

# Introductory of Bioinformatics?

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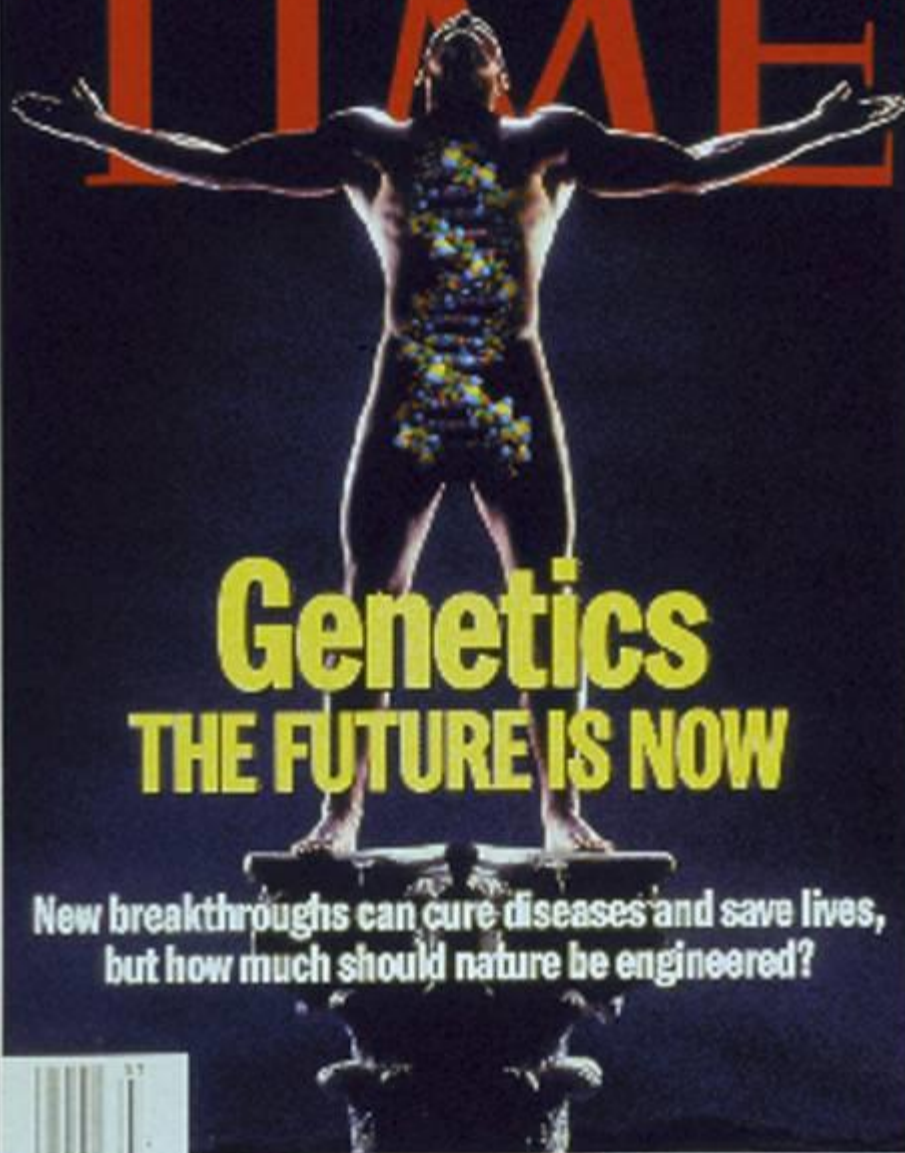
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**PhD. Technical University Of Munich, Germany**

**16-08-2015**

SPECIAL REPORT

# TIME



## Genetics THE FUTURE IS NOW

New breakthroughs can cure diseases and save lives,  
but how much should nature be engineered?



Newsweek

SHOWDOWN OVER ELIAN

THE RACE TO  
DECODE THE  
HUMAN  
BODY

CURING  
DISEASE  
DESIGNING  
BABIES  
PLAYING  
GOD

GENOME

LIVING  
LONGER  
PREDICTING  
HEALTH

INVESTING  
MILLIONS  
LOSING  
PRIVACY



www.newsweek.com



# TIME

SPECIAL REPORT

COUNTDOWN TO WAR

SOLVING  
THE  
MYSTERIES  
OF

## DNA

*The 50th Anniversary:*  
Reliving Watson and Crick's  
historic discovery

How gene science has  
changed our lives

Visions of the future



# Confirmed genetic contributors to common human diseases (April 2007)

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*Cholesterol*

*Obesity*

*Coronary Dz*

*Prostate cancer*

*Age Related Macular Degeneration*

*Crohn's Disease*

*Type 2 Diabetes*

*PPAR<sub>γ</sub>* *IBD5*  
*NOD2*

*KCNJ11*

*CFH*

*CFB/C2* *CDKN2A*  
*LOC387715* *IGF2BP2*  
*8q24* *CDKAL1*  
*IL23R* *HHEX*  
*TCF7L2* *SLC30A8*

*CF3*  
*GCKR*  
*FTO*  
*CDKN2A*  
*8q24 #2*  
*8q24 #3*  
*8q24 #4*  
*8q24 #5*  
*8q24 #6*  
*ATG16L1*  
*IRGM*  
*5p13*  
*3p21*  
*10q21*  
*NKX2*  
*PTPN2*  
*IL12B*

2000 2001 2002 2003 2004 2005 2006 2007

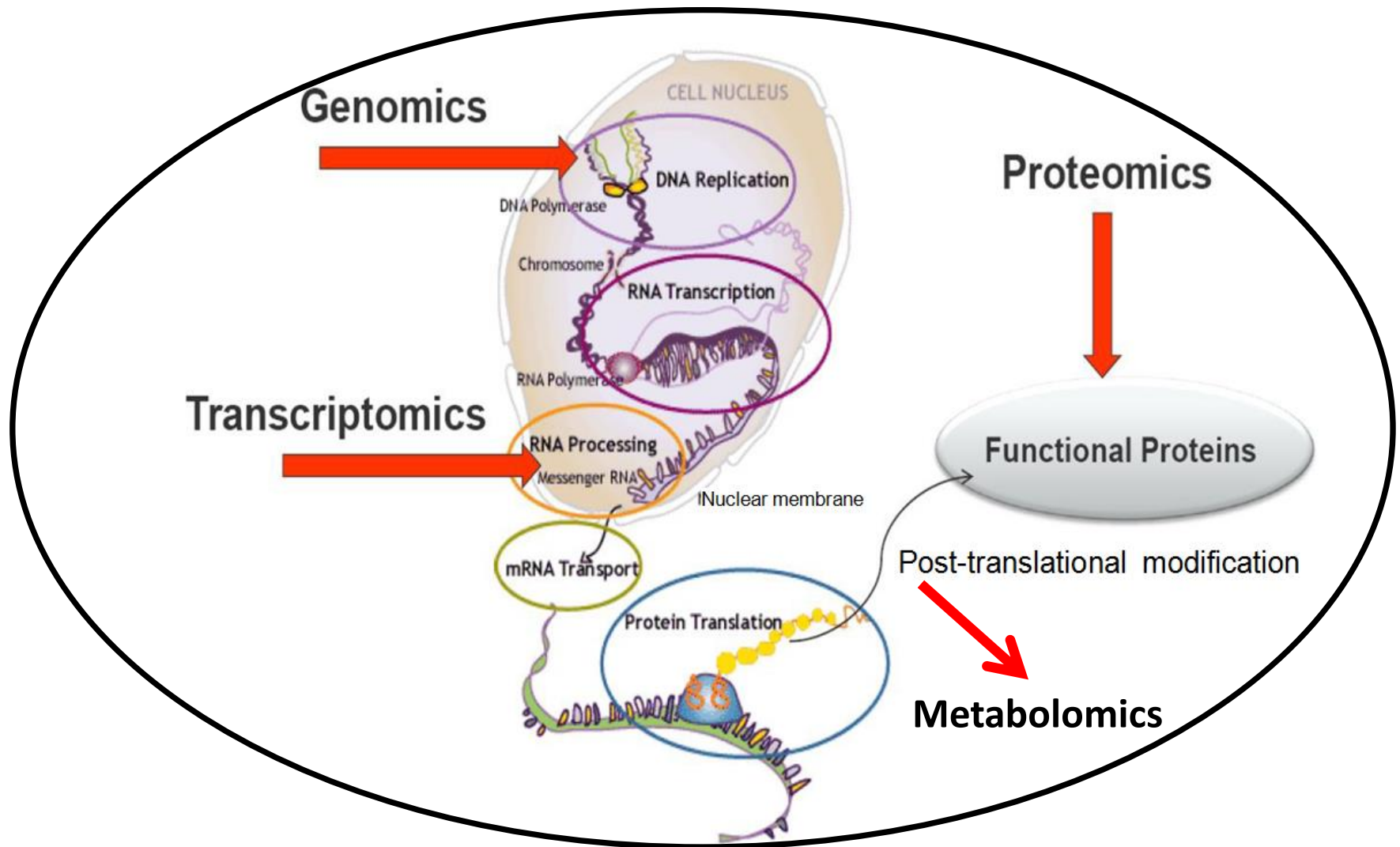
## Confirmed genetic contributors to common human diseases (Sept 2007)

Phenotype	Gene	Chromosome	Year
Cholesterol	ATG16L1	16p11.2	2000
Obesity	FTO	16p11.2	2007
Coronary Disease	GSK3B	5p13	2000
QT interval	SCN5A	3p21	2000
Atrial Fibrillation	KIF201	12p12	2006
Type 2 Diabetes	TCF7	10q26	2006
Prostate cancer	BRCA2	13q12	2000
Breast cancer	BRCA1	17q21	2000
Colon cancer	APC	5q21	2000
Age Related Macular Degeneration	CFH	1q32	2005
Crohn's Disease	NOD2	16p11.2	2001
Type 1 Diabetes	INS	6p22.3	2000
Systemic Lupus Erythematosus	IRF5	9p21.3	2005
Asthma	ORMDL3	8q24	2007
Restless leg syndrome	MEIS1	12p12	2006
Gallstone disease	ABCG8	3p21	2007
Multiple sclerosis	IL23R	16p11.2	2006
Rheumatoid arthritis	PTPN22	18p11.2	2004
Glaucoma	CDKN2B	12p12	2006
	CTLA4	2q37	2002
	KCNJ11	11p15.5	2003
	PPARγ	1p31	2000
	IBD5	16p11.2	2001
	CD25	12p12	2006
	LOC387715	12p12	2006
	IRF5	9p21.3	2005
	PCSK9	16p11.2	2006
	CFH	1q32	2005
	TCF7L2	10q26	2006
	IL23R	16p11.2	2006
	8q24	8q24	2007
	IGF2BP2	12p12	2006
	CDKAL1	12p12	2006
	HHEX	12p12	2006
	SLC30A8	12p12	2006
	FGFR2	10q26	2007
	TNRC9	10q26	2007
	MAP3K1	10q26	2007
	LSP1	10q26	2007
	GRIN3A	10q26	2007
	ANGPT3	10q26	2007
	SH2B3	10q26	2007
	PTPN2	18p11.2	2007
	CD226	1q32	2007
	GALNT2	1q32	2007
	PSRC1	16p11.2	2007
	NCAN	16p11.2	2007
	TBL2	12p12	2007
	TRIB1	12p12	2007
	KCTD10	12p12	2007
	LOXL1	16p11.2	2007
	IL7R	16p11.2	2007
	TRAF1	16p11.2	2007
	STAT4	16p11.2	2007
	ABCG8	3p21	2007
	KIAA030	3p21	2007
	ERBB3	3p21	2007
	C12orf0	3p21	2007
	NKX2-3	12p12	2007
	IRGM	10q21	2007
	GSK3B	5p13	2007
	TCF2	10q21	2007
	ATG16L1	16p11.2	2007

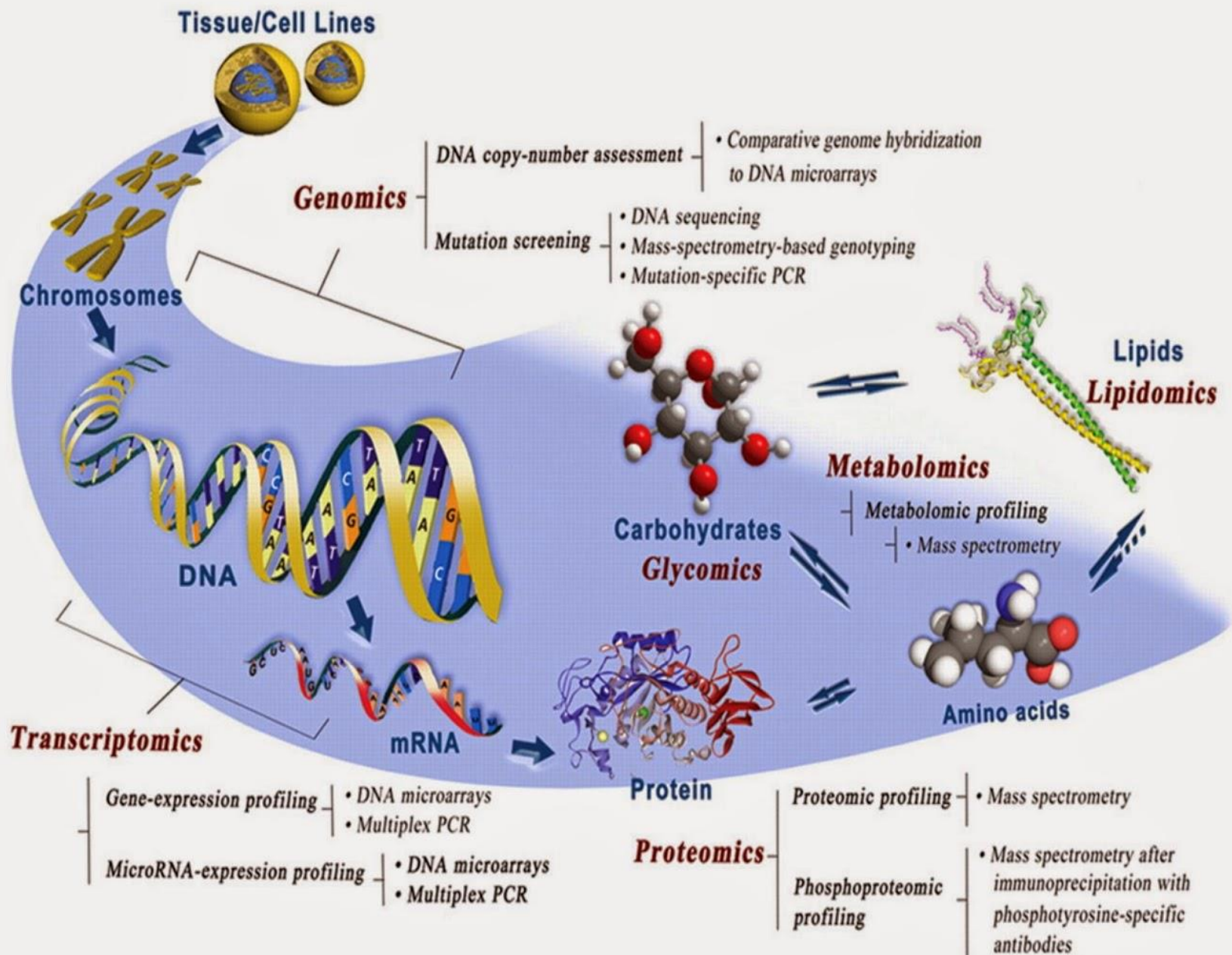
# Omic' Technologies

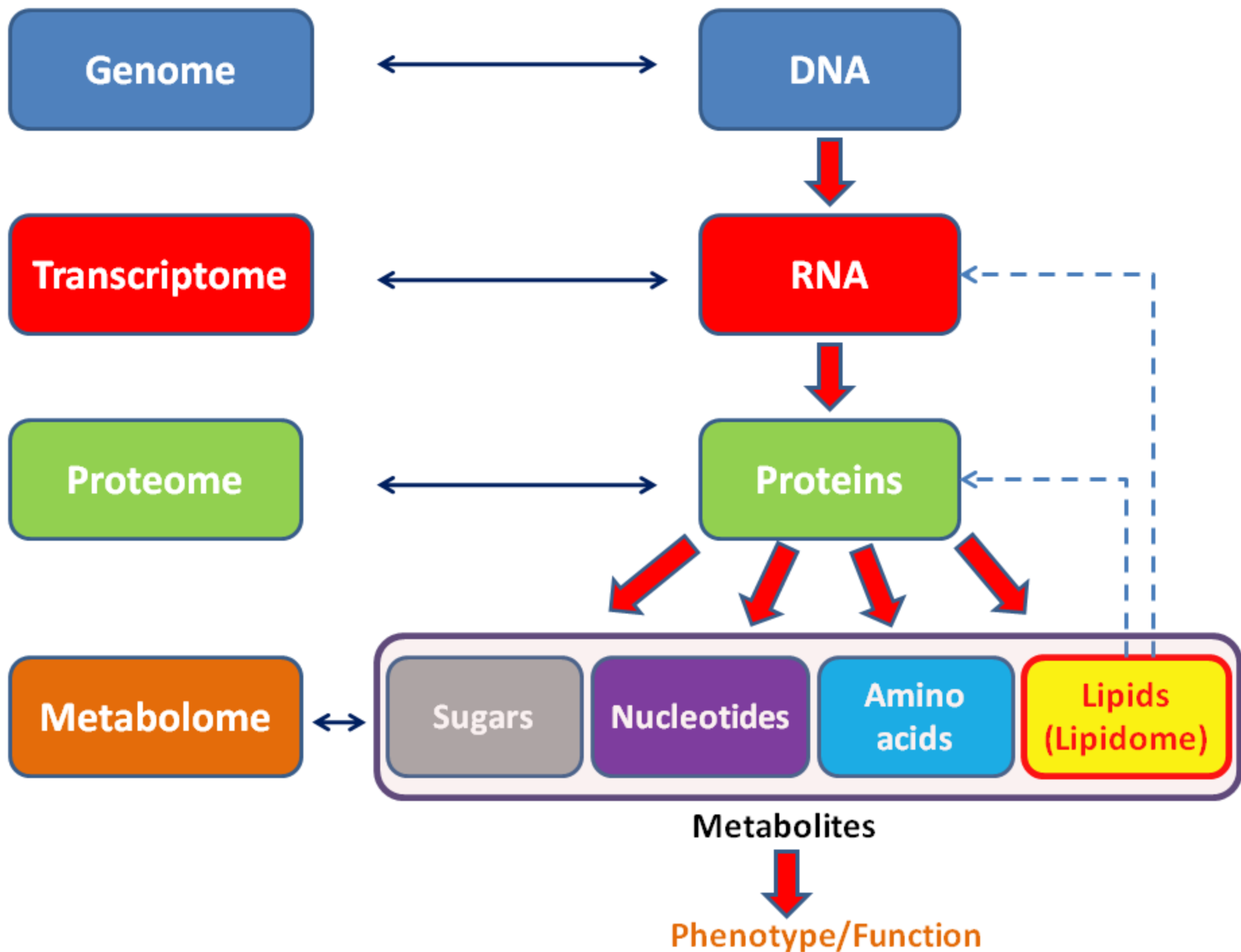
- Holistic view of the molecules that make up a cell, tissue or organism.
- They include the universal detection of **genes (genomics)**, **mRNA (transcriptomics)**, **proteins (proteomics)** and **metabolites (metabolomics)** in a specific biological sample in a non-targeted and non-biased manner.
- This can also be referred to as high-dimensional biology; the integration of these techniques is called **Systems Biology**

# Central Dogma of life

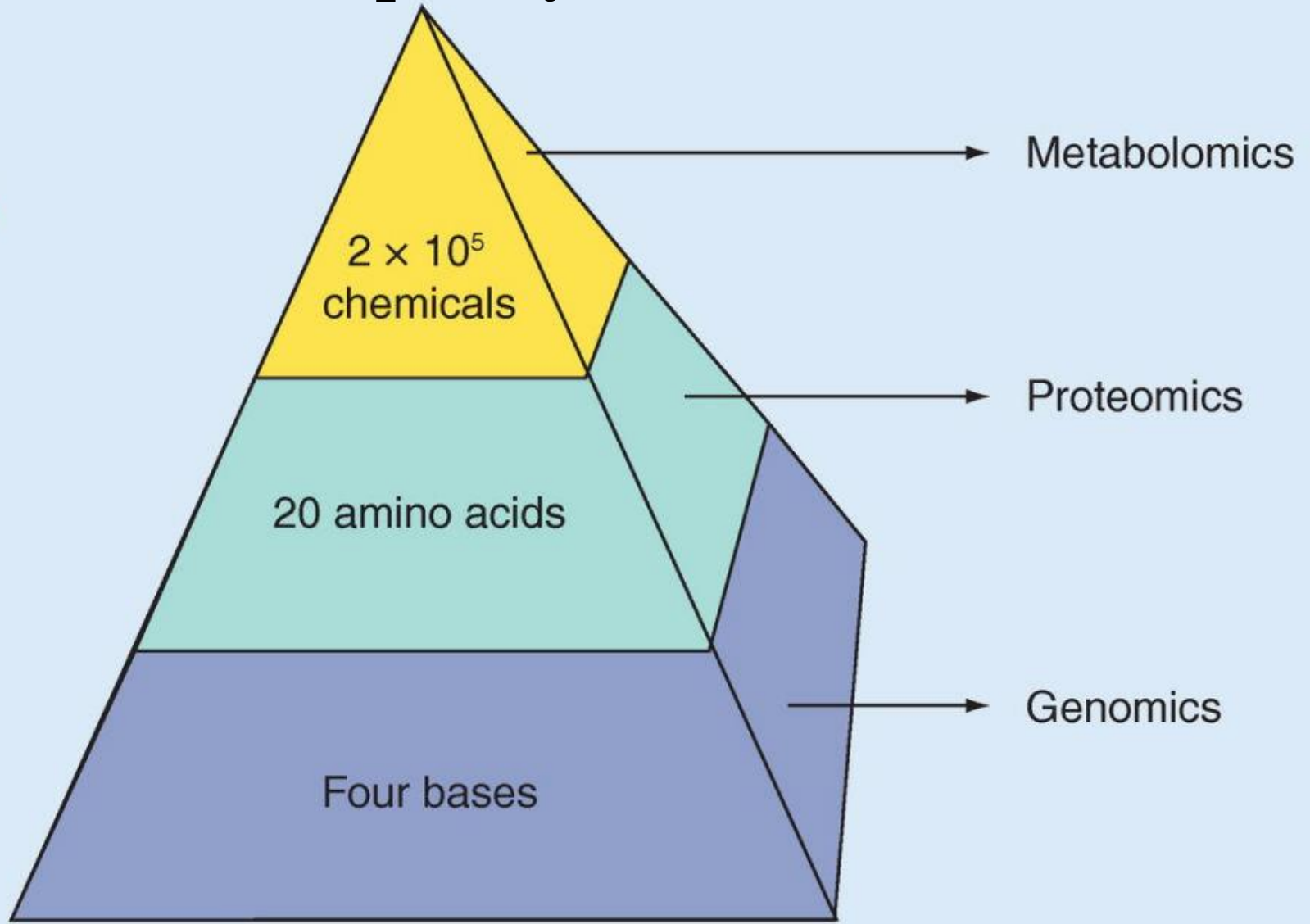








# Complexity level



# Genomics

- It is the systematic study of an organism's genome.
- The genome is the total DNA of a cell or organism.
- The human genome contains **3.2 billion bases**
- They can reveal **abnormalities** such as chromosomal **insertions** and **deletions** or **abnormal** chromosomal numbers in a process called **comparative genomic hybridisation**.

# Research area of Genomics

- **Functional genomics**

Describe gene (and protein) functions and interactions)

- **Structural genomics**

Describe the 3-dimensional structure of every protein encoded by a given genome).

- **Epigenomics**

Chemical changes to **DNA** and **histone** proteins of an organism that can be passed down to an offspring

- **Metagenomics**

Study of genetic material recovered directly from environment samples



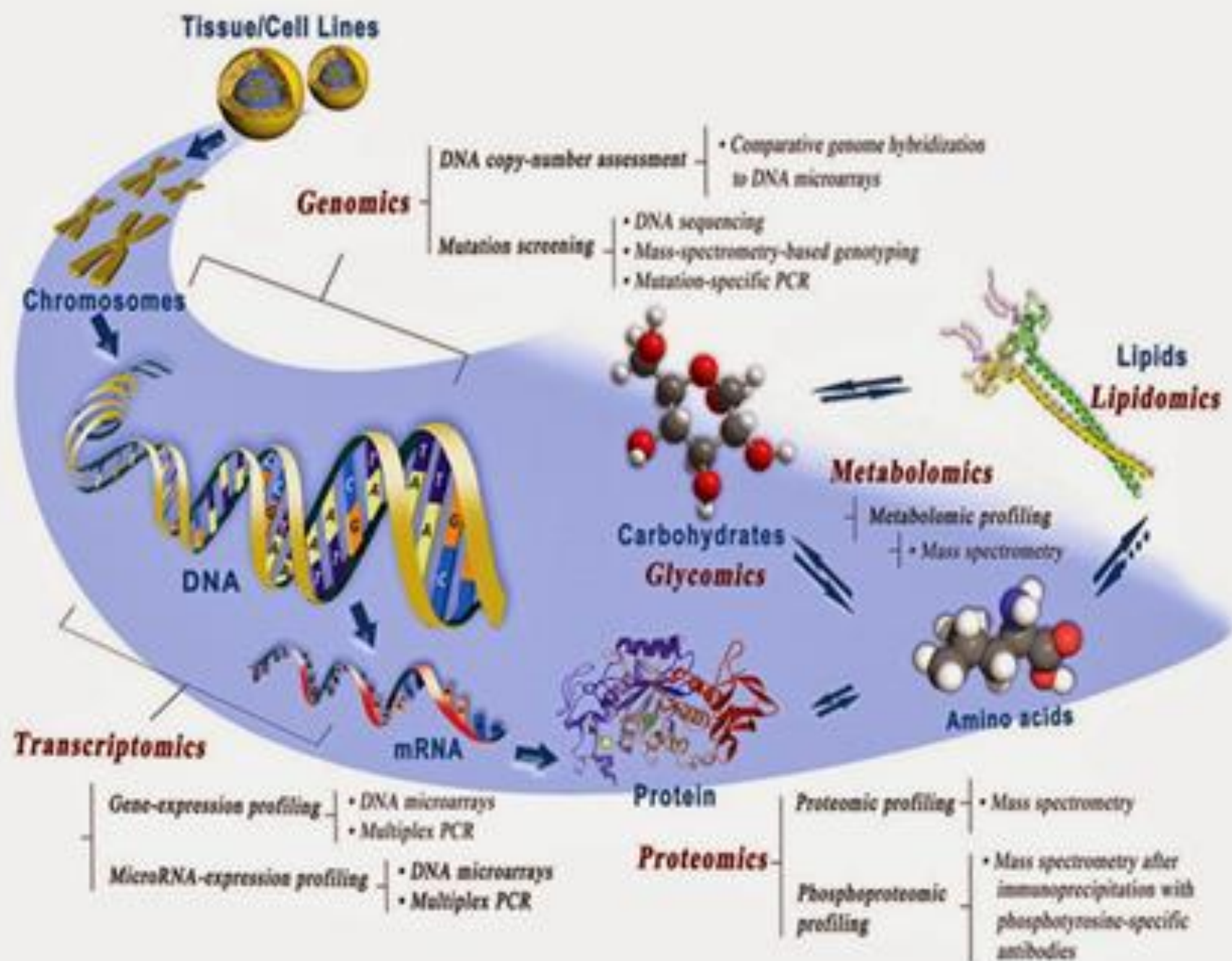
# Importance of Genomics for Human

- All humans have 99.9% identical genetic makeup.
- The remaining 0.1% may provide useful information about diseases.
- **Goal :**

To show why some people get sick from certain infections and environmental changes while others do not.



**Genetic Disorders**



# Transcriptomics

## **Specific gene expression**

Genes and signatures determined by particular genetic, epigenetic regulatory factors, environmental exposures

## **Exploratory approaches**

E.g global gene expression in tumors versus healthy tissues, differential responses to distinct environmental exposures

## **Disease etiology and classification**

Patterns/signatures rather than single markers can improve knowledge about etiology and diagnosis

International Agency for Research on Cancer



## **Biology**

- Development and Morphology (juveniles vs adults)
- Interactions between organisms (antagonistic, mutualistic)
- Interactions between organisms and their environments  
(temperature, radiation, draught, toxins and heavy metals)
- Evolution (within- and between species variation)
- Functional analyses (wild type vs mutant)

## **Medicine**

- Disease-associated expression patterns (diagnosis)
- Cell-cycle monitoring (cancer research)
- Treatment-induced expression pattern (drug development and response)

# Proteomics

- Set of all expressed proteins in a cell, tissue or organism.
- Proteomics aims to characterize information flow within the cell and the organism, through protein pathways and networks.
- The proteome is a dynamic reflection of both **genes** and the **environment** and is thought to hold special promise for **biomarker** discovery.



# Tumor markers

- **Diagnostic markers:** detection of malignant disease

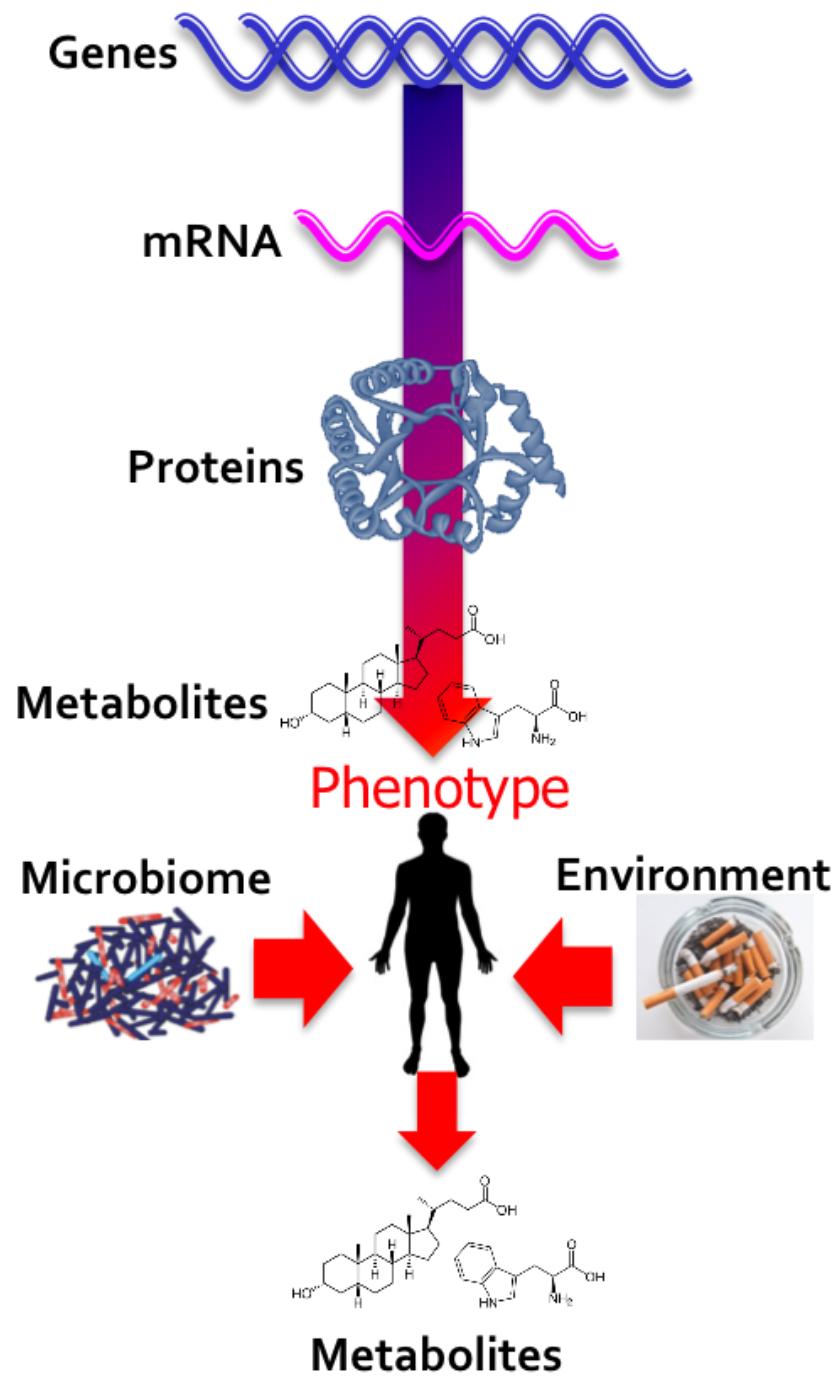
**Sensitivity =** detected positives / real positives

**Specificity =** detected negatives / real negatives

- **Prognostic markers:** malignant potential, disease recurrence
- **Predictive markers:** response to different therapies
- **Positioning markers:** positional information (e.g. for surgery)

# Metabolomics

- Study of global metabolite profiles in a system (cell, tissue or organism) under a given set of conditions.
- Additionally, as the downstream product, the metabolome is closest to the **phenotype** of the biological system studied.
- **Metabolom** is more **physically** and **chemically complex** than the other ‘omes’.



# Systems Biology

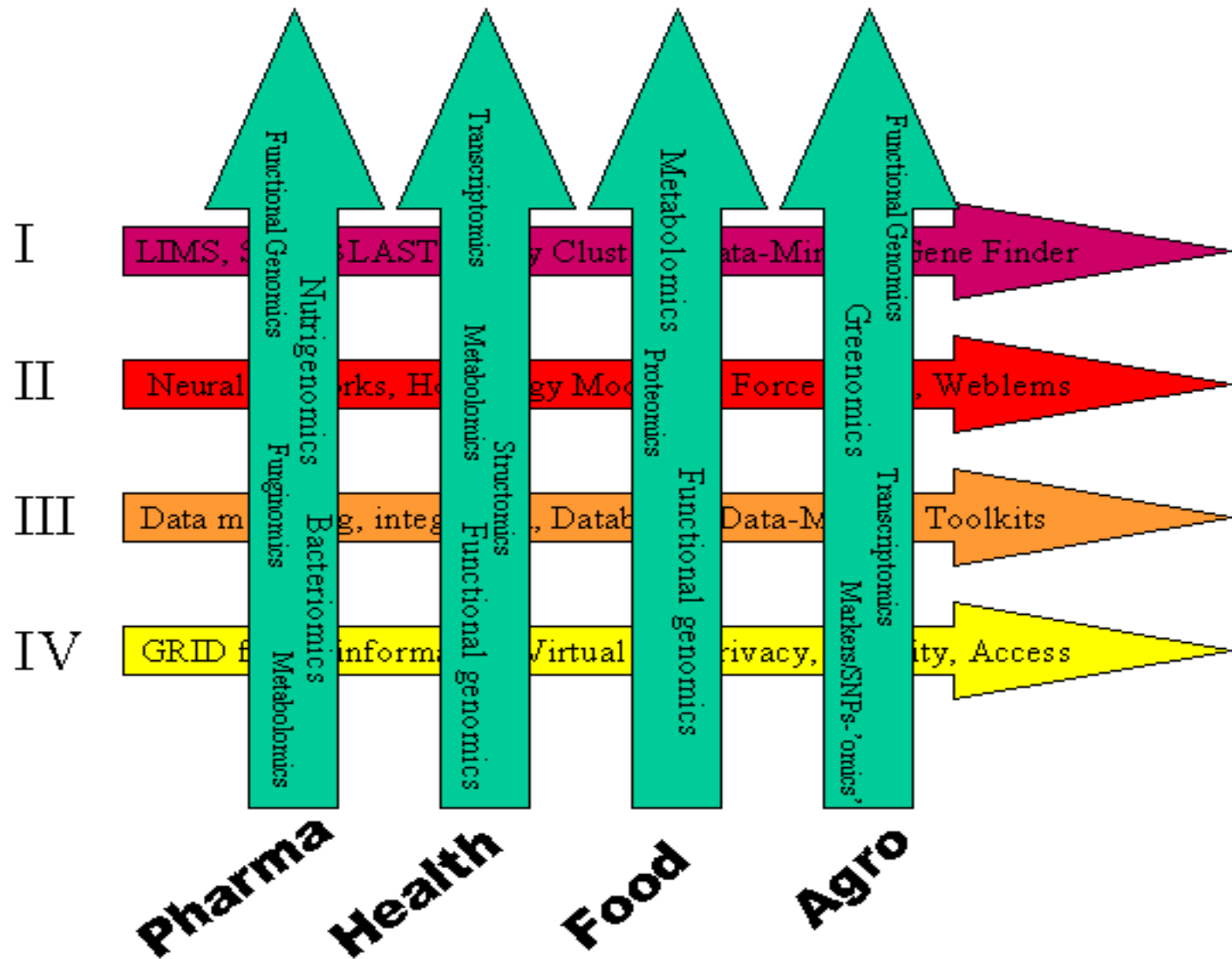
- Biological research focusing on the systematic study of complex interactions in biological systems using integration models.
- The ultimate aim is to understand whole systems, e.g. complex **cellular pathways**, by studying the effect of altered external factors on the **genome**, **transcriptome**, **proteome** and **metabolome** simultaneously

# Why Omics ?

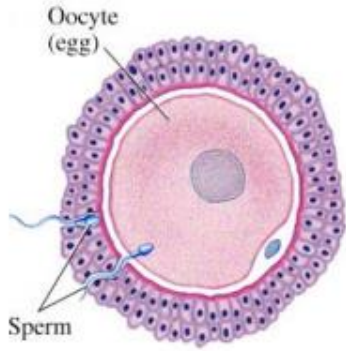
- The basic aspect of these approaches is that a **complex system** can be understood more thoroughly if considered as a whole.
- Omic technology can be applied not only for the greater understanding of **normal physiological** processes but also in disease processes where they play a role in **screening, diagnosis** and **prognosis** as well as aiding our understanding of the **aetiology** of diseases.



# Omics impact



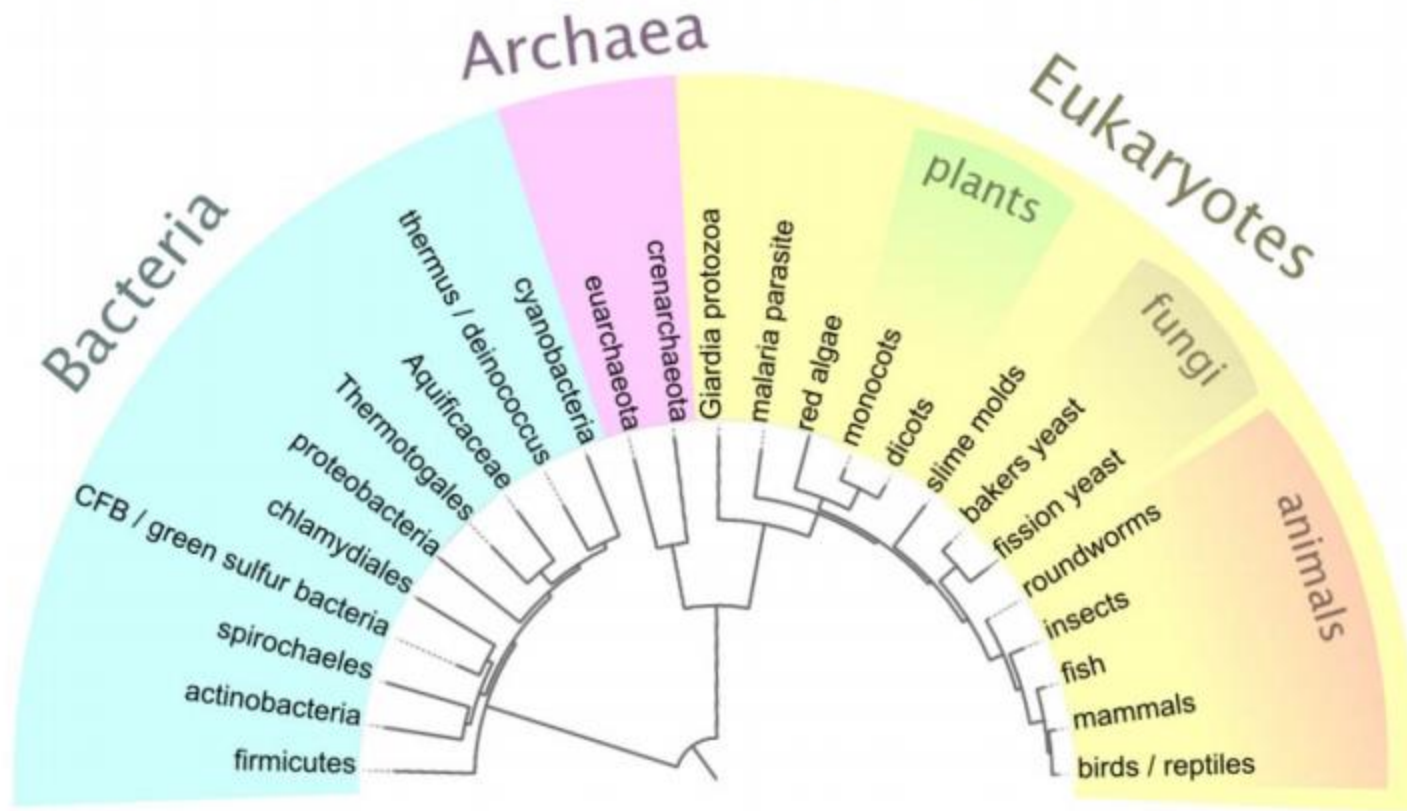
# The miracle of life





# The universal code: Other species' genomes

## The Tree of Life



[http://commons.wikimedia.org/wiki/File:Simplified\\_tree.png](http://commons.wikimedia.org/wiki/File:Simplified_tree.png)



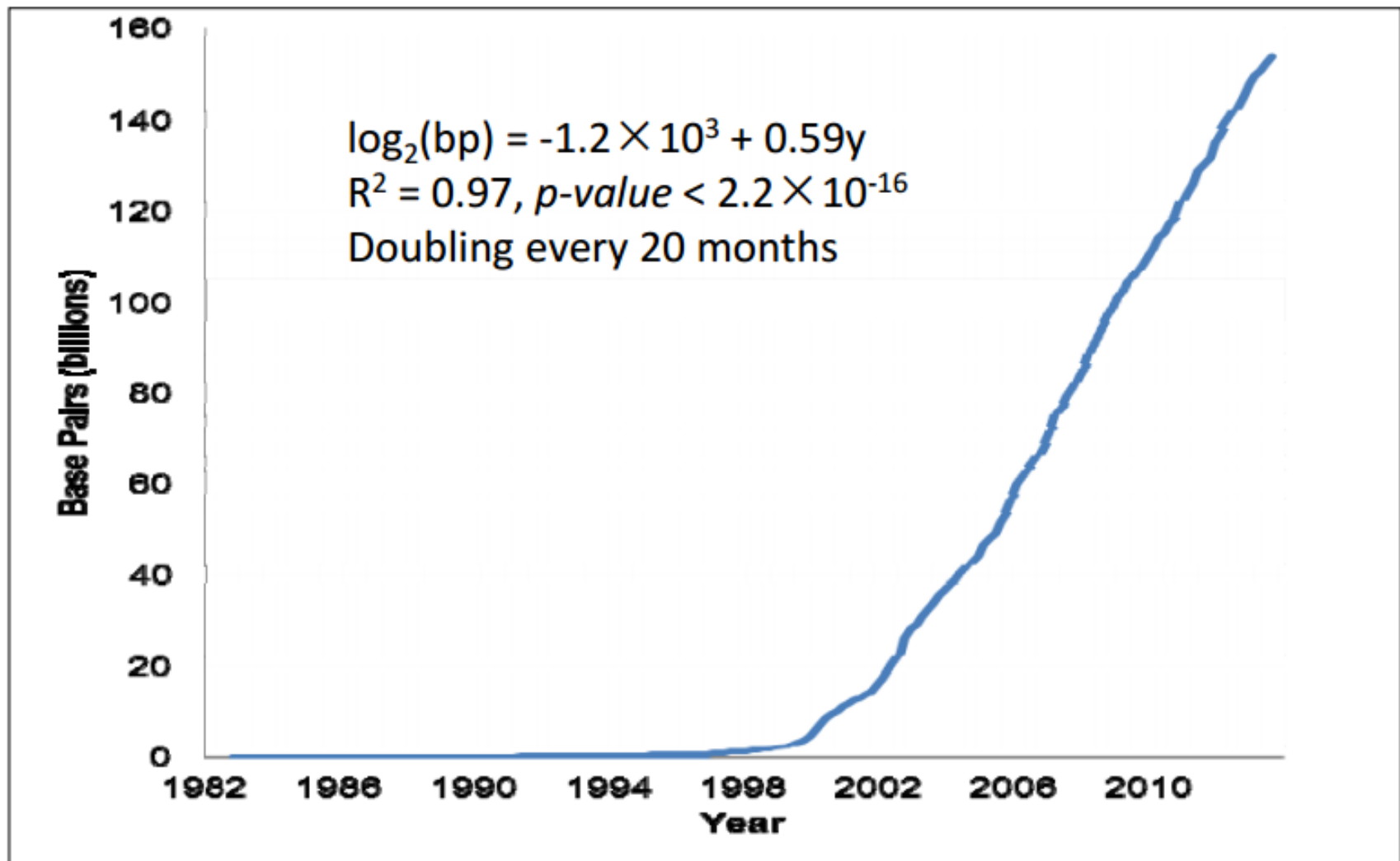
# Human genetic variation





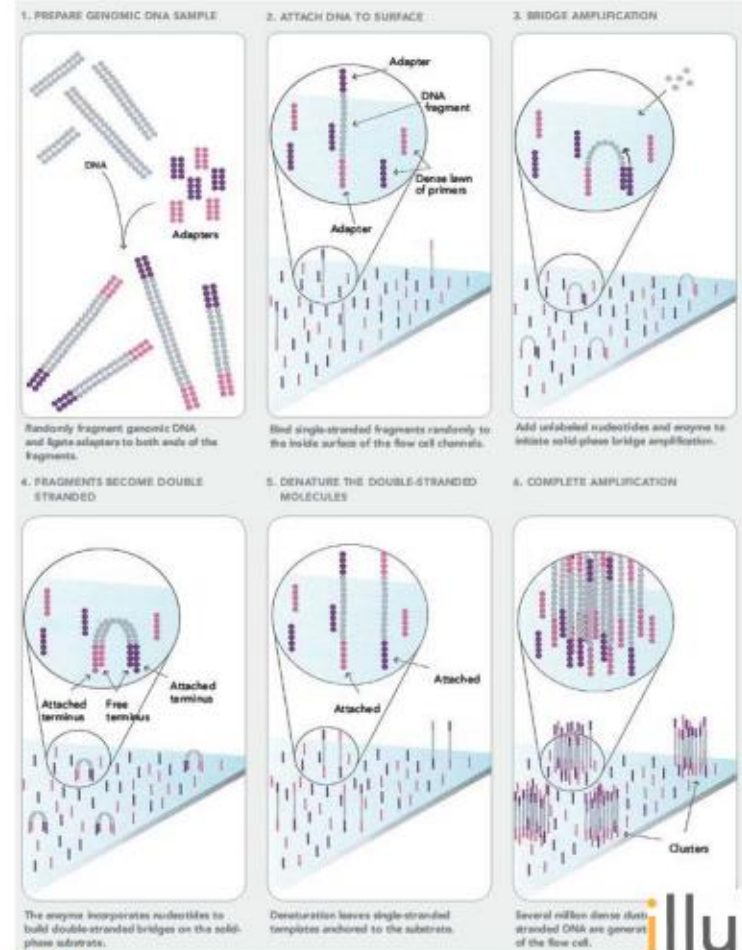


# Genbank growth



Data Source: <ftp://ftp.ncbi.nih.gov/genbank/gbrel.txt>

# Next-Generation Sequencing: Your genome, one day, \$3000!



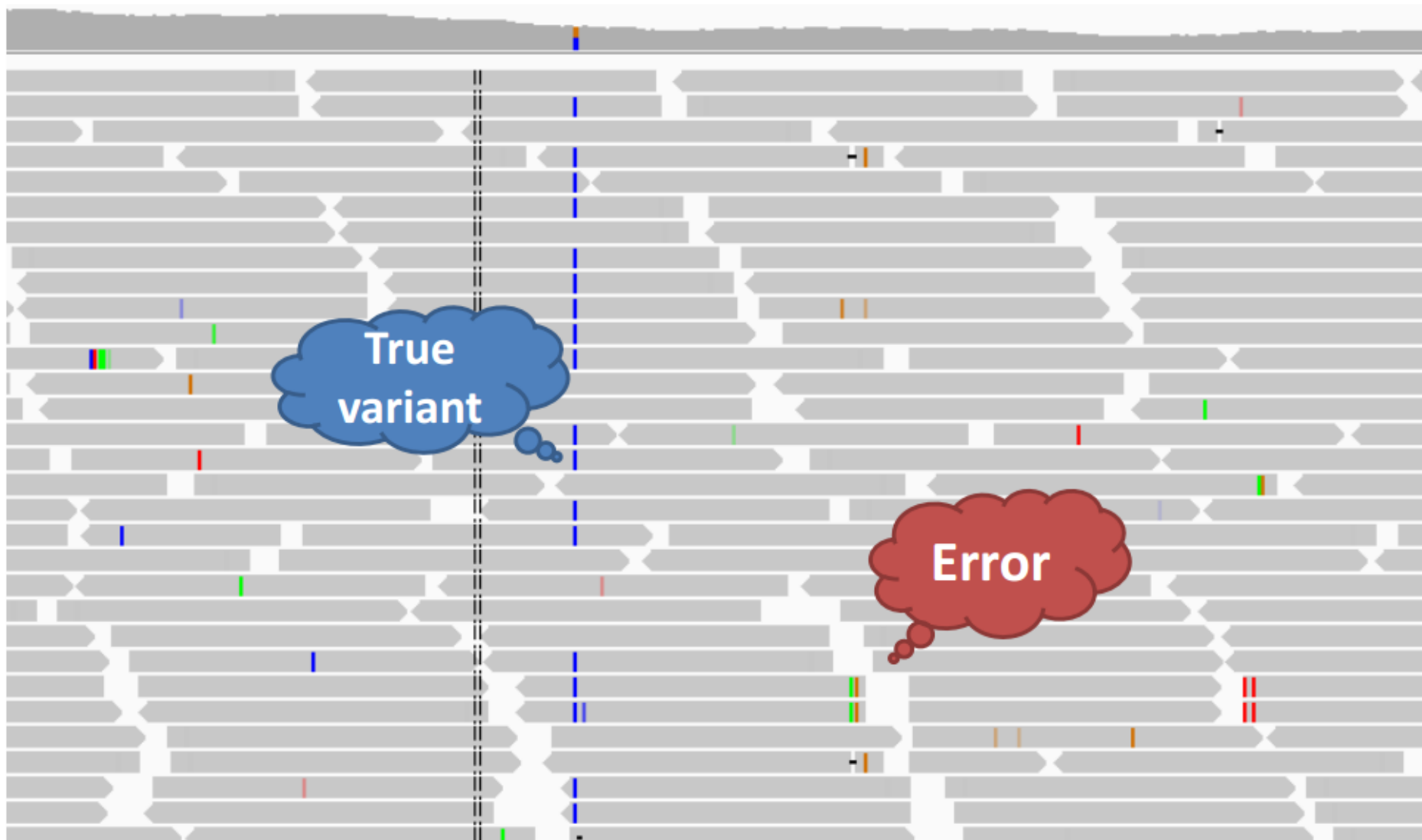
40 million clusters per flow cell

20 microns



Copyright © Peking University

illumina



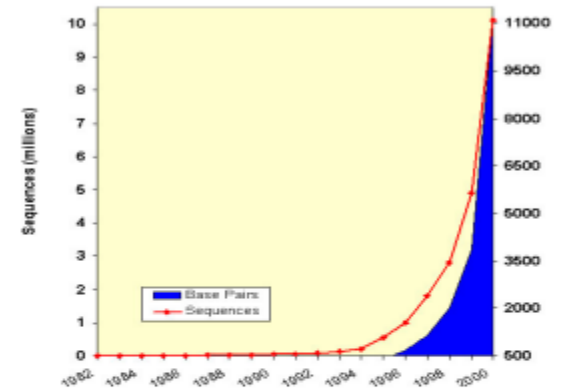
# Opportunities and challenges hand-in-hand: the driving forces of bioinformatics

## High-throughput data

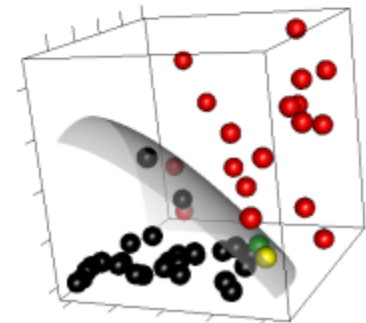
- Huge amount
- Explosive growth
- Low signal-to-noise ratio
- Multiple types

## Requirements for the methods

- Data needs to be stored in efficient **ontology-based database** systems
- The huge amount of data requires **efficient** algorithms
- Exponential growth requires **scalable** methods
- The low signal-to-noise ratio requires **accurate** methods
- Multiple types of data require data **integrative** methods



<ftp://ftp.ncbi.nih.gov/genbank/gbrel.txt>

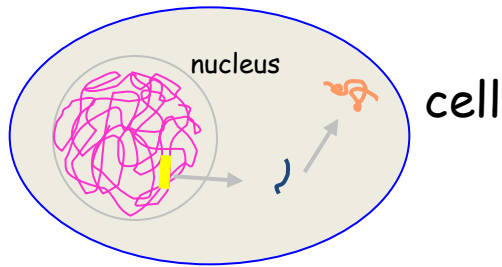


# Results in Paradigm shift in Life sciences

- Past experiments where hypothesis driven
  - Evaluate hypothesis
  - Complement existing knowledge
- Present experiments are data driven
  - Discover knowledge from large amounts of data



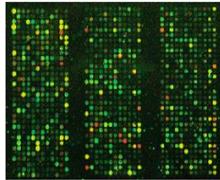
# Life sciences research: from gene to function



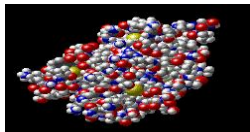
Whole-genome sequence projects



Genome-wide micro-array analysis



"High-throughput" protein-analysis



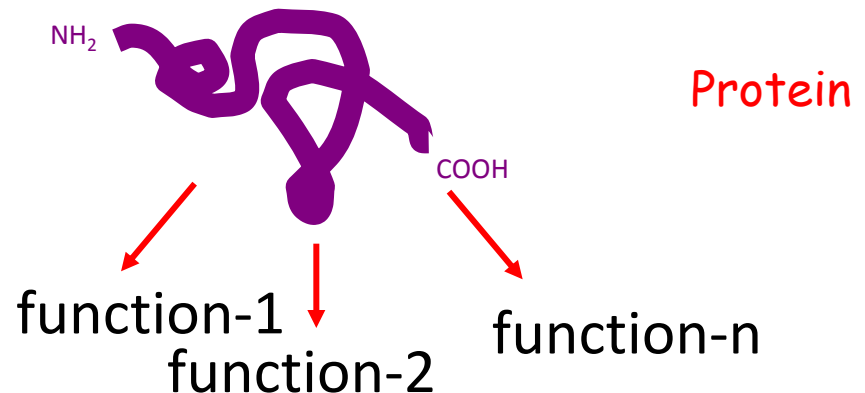
Protein function:  
-prediction by bioinformatics  
-proof by laboratory research



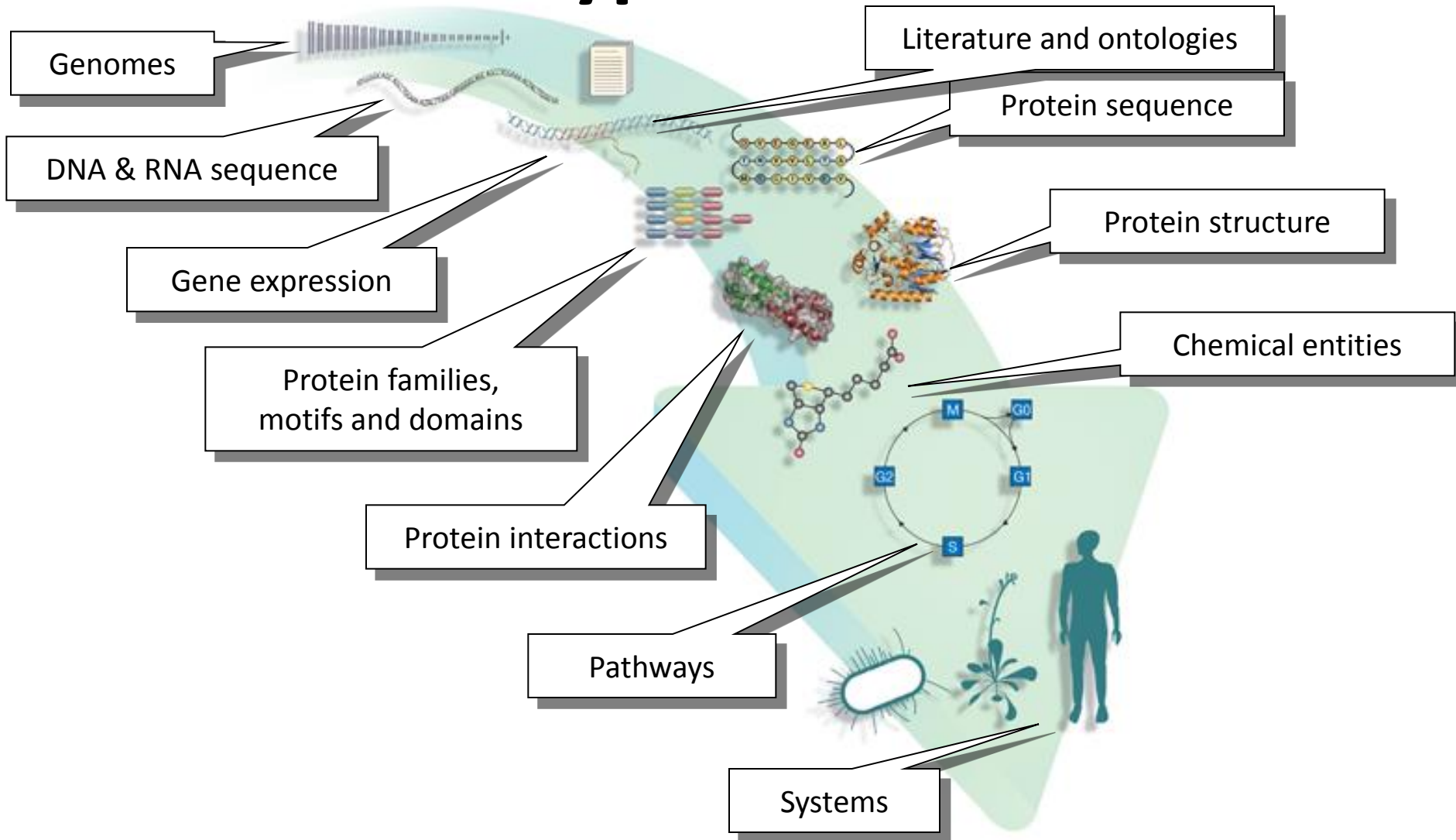
Gene expression by  
RNA synthesis



mRNA translation by  
protein synthesis

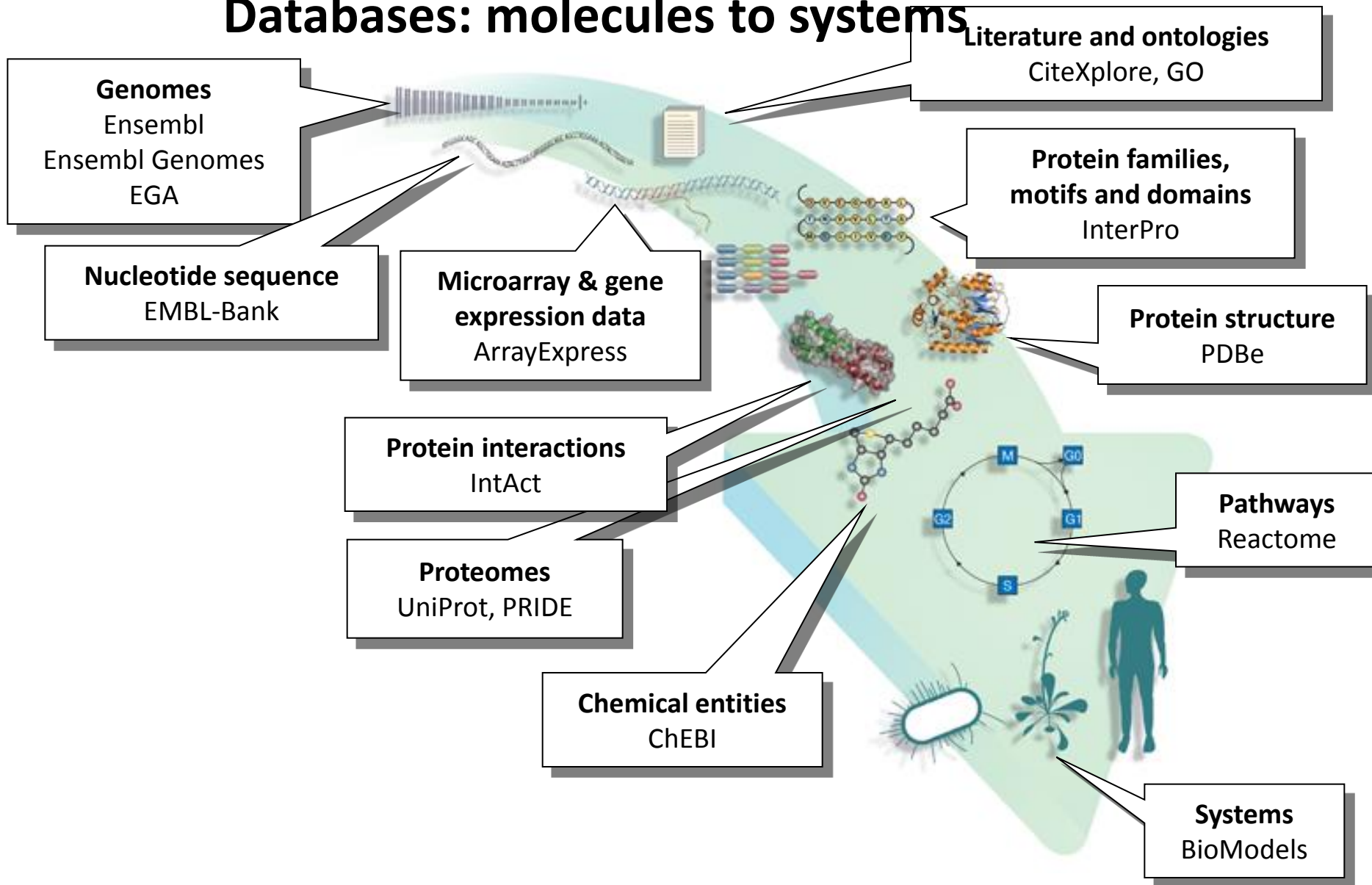


# New types of data





# Databases: molecules to systems

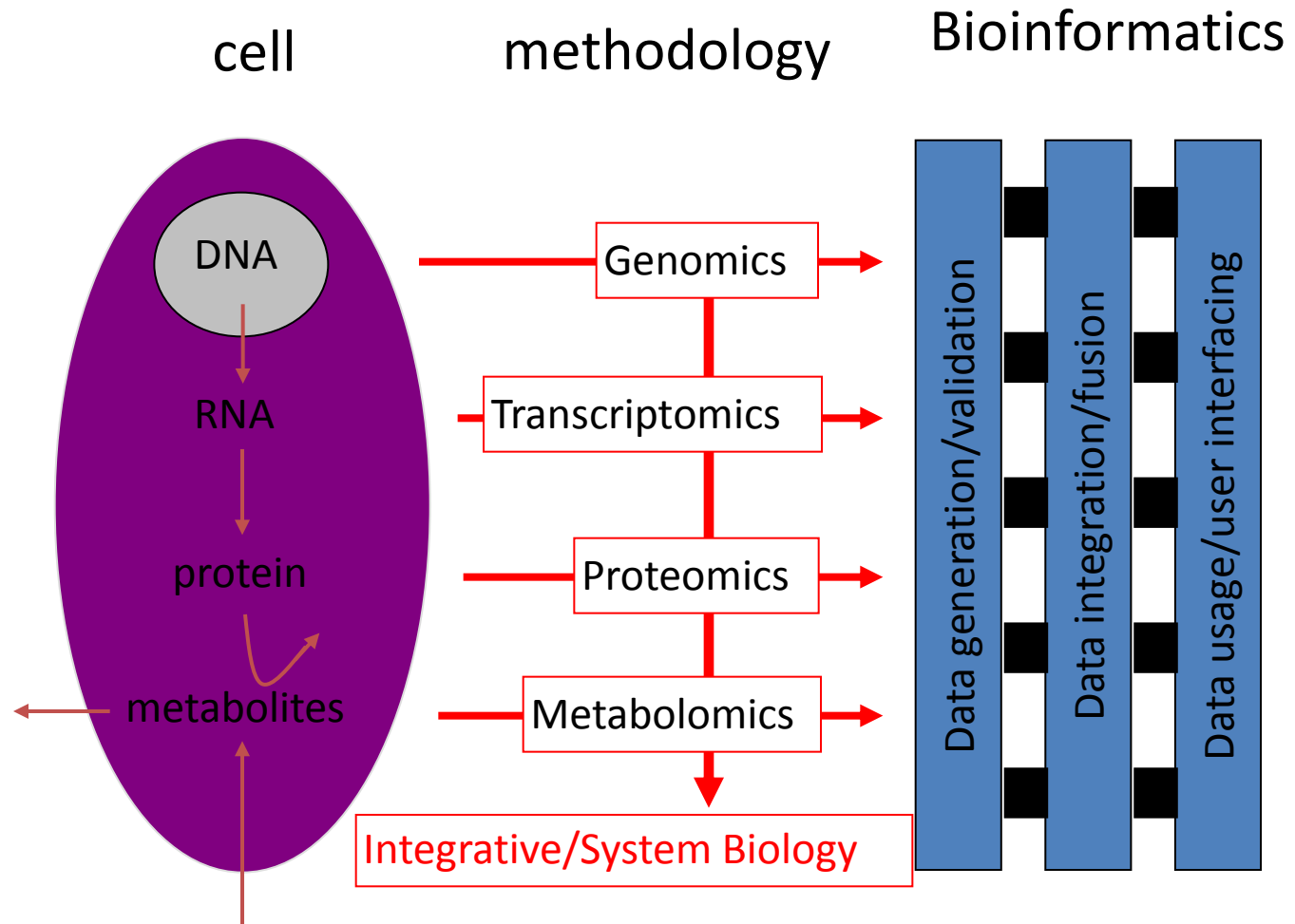


# Developments towards Bio-informatics & e-Science

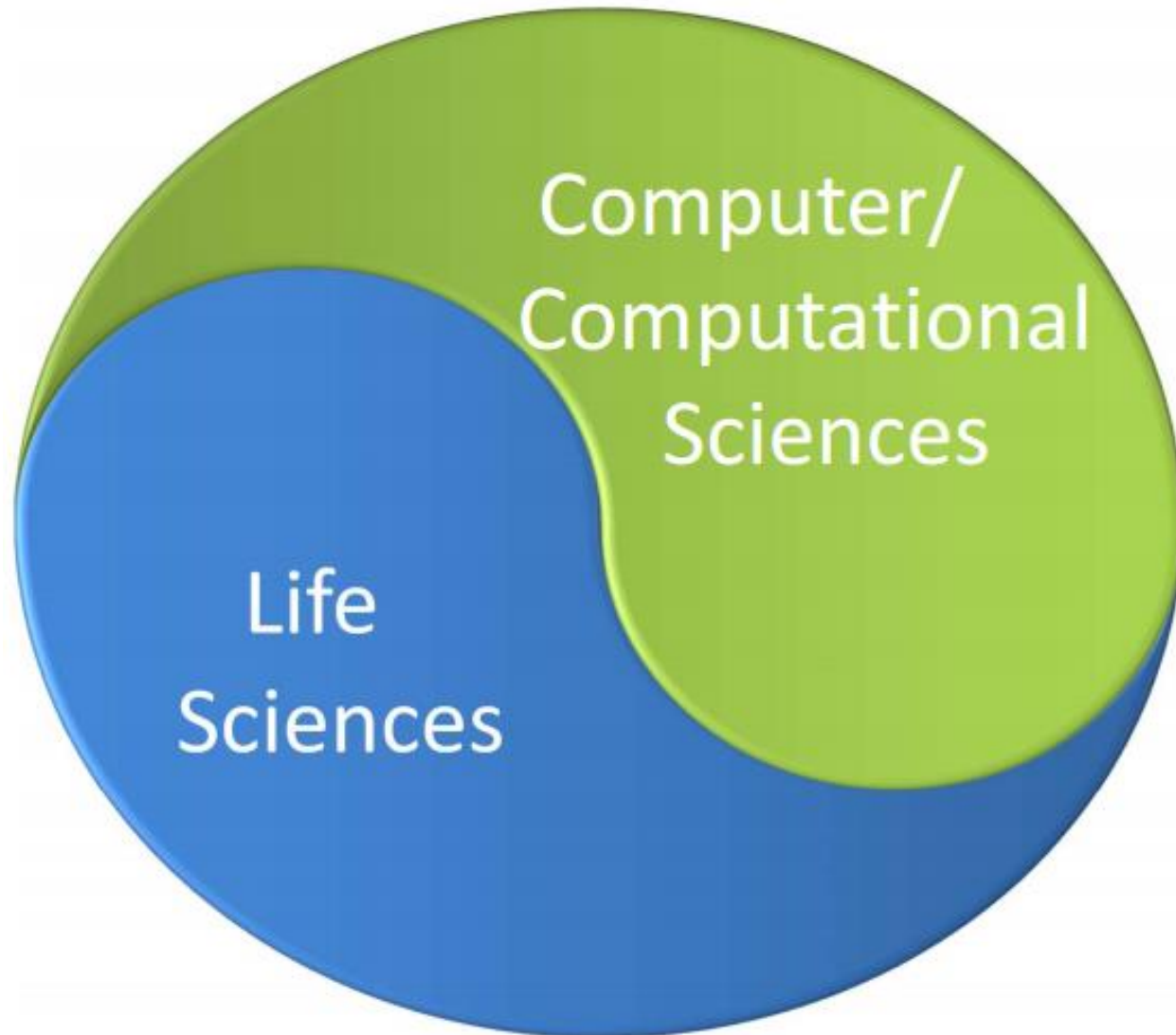
- Experiments become increasingly more complex
- Driven by increase of detector developments
- Results in an increase in **amount and complexity of data**
- Something has to be done to harness this development
  - **Bio-informatics** to translate data into useful biological, medical, pharmaceutical & agricultural knowledge



# Role of bioinformatics



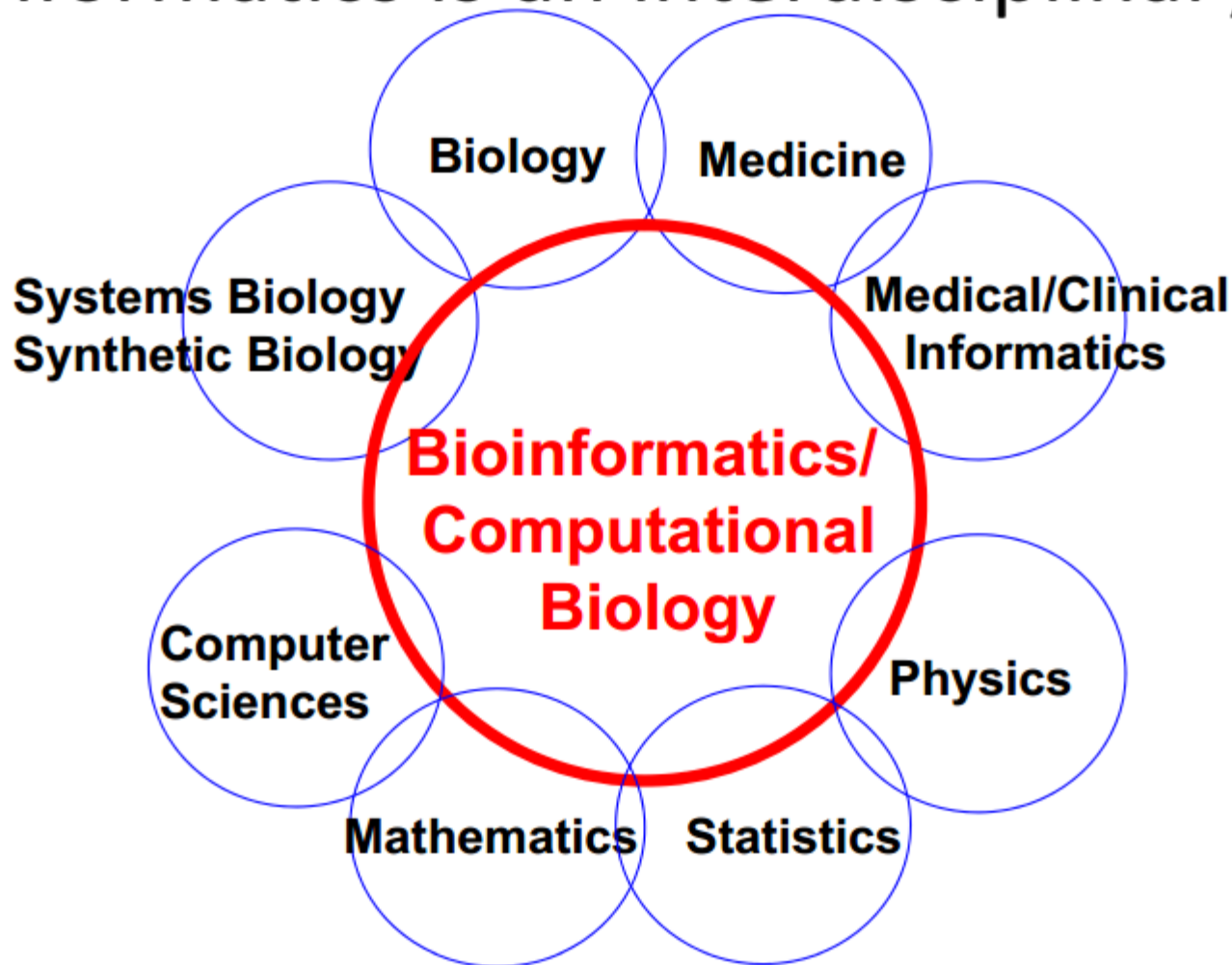
# Bioinformatics



## **Bioinformatics: an interdisciplinary field that develops and applies computer and computational technologies to study biomedical questions**





- As a technology, bioinformatics is a powerful technology to manage, query, and analyze big data in life sciences.
- As a methodology, bioinformatics is a top-down, holistic, data-driven, genome-wide, and systems approach that generates new hypotheses, finds new patterns, and discovers new functional elements.

# Bioinformatics is an interdisciplinary field



# The Bio- in Bioinformatics

**Genotype**  **Phenotype**

DNA/  
Genome  RNA  Proteins  Molecular  
Networks  Cells  Physiology/  
Disease

*Sequence alignment*  
*Database similarity search*  
*Motif finding*

*Gene finding*  
*Computational  
& comparative  
genomics*  
*Evolution*  
*DNA  
methylation*

*Differential  
expression*  
*Co-expression*  
*ncRNA*

*Mass spec protein  
identification*  
*Structure prediction*  
*Structure alignment*

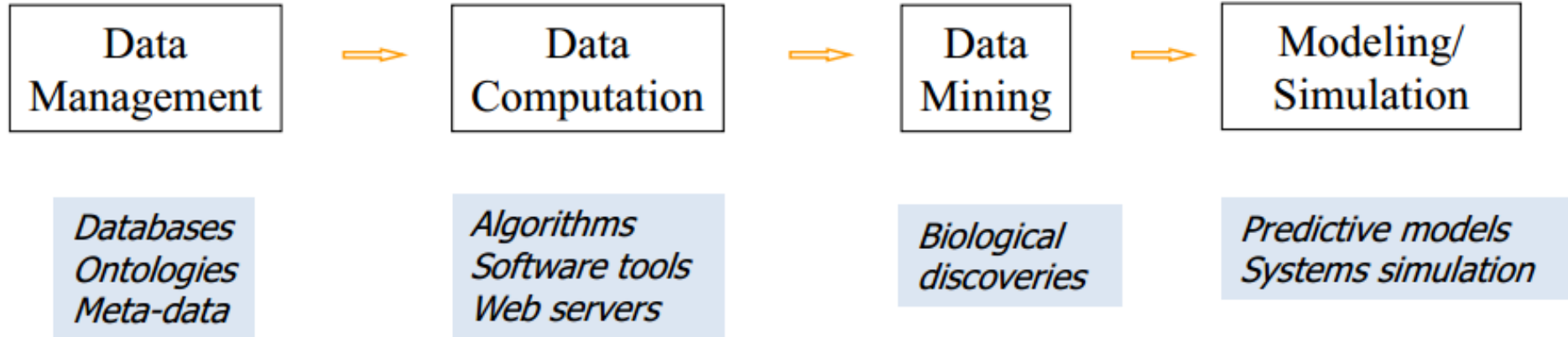
*Protein interaction  
networks*  
*Transcriptional  
regulation networks*  
*Metabolic and  
signaling networks*  
*Network dynamics*

*Virtual cell  
simulations*

*Population genetics*  
*Human genetics*

# The –informatics in Bioinformatics

**Data**  **Discovery**





# Genetic Research Deals with Inherited Traits

Genetic researchers study inherited traits by analyzing DNA sequences.



How are we similar?  
How are we different?

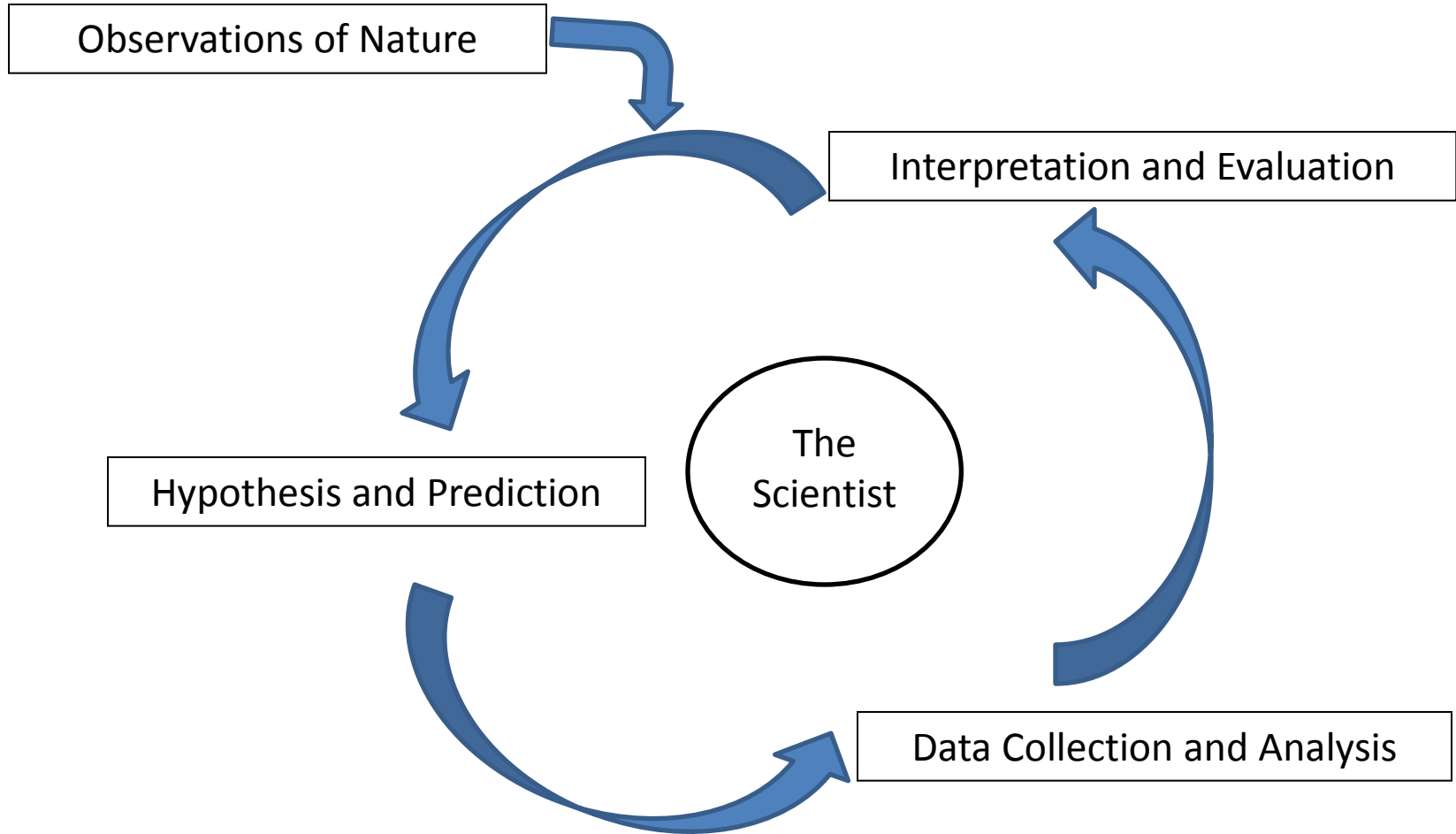
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ATGTTTCACCGACCGCTGATTATTCTCTACAAACCATA
ATGTTTCGCCGACCGCTGGCTATTCTCCACGAACCACA
ATGTTTCATAACTCGCTGATTATTCTCAACCAACCATA
.....GGTTATTCTCTACAAACCACA
ATGCTCATTAAATCGCTGACTCTTTTCAACAAATCACA
```

Use bioinformatics to  
research differences in DNA  
sequences.



DNA isolation.

# The Practices of Scientific Research



# ***What is Bioinformatics?***

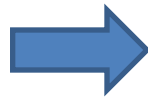
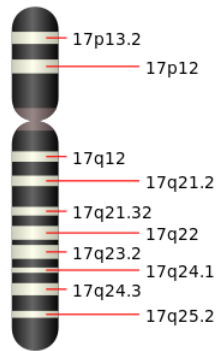
Bioinformatics is the application of computer science and information technology to biology and medicine.

Bioinformatics makes it possible to analyze large quantities of complex biological data and can be used to ***search biological databases, compare sequences, and draw molecular structures.***

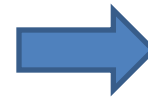
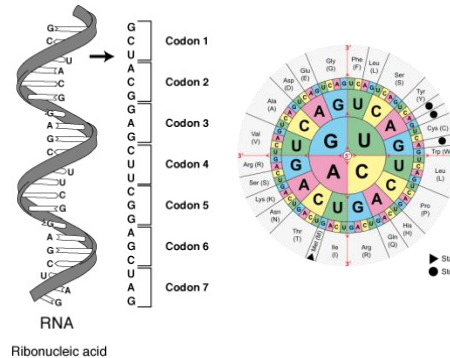
# Bioinformatics Tools Help Scientists:

Organize, Process, and Make Sense of Complex Biological Data Sets

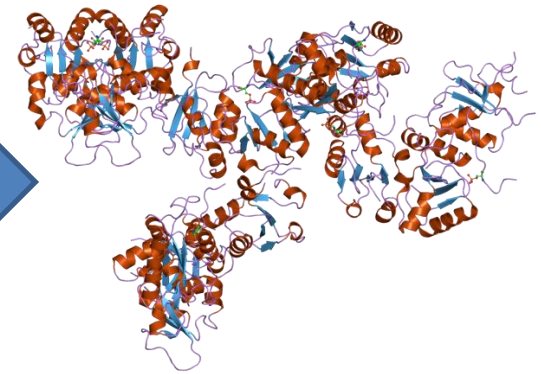
## DNA



## RNA



## Protein



*Bioinformatics Tools:*

DNA Sequencing  
Identify Mutations in  
DNA.

*Bioinformatics Tools:*

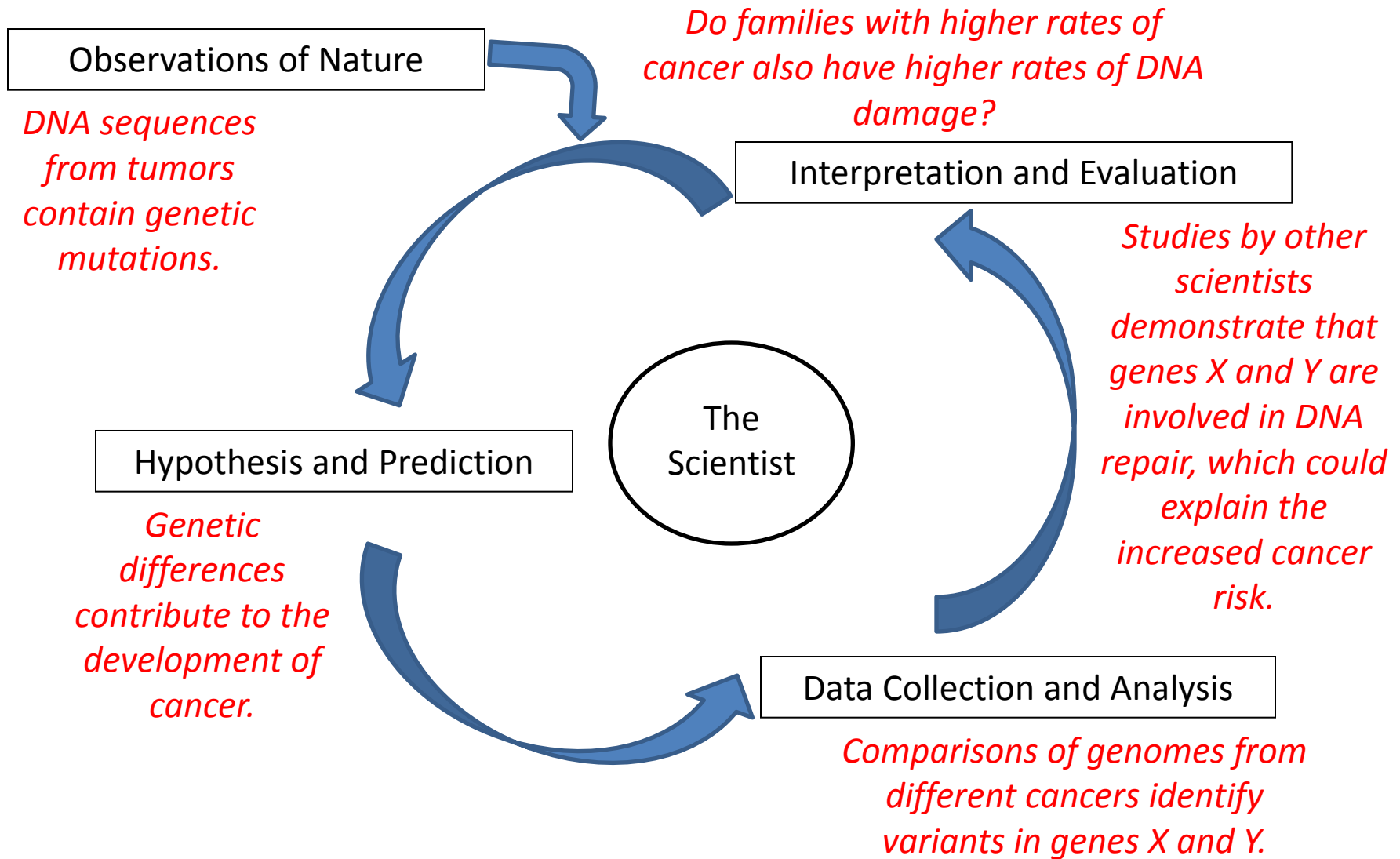
RNA Sequencing  
Identify tissue specific  
gene expression.

*Bioinformatics Tools:*

Protein 3D Structure  
visualization.

***Question: What kinds of scientific questions can we answer with bioinformatics tools?***

# The Practices of Scientific Research



# Inside the Gene Machine:

## How Information from DNA is Acquired and Used for Genetic Testing

**Patient Sample: Blood or Saliva.**



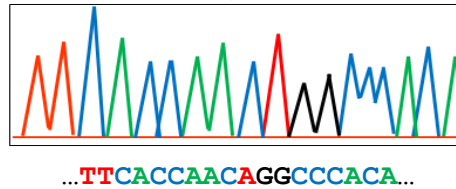
*Genetic Counselors* work with patients to help them decide whether or not to have a genetic test, and help them understand the results of the test.

**Extract DNA from Cells.**



*Lab Technicians* work with patient samples in the lab, purifying and sequencing the DNA.

**Sequence DNA.**



*Bioinformatics programmers* create computer programs to help biologists analyze data.

**Compare Patient DNA Sequence to Reference Sequence.**

Reference	...TTCACCAAC	ATG	CCCACA...
	F	T	N M P T
Patient	...TTCACCAAC	AGG	CCCACA...
	F	T	N R P T

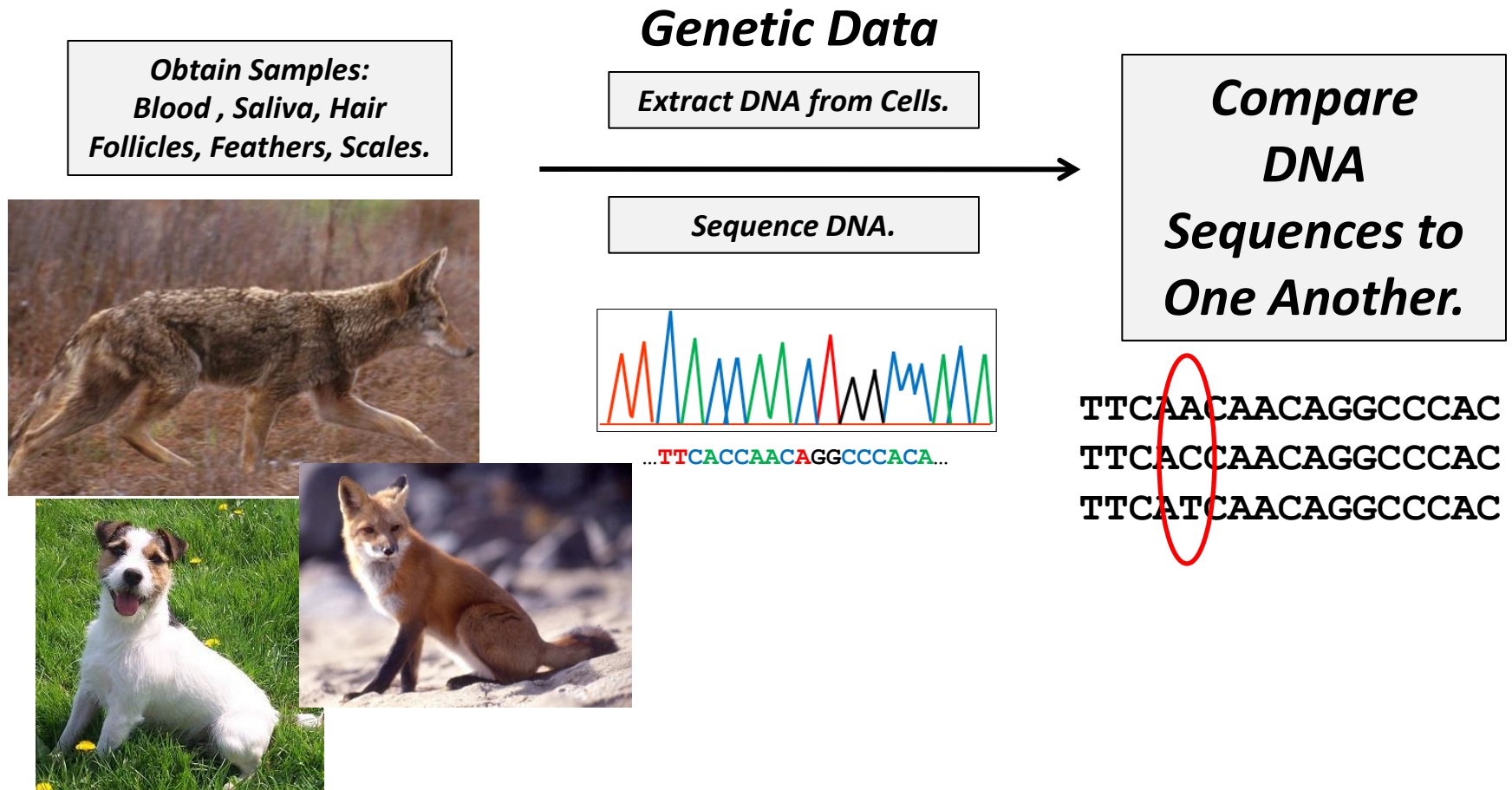
*Biomedical Researchers* perform experiments with patient samples to find different variations of genes that might cause disease. Bioinformatics tools like **BLAST** and **ClustalW** are used to compare sequences.

**Search Database to Determine if Patient Mutation is Associated with Disease.**



*Medical Doctors* and *Veterinarians* use the knowledge gained from genetic testing to care for their patients.

# How DNA Sequence Data is Obtained for Genetic Research





# ***Which Animals are Most Closely Related to One Another?***



Jack Russell



Labradoodle



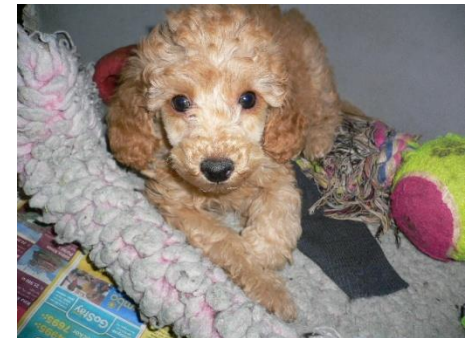
English Shepherd



Red fox



Coyote



Toy Poodle



Cocker Spaniel



# Multiple Sequence Alignment of Canine DNA Sequences

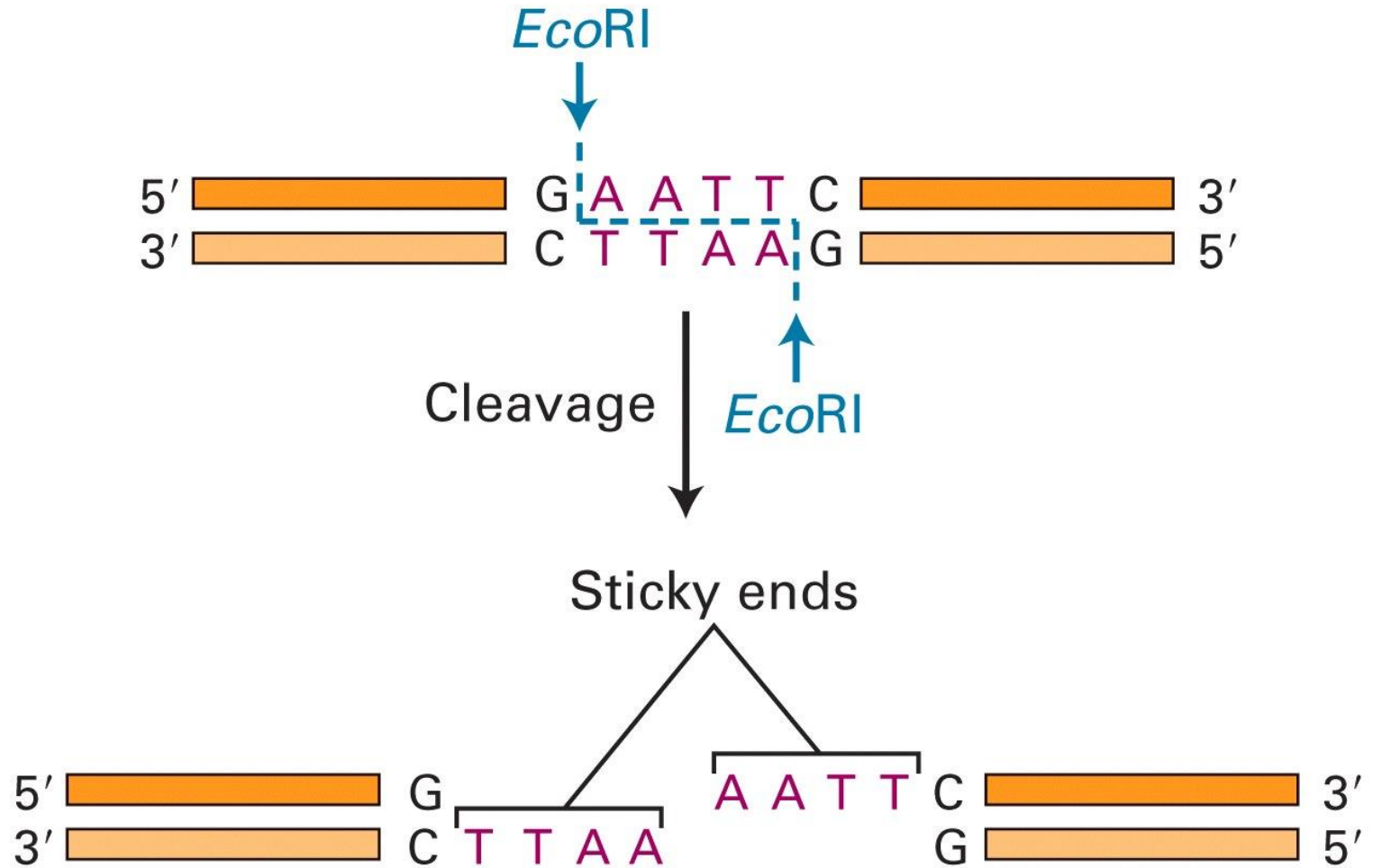
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<i>RedFox/1-880</i>	302	TTCCTCCATCCTTTCTTCTACTATTAGCATCTTCCATAGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATATCC	377
<i>Coyote/1-883</i>	305	TTCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGGACTGTATATCC	380
<i>Labradoodle/1-883</i>	305	TTCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
<i>JackRussell/1-883</i>	305	TTCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
<i>CockerSpaniel/1-883</i>	305	TTCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
<i>EnglishShepherd/1-883</i>	305	TTCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
<i>ToyPoodle/1-883</i>	305	TTCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
<i>GreyWolf/1-883</i>	381	CCCAGTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTTCTCCTTACACTTAGCCGGAGTC	456
<i>RedFox/1-880</i>	378	CCCATTAGCTGGTAACCTGGCTCATGCTGGAGCATCAGTGGACCTTACAATTTTCTCCTGACCTGGCCGGAGTC	453
<i>Coyote/1-883</i>	381	TCCAGTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGATCTTACAATTTTCTCCTTACATCTAGCTGGAGTC	456
<i>Labradoodle/1-883</i>	381	CCCAGTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTTCTCCTTACACTTAGCCGGAGTC	456
<i>JackRussell/1-883</i>	381	CCCAGTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTTCTCCTTACACTTAGCCGGAGTC	456
<i>CockerSpaniel/1-883</i>	381	CCCAGTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTTCTCCTTACACTTAGCCGGAGTC	456
<i>EnglishShepherd/1-883</i>	381	CCCAGTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTTCTCCTTACACTTAGCCGGAGTC	456
<i>ToyPoodle/1-883</i>	381	CCCAGTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTTCTCCTTACACTTAGCCGGAGTC	456
<i>GreyWolf/1-883</i>	457	TCTTCTATTTTAGGGGCAATTAATTTTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCAGTATCAAA	532
<i>RedFox/1-880</i>	454	TCTTCAATTTTAGGAGCTATTAATTTTCATCACTACTATTATCAATATAAAACCTCCCGCCATATCCCAATACCAA	529
<i>Coyote/1-883</i>	457	TCTTCTATTTTAGGGGCAATCAATTTTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCAGTATCAAA	532
<i>Labradoodle/1-883</i>	457	TCTTCTATTTTAGGGGCAATTAATTTTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCAGTATCAAA	532
<i>JackRussell/1-883</i>	457	TCTTCTATTTTAGGGGCAATTAATTTTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCAGTATCAAA	532
<i>CockerSpaniel/1-883</i>	457	TCTTCTATTTTAGGGGCAATTAATTTTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCAGTATCAAA	532
<i>EnglishShepherd/1-883</i>	457	TCTTCTATTTTAGGGGCAATTAATTTTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCAGTATCAAA	532
<i>ToyPoodle/1-883</i>	457	TCTTCTATTTTAGGGGCAATTAATTTTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCAGTATCAAA	532

# Color Coding Reveals Differences

GreyWolf/1-883	305	TTCCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
RedFox/1-880	302	TTCCCTCCATCCTTTCTTCTACTATTAGCATCTTCTCATAGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATATCC	377
Coyote/1-883	305	TTCCCTCCATCTTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGGACTGTATATCC	380
Labradoodle/1-883	305	TTCCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
JackRussell/1-883	305	TTCCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
CockerSpaniel/1-883	305	TTCCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
EnglishShepherd/1-883	305	TTCCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
ToyPoodle/1-883	305	TTCCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGTGCAGGAACGGGATGAACCGTATACCC	380
GreyWolf/1-883	381	CCCACCTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTCTCCTTACACTTAGCCGGAGTC	456
RedFox/1-880	378	CCCATTAGCTGGTAACCTGGCTTCATGCTGGAGCATCAGTGACCTTACAATTTCTCCTTACACTTAGCCGGAGTC	453
Coyote/1-883	381	TCCACTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGATCTTACAATTTCTCCTTACACTTAGCTGGAGTC	456
Labradoodle/1-883	381	CCCACCTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTCTCCTTACACTTAGCCGGAGTC	456
JackRussell/1-883	381	CCCACCTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTCTCCTTACACTTAGCCGGAGTC	456
CockerSpaniel/1-883	381	CCCACCTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTCTCCTTACACTTAGCCGGAGTC	456
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ToyPoodle/1-883	381	CCCACCTGGCTGGCAATCTGGCCCATGCAGGAGCATCCGTTGACCTTACAATTTCTCCTTACACTTAGCCGGAGTC	456
GreyWolf/1-883	457	TCTTCTATTTTAGGGGCAATTAATTTTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCAGTATCAAA	532
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ToyPoodle/1-883	457	TCTTCTATTTTAGGGGCAATTAATTTTCATCACTACTATTATCAACATAAAACCCCTGCAATATCCAGTATCAAA	532

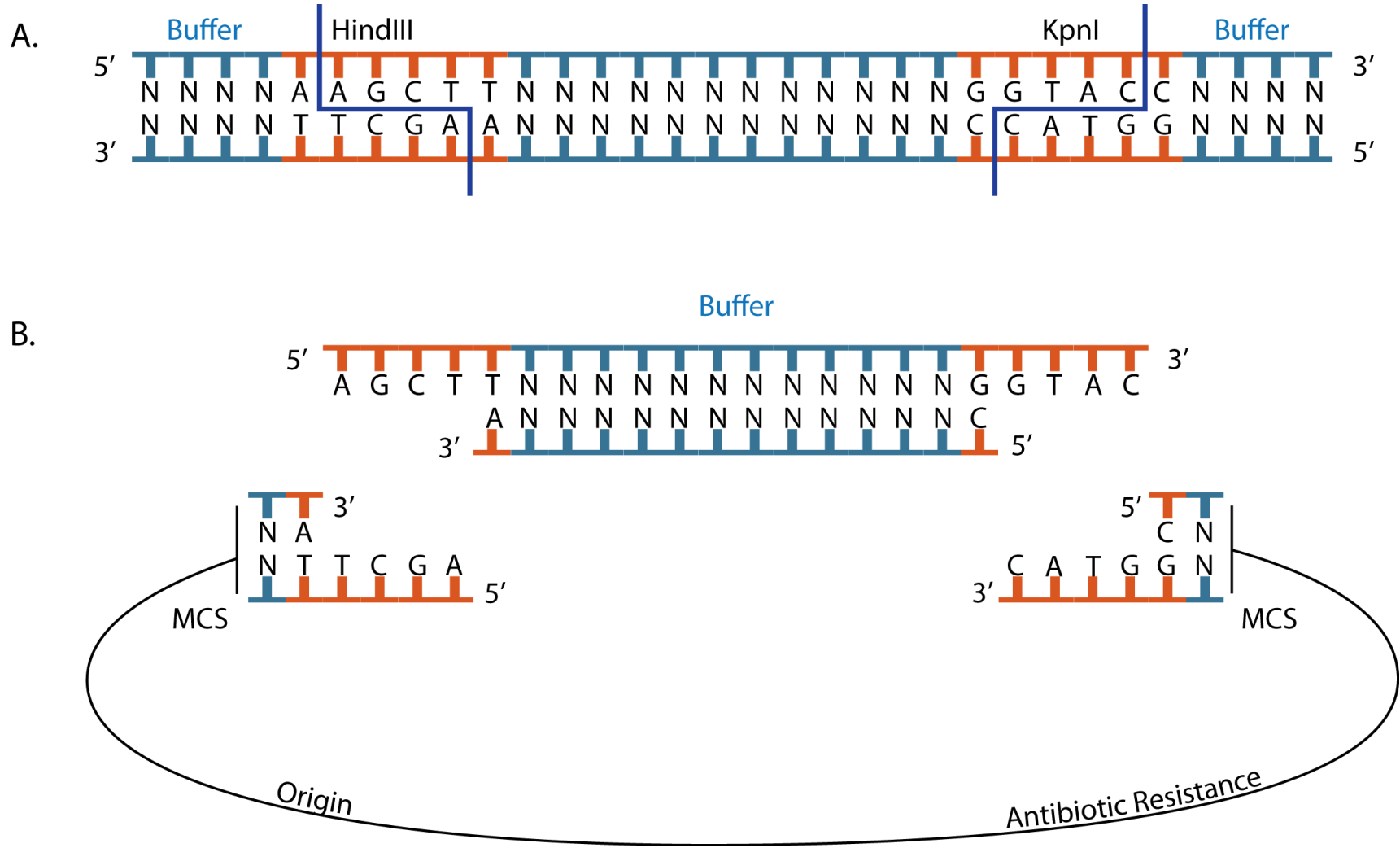
# Application of Bioinformatics

- Retrieving DNA sequences from databases .
- Identifying restriction sites.
- Designing polymerase chain-reaction (PCR) primers.
- Identifying open reading frames (ORFs).
- Predicting elements of DNA/RNA secondary structure .
- Finding repeats.
- Computing the optimal alignment between two or more DNA sequences
- Finding polymorphic sites in genes (single nucleotide polymorphisms, SNPs)
- Assembling sequence fragments
- Finding orthologous and paralogous genes.

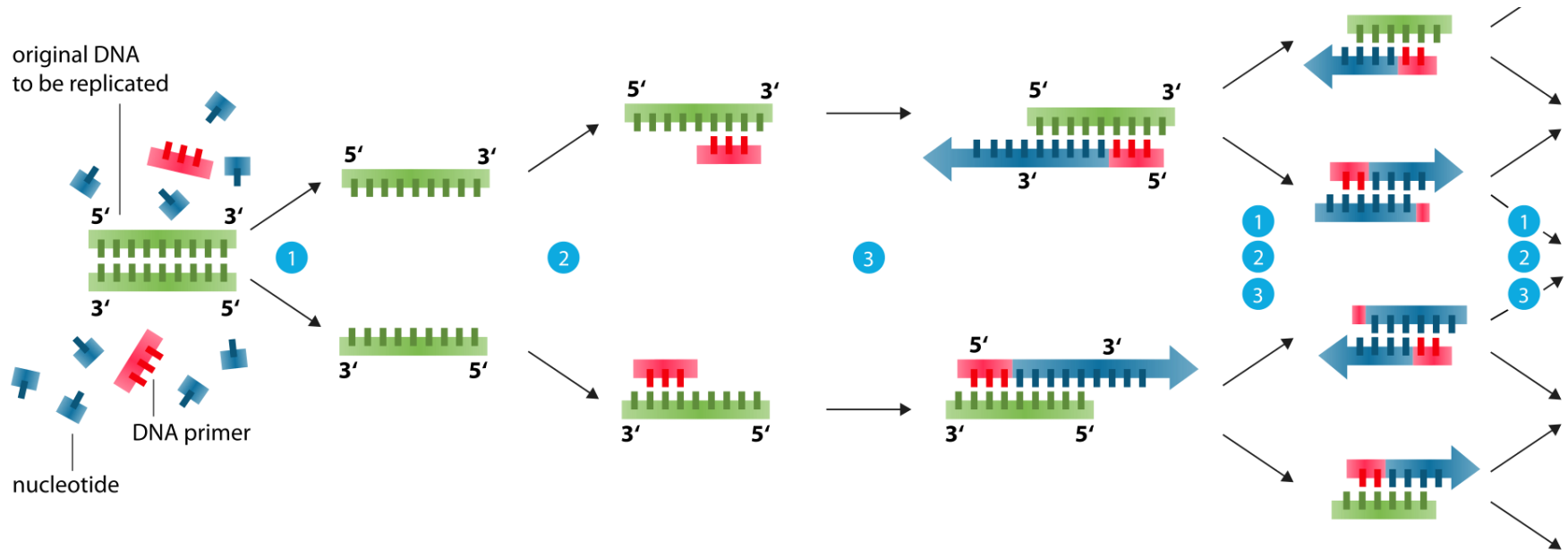




# Restriction sites

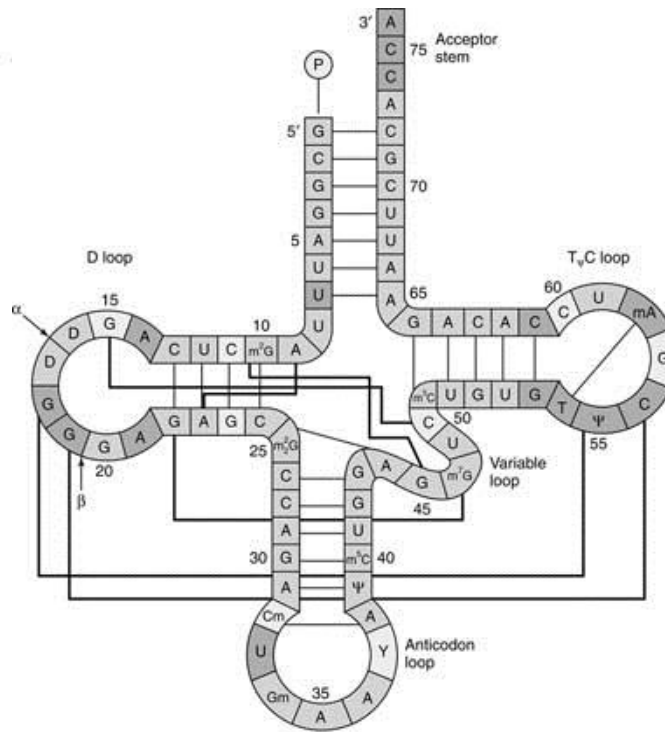
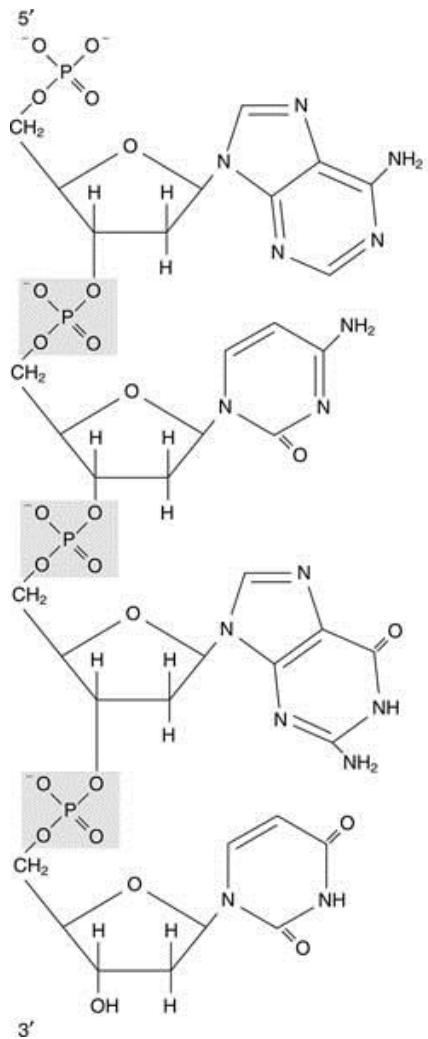


# Polymerase chain reaction (PCR)



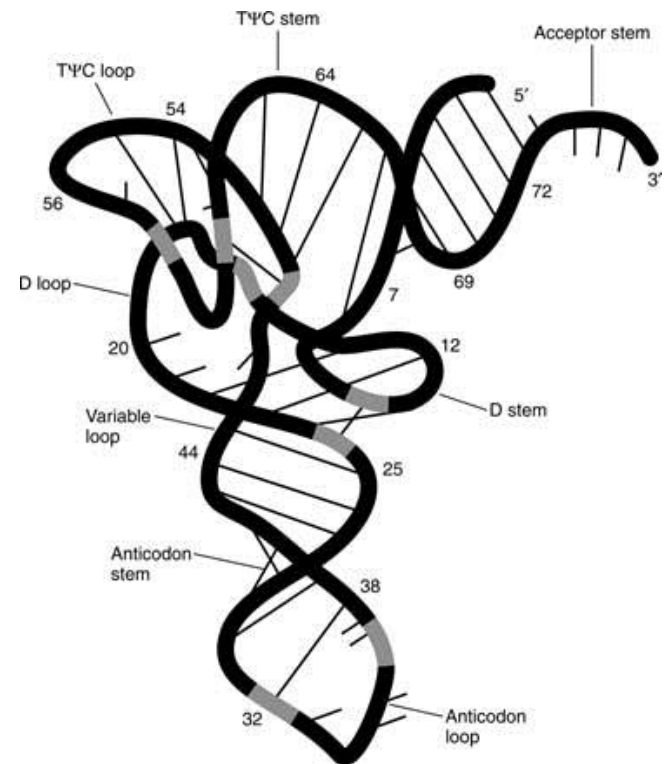
- 1 **Denaturation** at 94-96°C
- 2 **Annealing** at ~68°C
- 3 **Elongation** at ca. 72 °C





Secondary = Base pairs

(a)



Tertiary = Folded in 3 dimensions

(b)

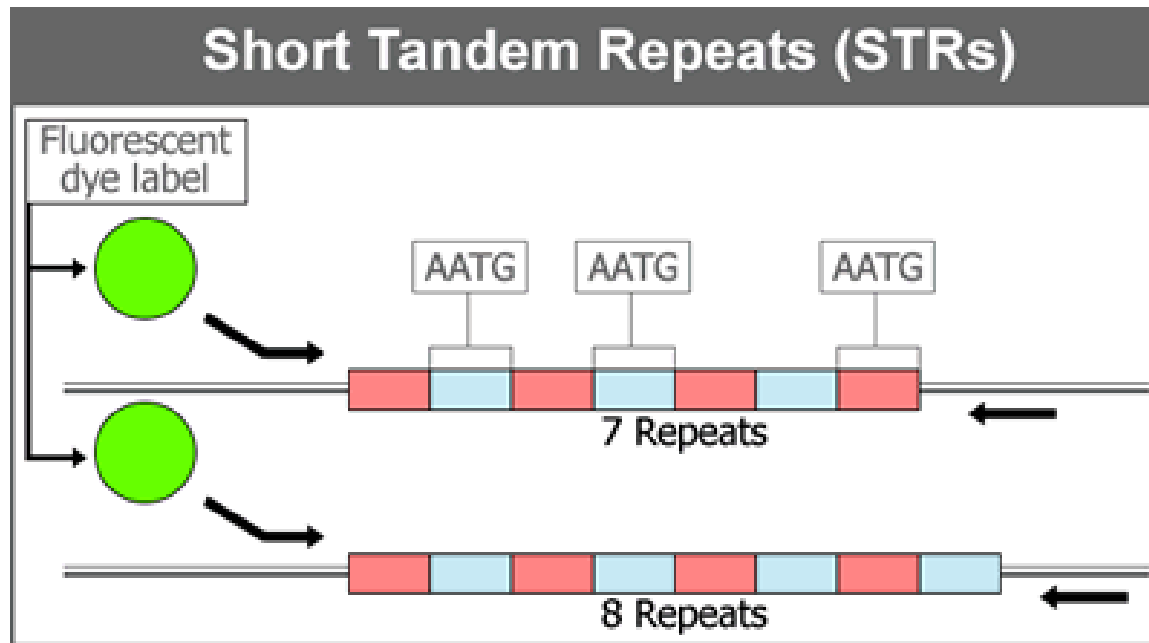
# Tandem repetitive DNA

Tandem repeats appear in genomic DNA with a wide variety.

A tandem repeat in DNA is two or more similar copies of a DNA sequence.

Tandem repeats may not have any functional role.

Tandemly repeated DNA sequences are widespread throughout the human genome.



The STR loci carry lots of desirable features which makes them an ideal candidate for diverse applications including:

**1- Forensic applications**

**2- Individual identification**

**3- True paternity/maternity detection**

**4- Fine scale genetic mapping**

**5- Inter and intra group phylogenetic reconstruction.**

# Who is the Murderer?

Hambozo

Cokrat

Dongule



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# Sequence Alignment

It is a way of arranging the sequences of [DNA](#), [RNA](#), or [protein](#) to identify regions of similarity that may be a consequence of functional, [structural](#), or [evolutionary](#) relationships between the sequences.

Aligned sequences of [nucleotide](#) or [amino acid](#) residues are typically represented as rows within a [matrix](#).

### Histone H1 (residues 120-180)

HUMAN	KKASKPKKAASKAPT	TKKPKATPVKKAKKK	LAATPKKAKKPKT	TVKAKPVKASKPKKAKPVK
MOUSE	KKAAKPKKAASKAPS	SKKPKATPVKKAKKK	PAATPKKAKKPKV	VVKVPVKASKPKKAKTVK
RAT	KKAAKPKKAASKAPS	SKKPKATPVKKAKKK	PAATPKKAKKPKI	VKVVPVKASKPKKAKPVK
COW	KKAAKPKKAASKAPS	SKKPKATPVKKAKKK	PAATPKKTKKPKT	TVKAKPVKASKPKKTKPVK
CHIMP	KKASKPKKAASKAPT	TKKPKATPVKKAKKK	LAATPKKAKKPKT	TVKAKPVKASKPKKAKPVK
	*** :	***** :	***** :	***** :

NON-CONSERVED AMINO ACIDS	Conservative	Conservative	Non-conservative	Conservative	Non-conservative	Semi-conservative	Conservative	Non-conservative
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A sequence alignment, produced by [ClustalO](#), of mammalian [histone](#) proteins.

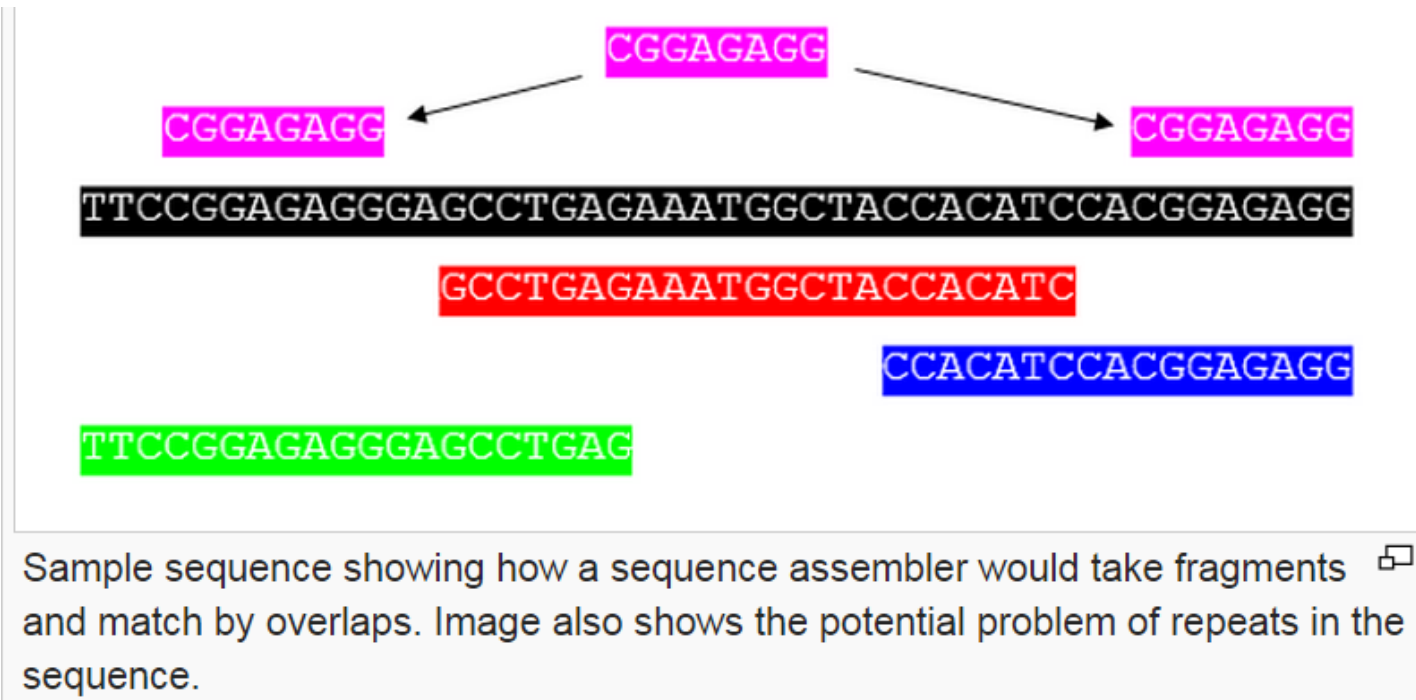
Sequences are the [amino acids](#) for residues 120-180 of the proteins. Residues that are conserved across all sequences are highlighted in grey. Below the protein sequences is a key denoting [conserved sequence](#) (\*), [conservative mutations](#) (:), semi-conservative mutations (.), and [non-conservative mutations](#) ( ).<sup>[2]</sup>



# Sequence Assembly

Aligning and merging fragments of a much longer DNA sequence in order to reconstruct the original sequence.

In DNA sequencing technology cannot read whole genomes in one go, but rather reads small pieces of between 20 and 30000 bases, depending on the technology used.



# Orthologs vs Paralogs

## Orthologs

They are genes of common ancestry between species.

Eg: Dog hemoglobin and human hemoglobin, for example are orthologous.

## Paralogs

They are when genes are duplicated then one of the copies evolves a new function.

Eg: Humans would be myoglobin and hemoglobin; both are oxygen storage proteins derived from the same ancestor gene, but have different functions (one is a transport protein in red blood cells, the other is a storage protein in muscle cells).

# **Impact of Genomics in Medicine**



# Fungal bioinformatics

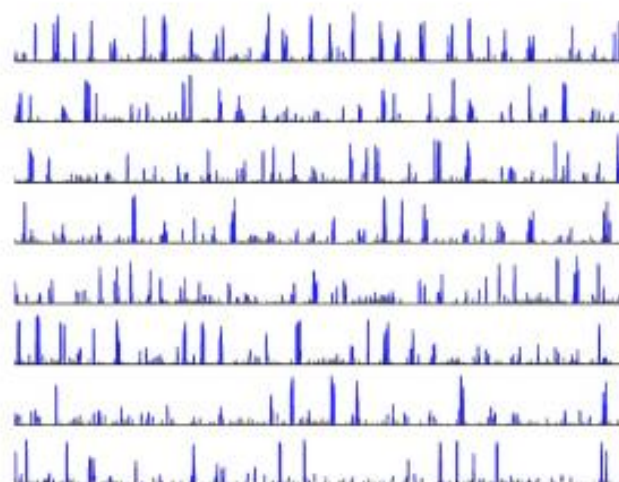
**Programme Leader(s):** Murray Cox

**Team Member(s):** Pierre-Yves Dupont

*We are identifying lateral gene transfer events in fungi by developing evolutionary algorithms and computational tools.*

## Lateral gene transfer

Organisms typically evolve by vertical transmission, where genes are passed from parents to offspring. However, genes are sometimes passed between organisms in a process known as lateral, or horizontal, gene transfer.



## Fungal adaptability and gene transfer

Assoc Prof Murray Cox and colleagues at Massey University are investigating whether lateral gene transfer between fungi is a key driving force in the adaptability of fungal species. Laterally transferred genes have been shown to confer new functions or traits, such as pathogenicity. Recent research has shown that entire metabolic pathways, as well as individual genes, have been transferred between fungi.

## Bioinformatics and fungal genomes

The researchers are comparing genomes in two case study systems with major relevance to the New Zealand economy:

1. *Dothistroma septosporum*, a fungus which causes pine needle blight, costing New Zealand's pine plantation industry \$200 million each year.
2. *Epichloë festucae*, a fungal endophyte which protects New Zealand's pasture grasses from insect damage.

## Fungal & Microbial Genomics



- About us
- Staff
- Resources
- Projects
- Publications
- News

### Welcome to the MIPS Fungal & Microbial Genomics Group

The group focuses on the analysis of fungal and microbial genomes. With former efforts on the model systems yeast and Neurospora we now work on plant pathogenic fungi and advanced model systems, mainly Fusarium spec., Ustilaginaceae and selected human pathogenic bacteria. We also provide comprehensive analysis of further public genome data for comparative analysis.

The basis to explore the species specific properties are correct structural annotations. Thus we improve the gene sets of our core projects and related genome data by applying comparative gene calling procedures. The resulting structurally annotated genomes are used for integration of further omics datasets and comparative studies.

#### Contact

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**Fungal & Microbial Genomics**  
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Germany

[Email](#)

Phone: +49 (0) 89 3187-3582  
Fax: +49 (0) 89 3187-3585

#### Featured Resources

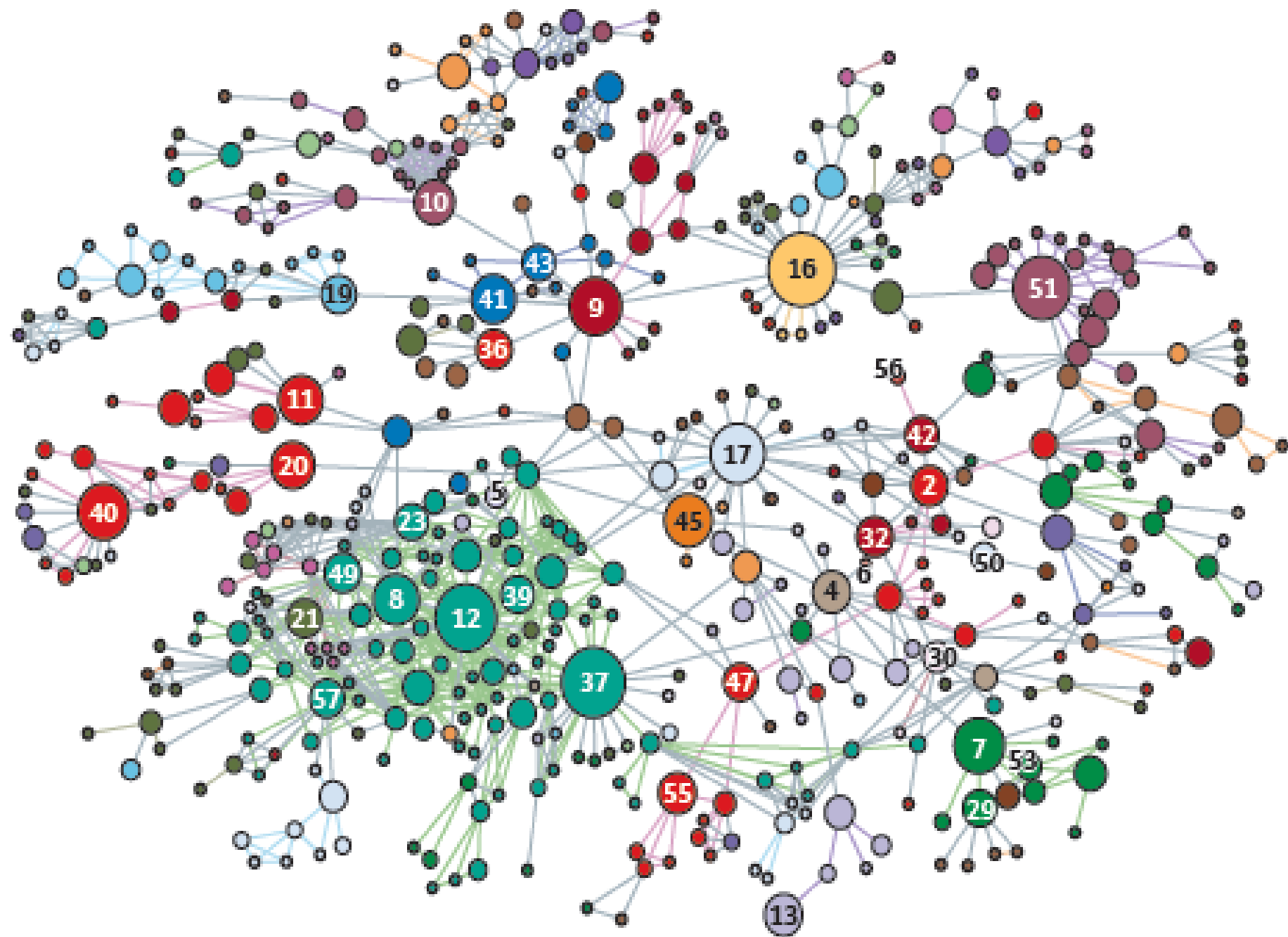
- List all analyzed Fungal Genomes - PEDANT >
- <ftp://ftpmips.gsf.de/fungi/> >
-  **Fusarium** species groups >



## Network medicine: a network-based approach to human disease

*Albert-László Barabási<sup>\*†§</sup>, Natali Gulbahce<sup>\*†||</sup> and Joseph Loscalzo<sup>§</sup>*

**Abstract** | Given the functional interdependencies between the molecular components in a human cell, a disease is rarely a consequence of an abnormality in a single gene, but reflects the perturbations of the complex intracellular and intercellular network that links tissue and organ systems. The emerging tools of network medicine offer a platform to explore systematically not only the molecular complexity of a particular disease, leading to the identification of disease modules and pathways, but also the molecular relationships among apparently distinct (patho)phenotypes. Advances in this direction are essential for identifying new disease genes, for uncovering the biological significance of disease-associated mutations identified by genome-wide association studies and full-genome sequencing, and for identifying drug targets and biomarkers for complex diseases.



- ① Aldosteronism
- ② Alzheimer's disease
- ③ Anaemia, congenital deserythropoietic
- ④ Asthma
- ⑤ Ataxia-telangiectasia
- ⑥ Atherosclerosis
- ⑦ Blood group
- ⑧ Breast cancer
- ⑨ Cardiomyopathy
- ⑩ Cataract
- ⑪ Charcot-Marie-Tooth disease
- ⑫ Colon cancer
- ⑬ Complement component deficiency
- ⑭ Coronary artery disease
- ⑮ Coronary spasm
- ⑯ Deafness
- ⑰ Diabetes mellitus
- ⑱ Enolase- $\beta$  deficiency
- ⑲ Epidermolysis bullosa

- ⑳ Epilepsy
- ㉑ Fanconi's anaemia
- ㉒ Fatty liver
- ㉓ Gastric cancer
- ㉔ Gilbert's syndrome
- ㉕ Glaucoma 1A
- ㉖ Goitre congenital
- ㉗ HARP syndrome
- ㉘ HELLP syndrome
- ㉙ Haemolytic anaemia
- ㉚ Hirschprung disease
- ㉛ Hyperbilirubinaemia
- ㉜ Hypertension
- ㉝ Hypertension diastolic
- ㉞ Hyperthyroidism
- ㉟ Hypoaldosteronism
- ㊱ Leigh syndrome
- ㊲ Leukaemia
- ㊳ Low renin hypertension
- ㊴ Lymphoma
- ㊵ Mental retardation
- ㊶ Muscular dystrophy

- ㊷ Myocardial infarction
- ㊸ Myopathy
- ㊹ Nucleoside phosphorylase deficiency
- ㊺ Obesity
- ㊻ Paraganglioma
- ㊼ Parkinson's disease
- ㊽ Pheochromocytoma
- ㊾ Prostate cancer
- ㊿ Pseudohypoaldosteronism
- ⑤① Retinitis pigmentosa
- ⑤② Schizoaffective disorder
- ⑤③ Spherocytosis
- ⑤④ Spina bifida
- ⑤⑤ Spinocerebellar ataxia
- ⑤⑥ Stroke
- ⑤⑦ Thyroid carcinoma
- ⑤⑧ Total iodide organification defect
- ⑤⑨ Trifunctional protein deficiency
- ⑥① Unipolar depression

# **Top Reasons To study Bioinformatics/Computational Biology**

**Computing is the key skill set for 21st century biology**

Biology is becoming a more quantitative science.

In the future, new discoveries will require leveraging big datasets and using advanced analytical methods.

Big data and complex models require computational skills.

**There is no way to escape this reality.**

# Nobel-prize winning pioneer

- [Walter Gilbert:](#)

*“To use this flood of [sequence] knowledge, which will pour across the computer networks of the world, biologists not only must become computer literate, but also change their approach to the problem of understanding life”*

- [Sydney Brenner:](#)

*“I spent many hours persuading people that computing was not only going to be the essential tool for biological research but would also provide models for analyzing”*



# **Computational skills are highly transferable**

Computational skills transfer across this sector, plus a much wider market outside of the (bio)science.

Increasing your computational chops will give you a better chance at landing a job.

You will have a deeper appreciation for how computers work and more mastery of when you interact with computers in your daily life

# Computing will help improve your core scientific skills

Computing forces you to confront and tame the very human tendency to do science in *ad hoc* ways and therefore it naturally develops core scientific skills such as:

- Logically planning experiments
- Collecting data consistently
- Developing reproducible methodology
- Analyzing your data with proper statistical methodology.

# **You should use you Ph.D./Post-Doc to develop new skills**

Majority of Biology Ph.D. students have no training in scientific computing skills beyond using Excel or statistics package.

So you have to start training in something new, not just further developing a skill set that you already have.

## **You will develop a more unique skill set in Biology**

Majority of Biologists have experimental training, but very few have advanced Computational training.

And because you will be able to get results that many others cannot, plus the fact that you will have skills that set you apart from the herd, you will be more competitive on the job market.

# **You will publish more papers**

Computational Biology will provide you more than your fair share of failed experiments.

As a result, you are very likely to publish more papers per unit time in Computational Biology.

Funding agencies want to see the junior researchers who have good ideas and can take them to completion.

Publication is the proof that you can finish projects.

# **You will have more flexibility in your research**

You can move from flexibly from topic to topic more easily than you can if your skill set is linked to specific experimental techniques.

This flexibility in scope allows you to satisfy your intellectual curiosity or chase the latest trend as you wish.



# You will have more flexibility in working practices

- Unlike being chained to the bench, you can do working from home.



**Nick Loman**

@pathogenomenick

 Follow

Best thing about doing bioinformatics; still being able to work with the baby sleeping on you. Try that in the lab.

3:58 PM - 31 Jul 2012

28 RETWEETS 16 FAVORITES



# Computational research is cost-effective

- Computational Biology research is cheaper than most experimental work that requires a large consumables budget.
- Cost-efficiency is also very important when you are starting your group and for maintaining continuity of productivity when riding out troughs in funding or group size.

# A successful scientist ends up in an office

- The truth is that the native habitat for an academic researchers is sitting in their office in front of their computer.

[Webb Miller](#) (most highly-cited bioinformaticians)

- If you've really wanted to do research since you were young, then ask yourself: why train in skills you will never ultimately use for the majority of your career, while somebody else in your lab gets to have fun making all the discoveries?

# **According to Fast Future report**

- Computational biology is going to be among the most popular jobs of the future.
- Besides, most NGS data will sit untouched and unloved unless there are better methods to collect information about phenotype.

# **Safer and Environment friend**

**Mason Vail :**

“You’re far less likely to spill a pathogen on yourself if you avoid the wet lab altogether “.

Another reason that came up in recent discussions is that computational work is more environmentally friendly.

Less plastic waste, less energy spent on autoclaving, etc.

*The  
End*