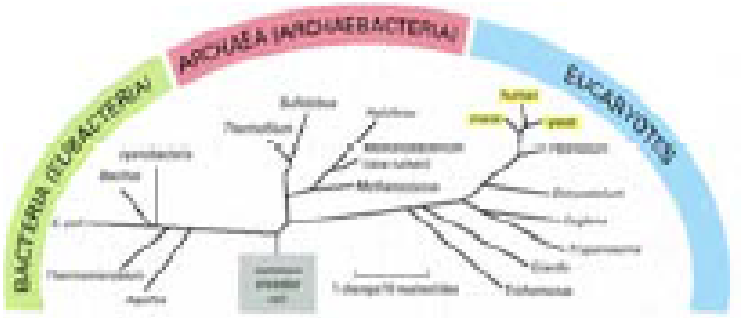
- amino acids ——— subunits of *proteins*, the "workhorses" of the cells



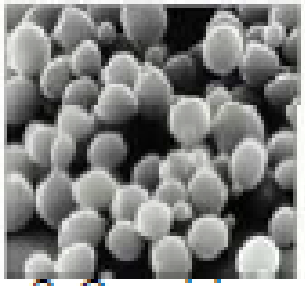
And also ions (Ca^{2+}, Mg^{2+}, Cl^-, K^+, etc), lots of water, some other organic molecules, and structures that arise by combining these basic constituents

Two classes of cells

E. Coli



[adapted from Alberts et al, Molecular Biology of the Cell]



S. Cerevisiae

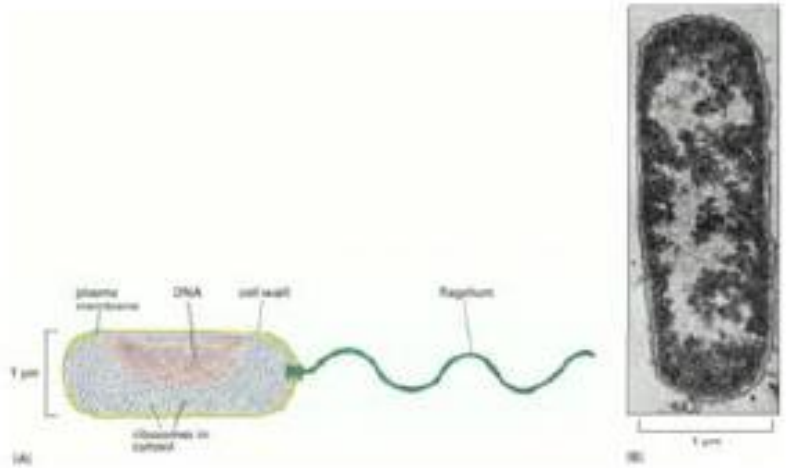
- bacteria and cyanobacteria
- 1 to 10 μm
- anaerobic or aerobic
- few or none organelles
- circular DNA in cytoplasm
- RNA and protein synthesis in same compartment
- no cytoskeleton
- chromosomes pulled apart by attachments to plasma membrane
- mainly unicellular

bacteria

- protists, fungi, plants and animals
- 5 to 100 μm
- aerobic
- many organelles
- long linear DNA bounded by nucleus
- RNA synthesis in nucleus, protein synthesis in the cytoplasm
- cytoskeleton
- chromosomes pulled apart by spindle apparatus
- mainly multicellular

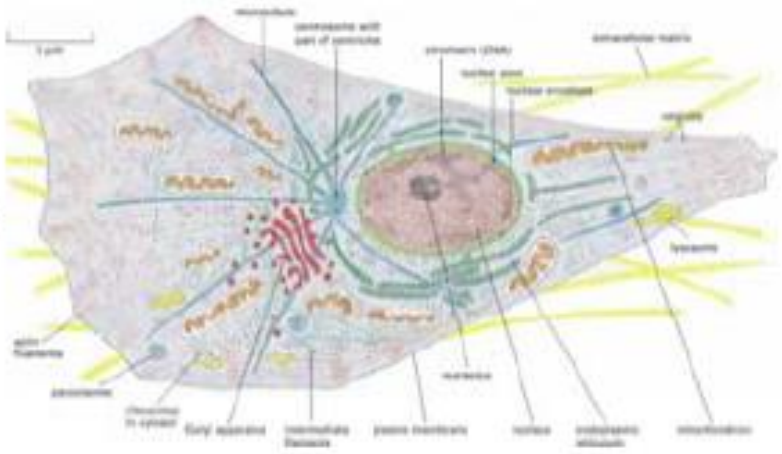
eukaryotes

Cell structure

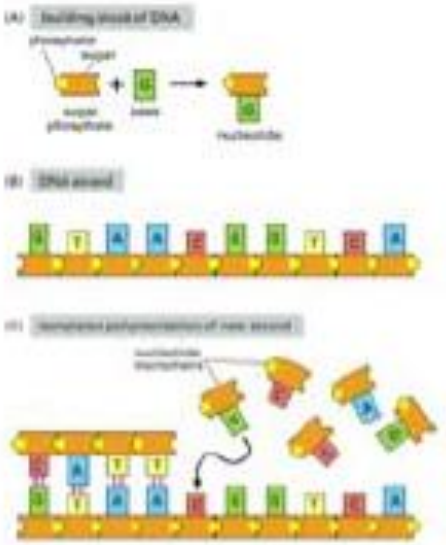


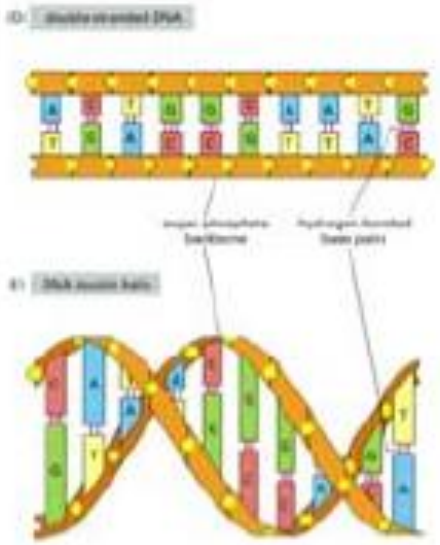
"typical" prokaryote

"typical" eukaryote



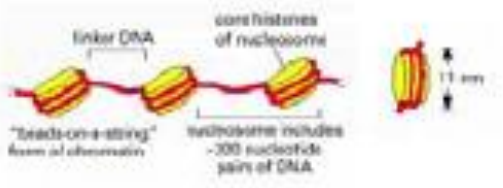
DNA



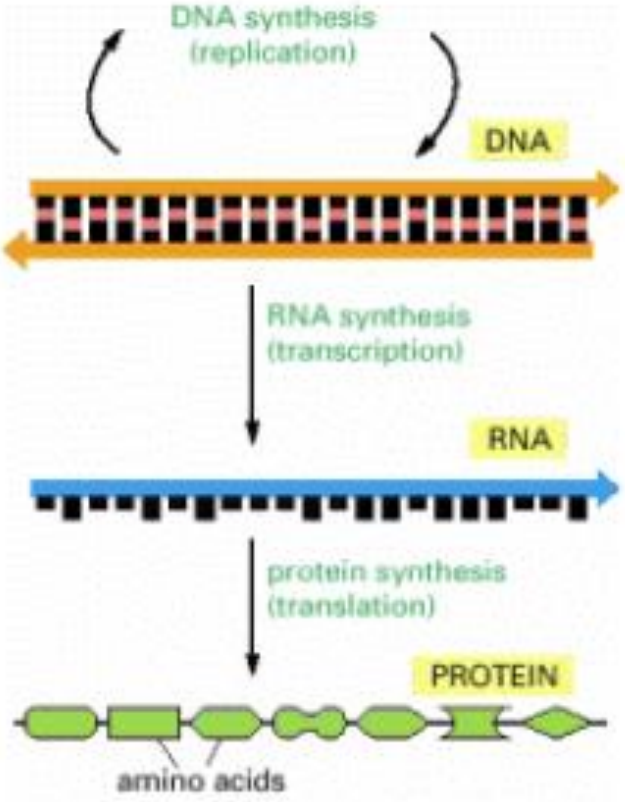


DNA encodes information. It defines the *genotype* of a cell.

- In prokaryotes it is a circular chain that floats around in the cytoplasm.
- In eukaryotes it consists of several long linear chains called *chromosomes*, with specialized structures that guarantee a faithful duplication (centromere, telomeres); everything heavily packed inside the nucleus.
- The collection of all the DNA in one cell is referred to as its *genome*.
- Composed of A, T, C, G bases
- Double helix structure, but it can also be fold in other ways.
- Negatively charged
- Human: 24 chromosomes, each with 10^7 - 10^8 base pairs.

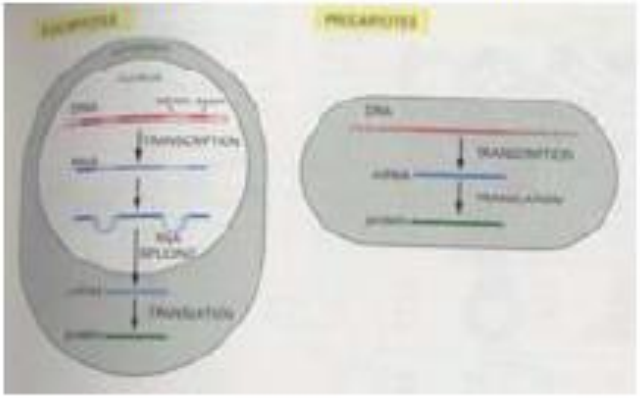


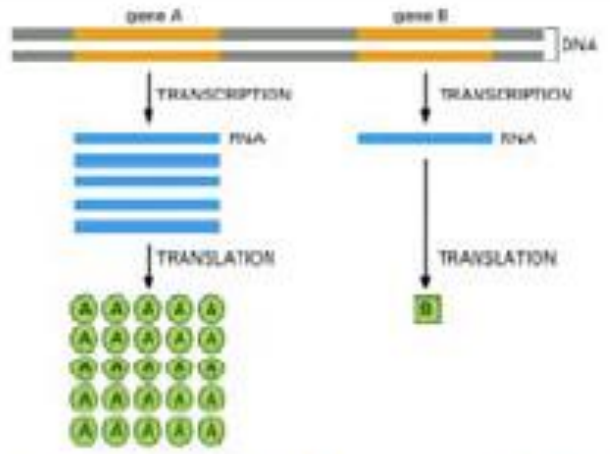
The central dogma



A portion of *DNA*, called a *gene*, is *transcribed* into *RNA*.
RNA is *translated* into *proteins*.

Details of the process are different in eukaryotes / prokaryotes.



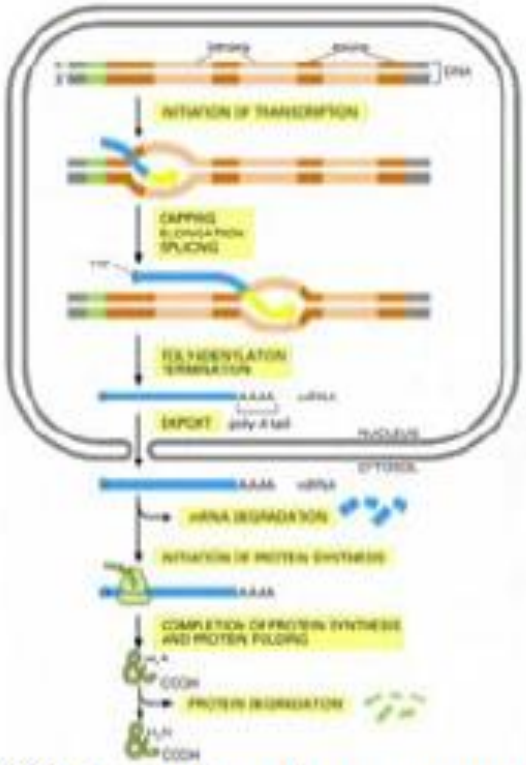


Expression might depend on the gene.

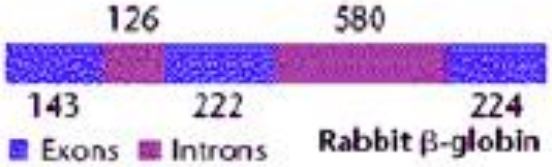
More details…

GCA GCC GCG GCU	AGA AGG CGA CGC CGG CGU	GAC GAU	AAC AAU	UGC UGU	GAA GAG	CAA CAG	GGA GGC GGG GGU	CAC CAU	AUA AUC AUU	UUA UUG CUA CUC CUG CUU	AAA AAG	AUG	UUC UUU	CCA CCC CCG CCU	AGC AGU UCA UCC UCG UCU	ACA ACC ACG ACU	UGG	UAC UAU	GUA GUC GUG GUU	UAA UAG UGA
Ala	Arg	Asp	Asn	Cys	Glu	Gln	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	stop
A	R	D	N	C	E	Q	G	H	I	L	K	M	F	P	S	T	W	Y	V	

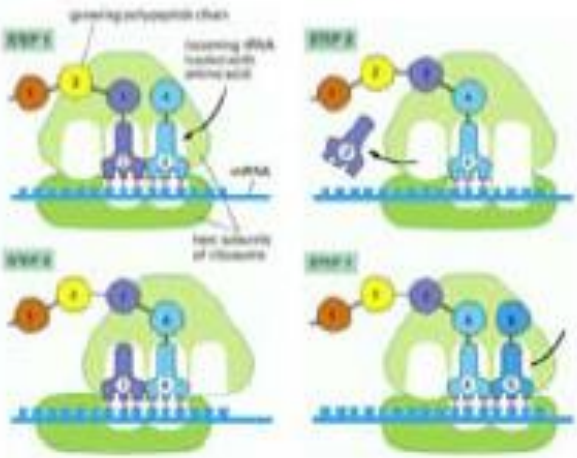
The genetic code



From DNA to proteins in an eucaryotic cell.

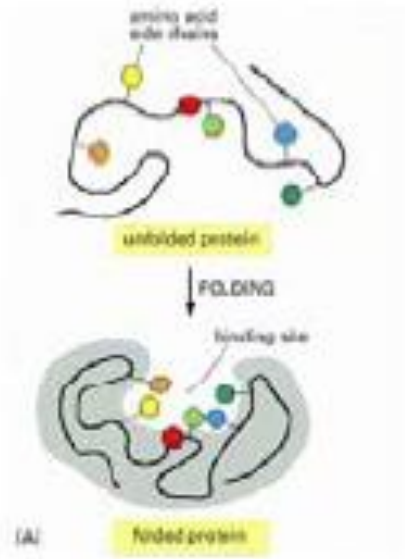


Introns and exons



tRNA and *ribosomes*

Proteins

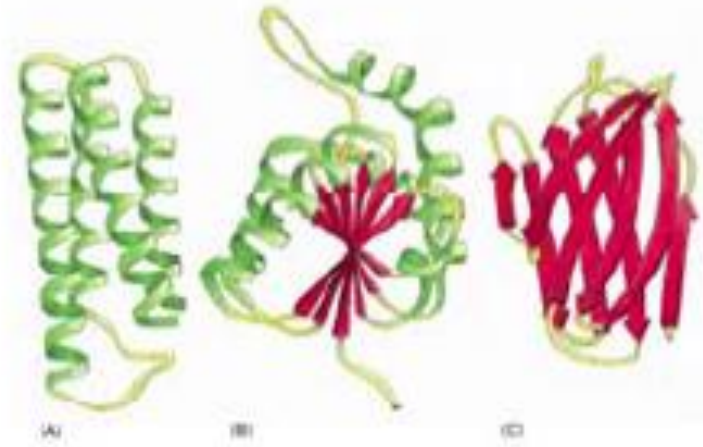


AMINO ACID			SIDE CHAIN
Aspartic acid	Asp	D	negative
Glutamic acid	Glu	E	negative
Arginine	Arg	R	positive
Lysine	Lys	K	positive
Histidine	His	H	positive
Asparagine	Asn	N	uncharged polar
Glutamine	Gln	Q	uncharged polar
Serine	Ser	S	uncharged polar
Threonine	Thr	T	uncharged polar
Tyrosine	Tyr	Y	uncharged polar

POLAR AMINO ACIDS

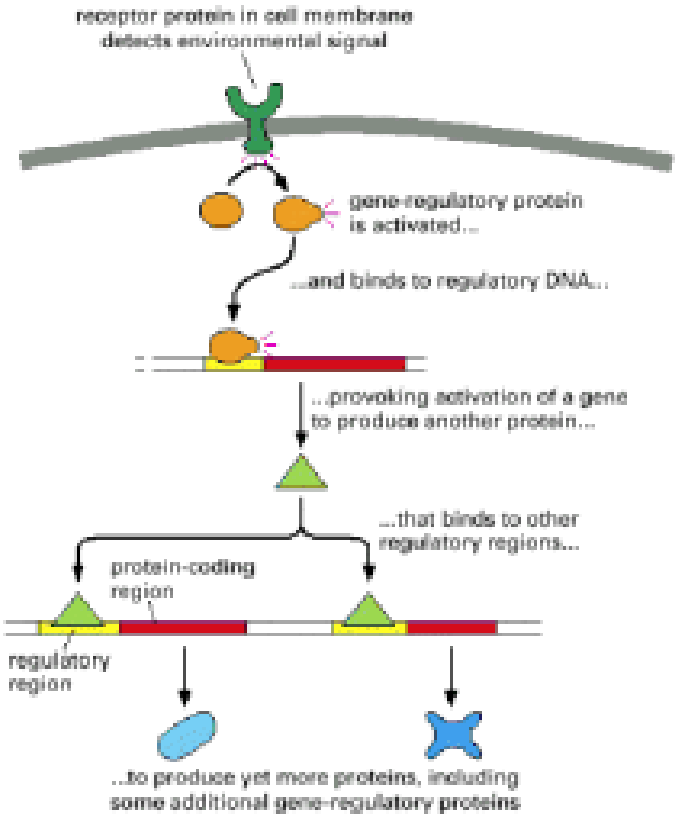
AMINO ACID			SIDE CHAIN
Alanine	Ala	A	nonpolar
Glycine	Gly	G	nonpolar
Valine	Val	V	nonpolar
Leucine	Leu	L	nonpolar
Isoleucine	Ile	I	nonpolar
Proline	Pro	P	nonpolar
Phenylalanine	Phe	F	nonpolar
Methionine	Met	M	nonpolar
Tryptophan	Trp	W	nonpolar
Cysteine	Cys	C	nonpolar

NONPOLAR AMINO ACIDS



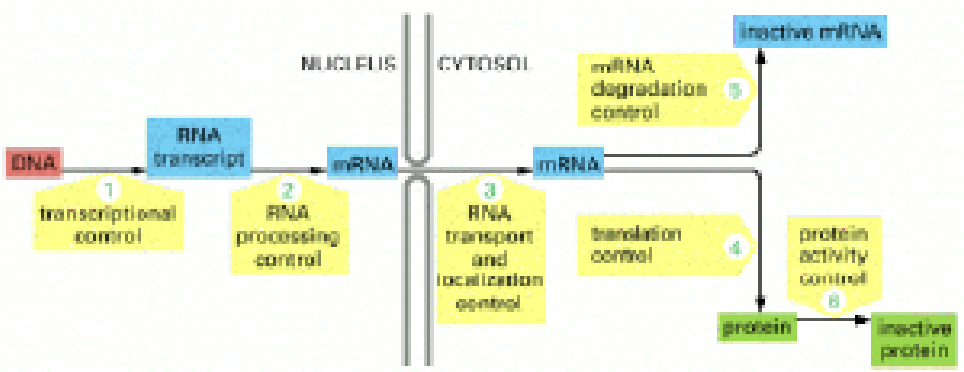
- The function of a protein is basically given by its geometric shape.
- After translation a protein has to be folded properly for rendering it functional.
- Predicting the shape of a protein given its sequence is a huge open problem!

Regulation of ***gene expression***



Some proteins, known as *transcription factors*, bind to DNA and regulate the activity of RNA polymerase, the enzyme in charge of the transcription process.

Regulation can take place all along the protein synthesis process.



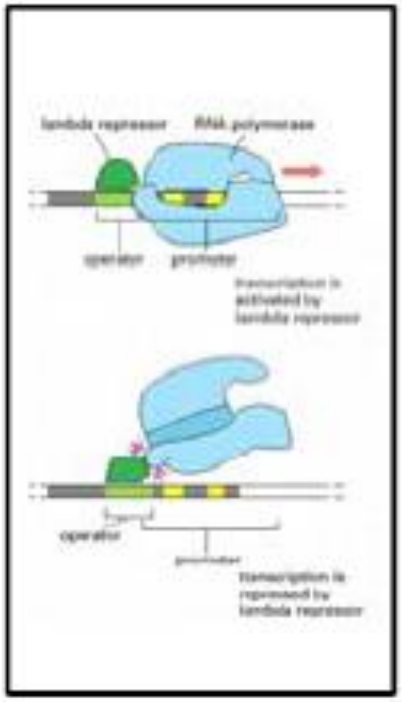
To start transcription, RNA polymerase has to bind to a portion of DNA right before the gene to be translated. That region is known as the gene *promoter*.

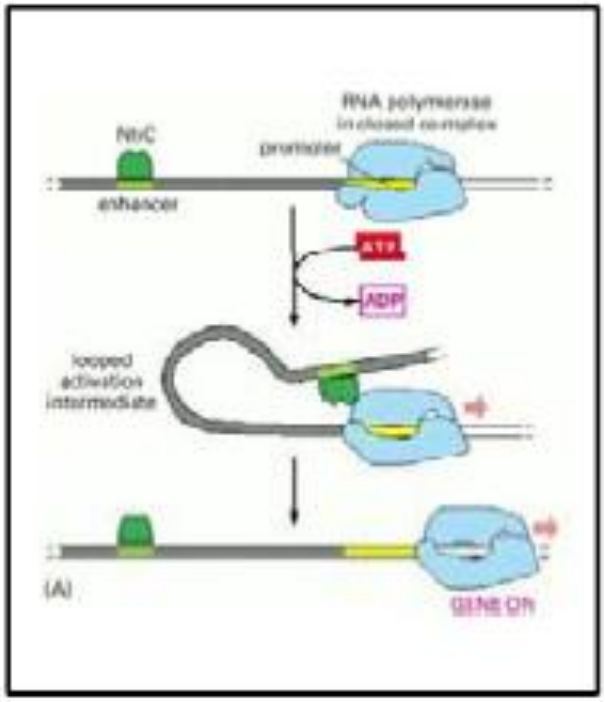
"Activity" of promoters is regulated by the binding / unbinding of transcription factors to some "neighboring" pieces of DNA

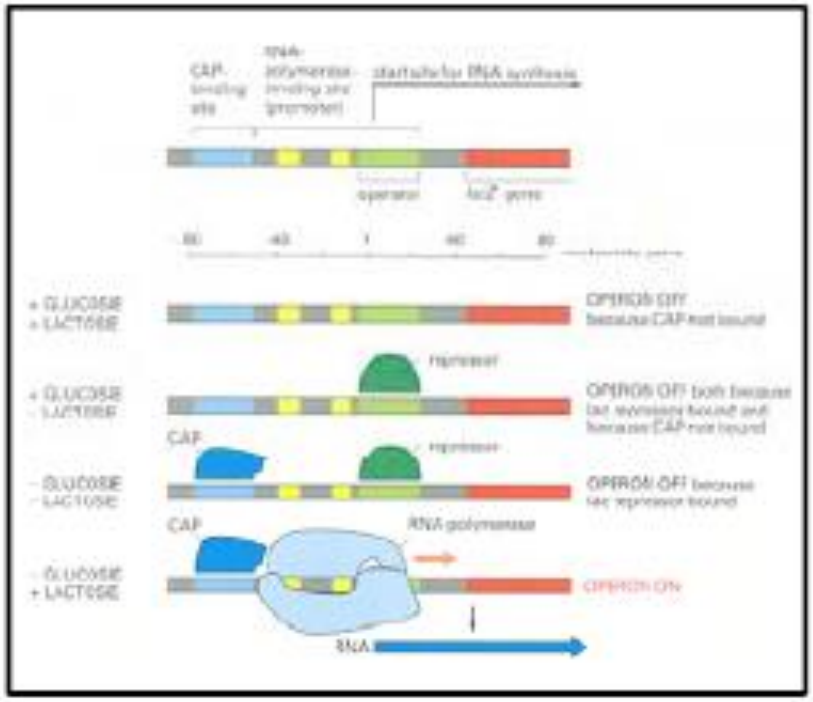
Being able to predict where a transcription factor will bind to and what its effect will be it is also a huge open problem.

Regulation of ***gene expression***

Examples of models of regulation of gene expression at the transcriptional level.
Transcription factors bind to *promoter* sites and influence the rate of transcription of a *gene*.

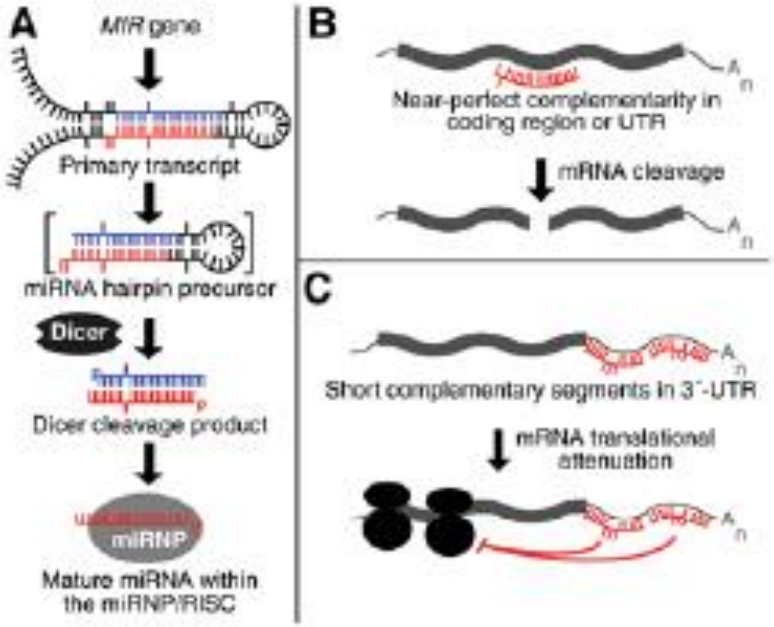






Regulation of ***gene expression***

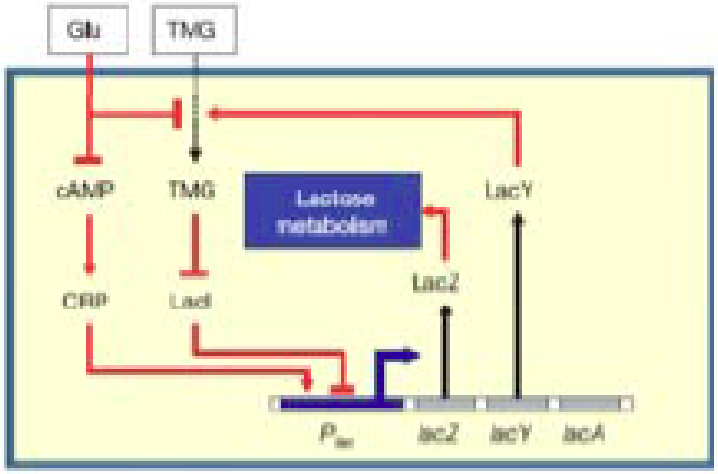
Gene expression can also be regulated at the *RNA* level, for instance through micro RNAs (*miRNA*) and/or short interfering RNA molecules (*siRNA*)



[Douglas Steinberg, The Scientist, **17**(12):22 (2003)]
[see also B. Bartel and D. P. Bartel, Plant Physiol, **132**:1-9 (2003)]

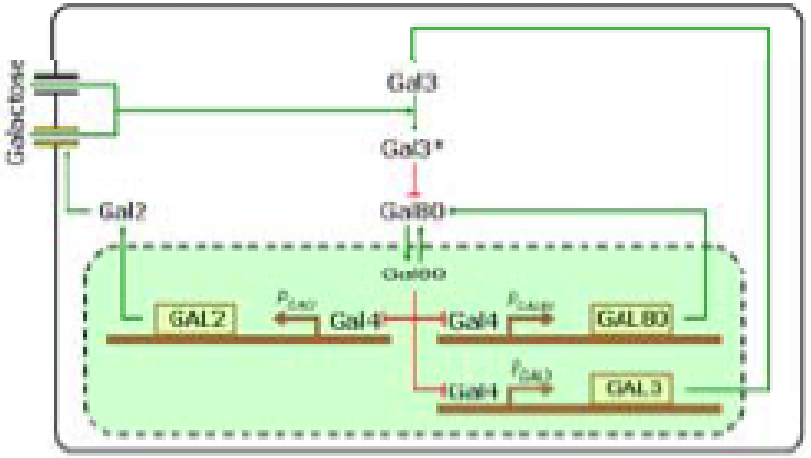
Gene expression

Two examples



Ozbudak *et al*, Nature **427** (2004)

Lactose consumption regulation in *E.Coli*.



Galactose signaling network in *S. Cerevisiae*.

The amount of proteins produced is a dynamic process. It is not entirely determined by the genotype, it will also depend on the environment and the cell history. Cells can use this fact to store information in the amounts of proteins that they hold; different patterns of protein concentrations can lead to macroscopic changes in cell behavior. Any information encoded in this way is referred to as the *phenotype* of a cell.

Part I

Single reaction

‘A living cell is a well-stirred bioreactor’

Michaelis-Menten Kinetics

To develop the mathematical techniques to model fundamental biochemical reactions, e.g.

1. Conversion of glucose (S) into glucose-6-phosphate (P) by protein hexokinase (E)
2. Transcription: binding of RNA polymerase (E) to the promoter of the DNA (S) results in the transcription of the mRNA (P)
3. Phosphorylation of a protein: CheY (S) is phosphorylated by CheZ (E) resulting in CheY-p (P)

The reaction

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P$$

$$\frac{d[S]}{dt} = -k_1[E][S] + k_{-1}[ES]$$

$$\frac{d[E]}{dt} = -k_1[E][S] + (k_{-1} + k_2)[ES]$$

$$\frac{d[ES]}{dt} = k_1[E][S] - (k_{-1} + k_2)[ES]$$

$$\frac{d[P]}{dt} = k_2[ES] \equiv v$$

Simplified equations

$$E_o = [E] + [ES]$$ Total amount of enzyme is constant

$$\frac{d[S]}{dt} = -k_1 E_o [S] + (k_1 [S] + k_{-1})[ES]$$

$$\frac{d[ES]}{dt} = k_1 E_o [S] - (k_1 [S] + k_{-1} + k_2)[ES]$$

$$\frac{d[P]}{dt} = k_2 [ES] \equiv v$$

psuedo-steady state

Assuming formation and breaking of enzyme-substrate reach a balance

$$d[ES]/dt = d[E]/dt = 0$$

$$[ES] = \frac{k_1[S]E_o}{k_1[S] + k_{-1} + k_2}$$

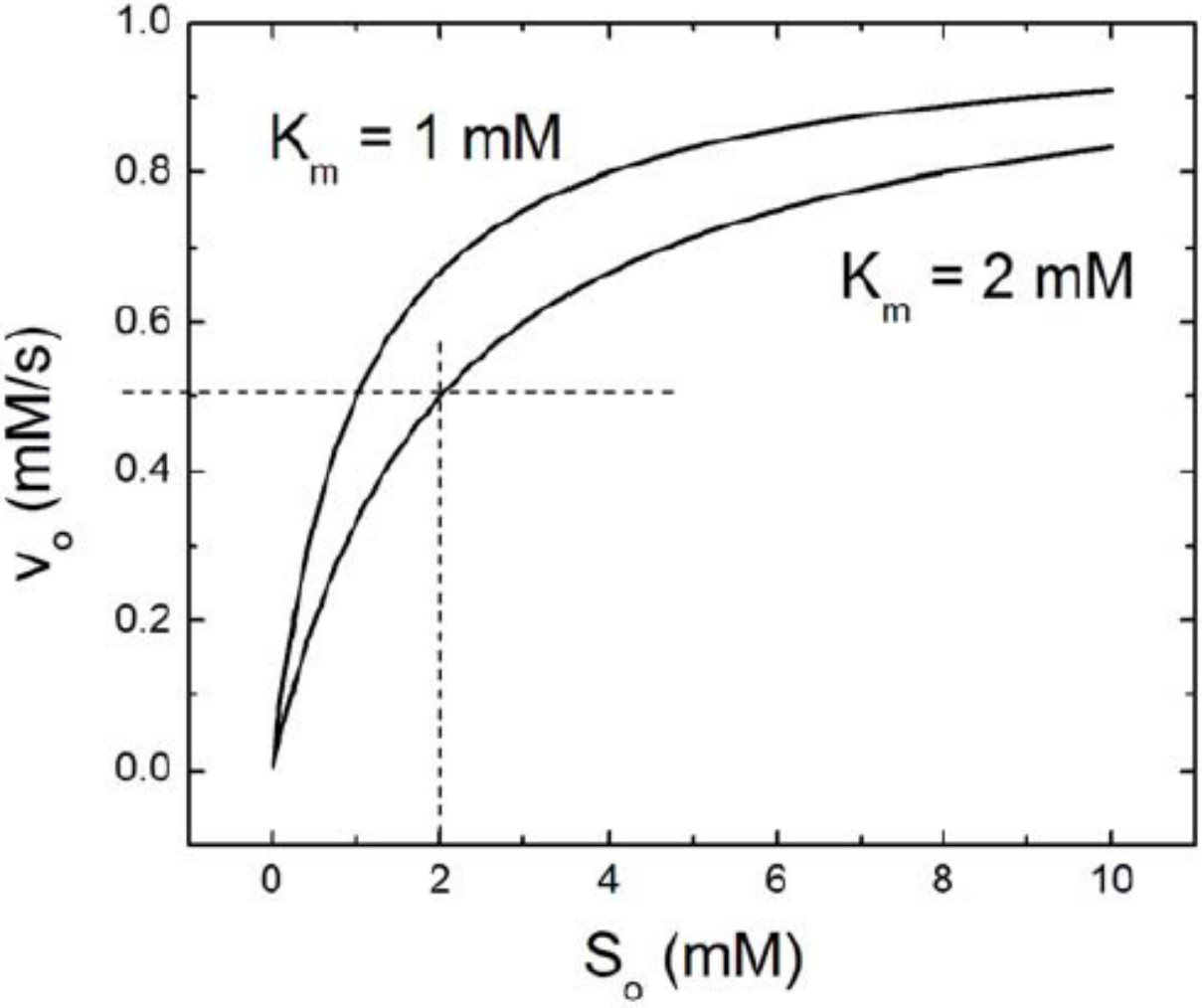
$$v = \frac{dP}{dt} = \frac{k_2[S]E_o}{\frac{k_{-1} + k_2}{k_1} + [S]}$$

Michaelis-Menten equation

$$v_o = \frac{v_{max} S_o}{K_m + S_o}$$

$$K_m = (k_{-1} + k_2)/k_1$$

$$v_{max} = k_2 E_o$$



The initial turnover rate as given by the Michaelis-Menten formula

How about the dynamics of the reaction?

Solve the equations

$$\frac{d[S]}{dt} = -k_1 E_o [S] + (k_1 [S] + k_{-1})[ES]$$

$$\frac{d[ES]}{dt} = k_1 E_o [S] - (k_1 [S] + k_{-1} + k_2)[ES]$$

$$\frac{d[P]}{dt} = k_2 [ES] \equiv v$$

With initial condition: $[S]_{t=0}=S_0$, $[ES]_{t=0}=0$ and $[P]_{t=0}=0$

How do we do that?

Meet your next best friend

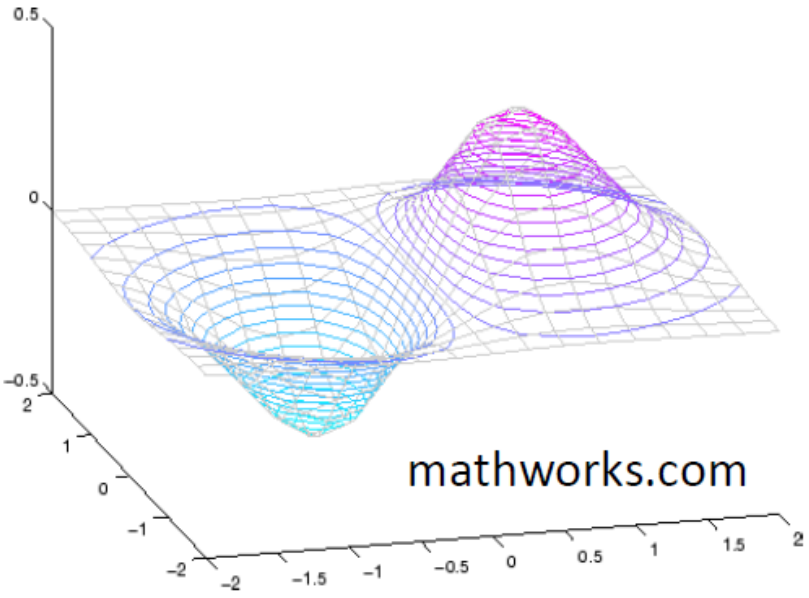
Matlab!

What is Matlab?

- Matlab = Matrix Laboratory
- Problem-solving environment
- Designed for convenient *numerical* computations (e.g. matrix manipulation, differential eqns, stats, and graphics)
- Developed by Cleve Moler in 1970s as a teaching tool
- Now ubiquitous in education and industry

Why Matlab?

- Great tool for simulation and data analysis
- User-friendly interface
- Many easy to use built-in functions and tool boxes
- Easy visualization
- Easy to get help:
  - help *function_name*
  - lookfor *topic*
  - www.mathworks.com



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商业数学软件——MATLAB（数学系采购）

软件介绍:

MATLAB 是美国MathWorks公司出品的商业数学软件，用于算法开发、数据可视化、数据分析以及数值计算的高级技术计算语言和交互式环境，主要包括MATLAB和Simulink两大部分。

安装激活指南:

南科大正版matlab安装激活指南

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MATLAB技术支持电话：86-10-5982-7000