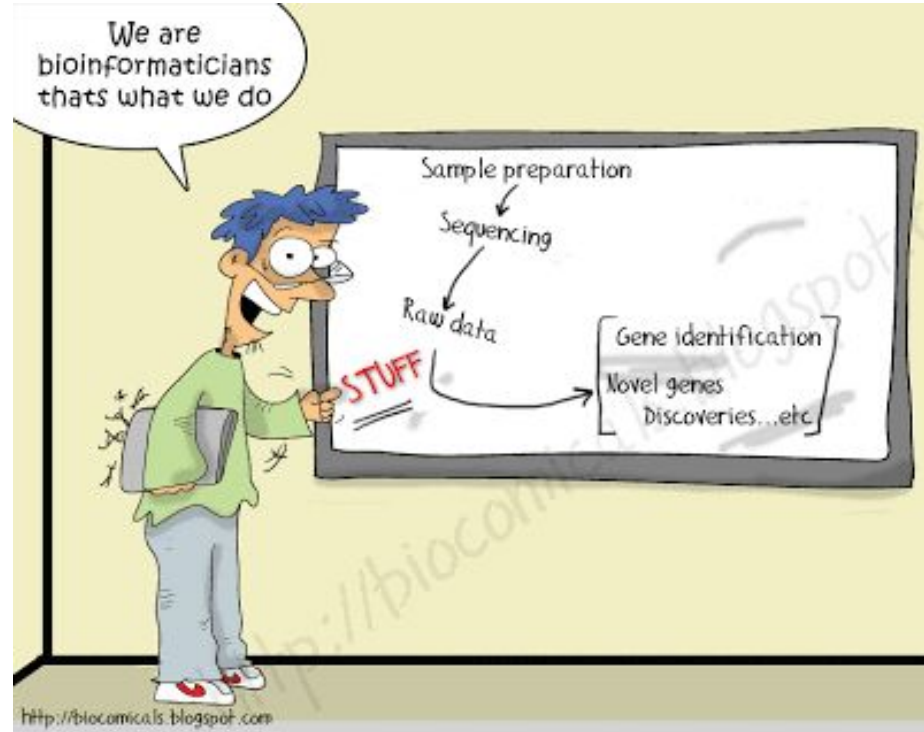


Introduction to Bioinformatics

Summer 2021

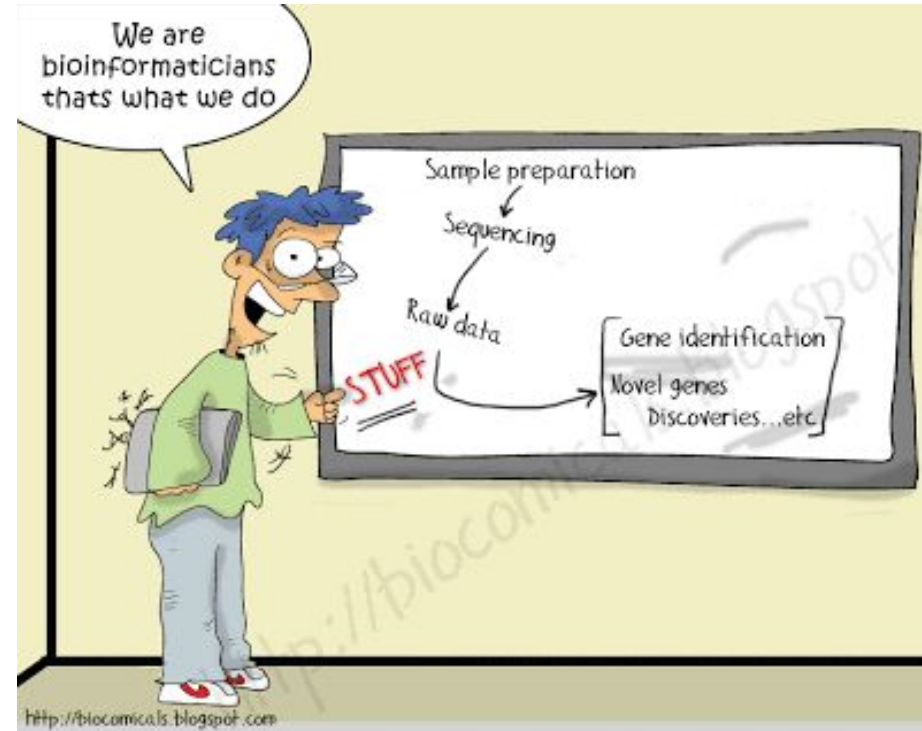
Emilie Skoog

What is bioinformatics?



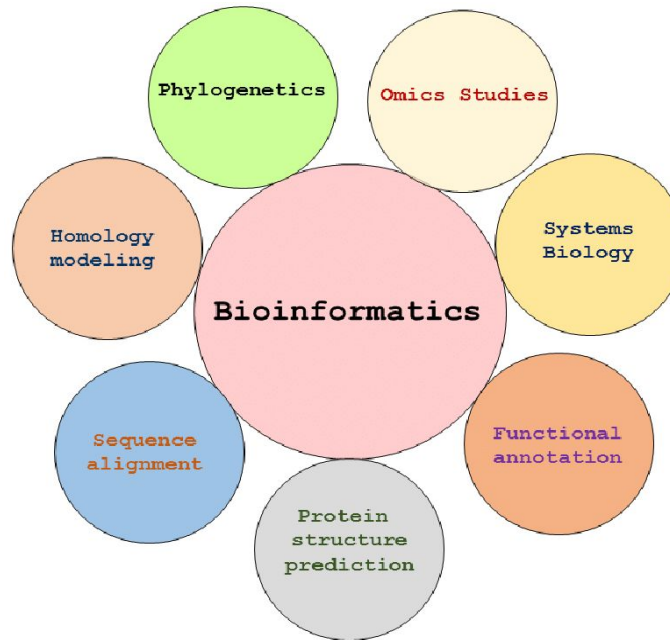
What is bioinformatics?

- Bioinformatics is a subdiscipline of biology and computer science concerned with the acquisition, storage, analysis, and dissemination of biological data, most often DNA and amino acid sequences. Bioinformatics uses computer programs for a variety of applications, including determining gene and protein functions, establishing evolutionary relationships, and predicting the three-dimensional shapes of proteins.



What is bioinformatics?

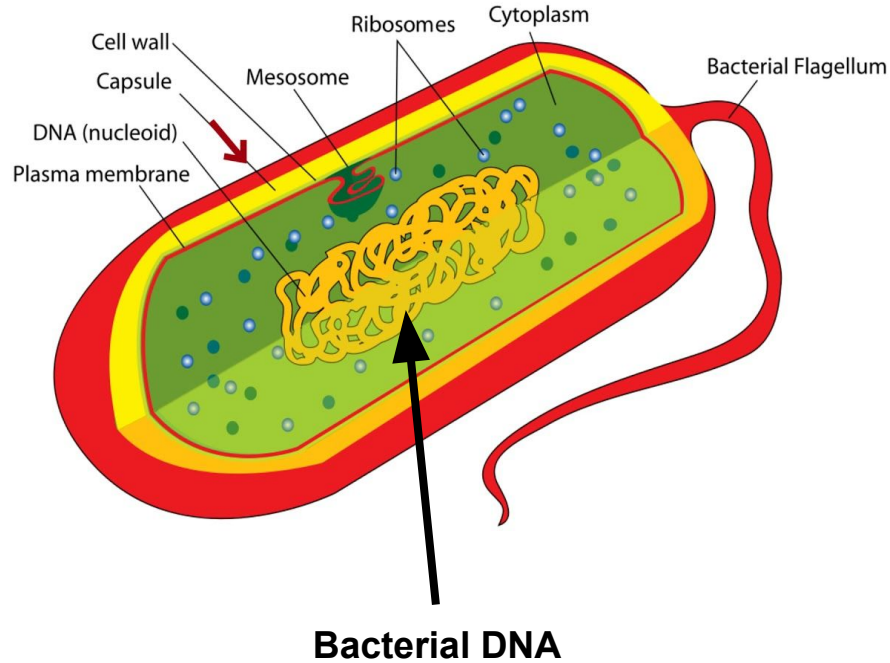
- Combines biology and computer science to **interpret biological data**



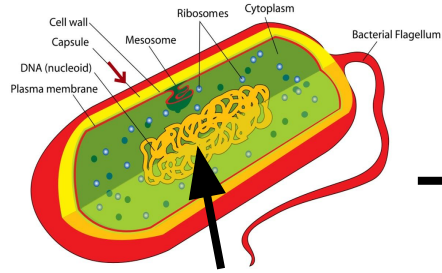
Usually DNA and amino acid sequences!

Mini crash course/ biology refresher

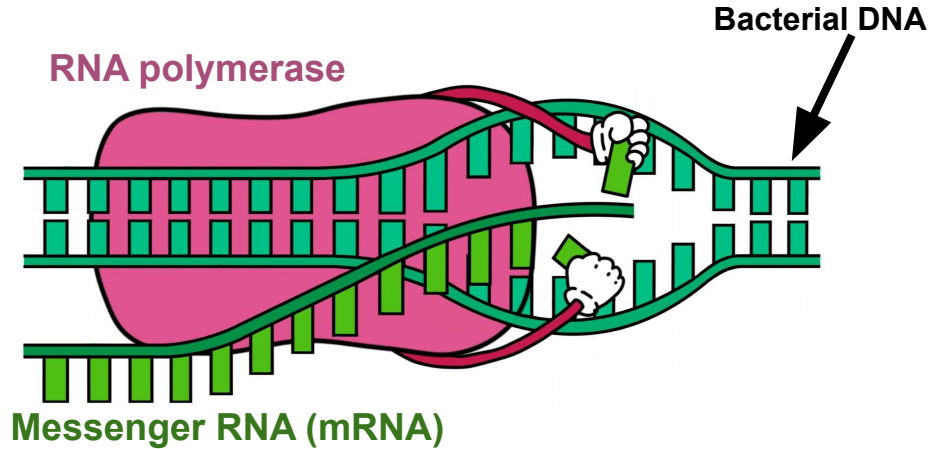
Mini crash course/ biology refresher



Mini crash course/ biology refresher

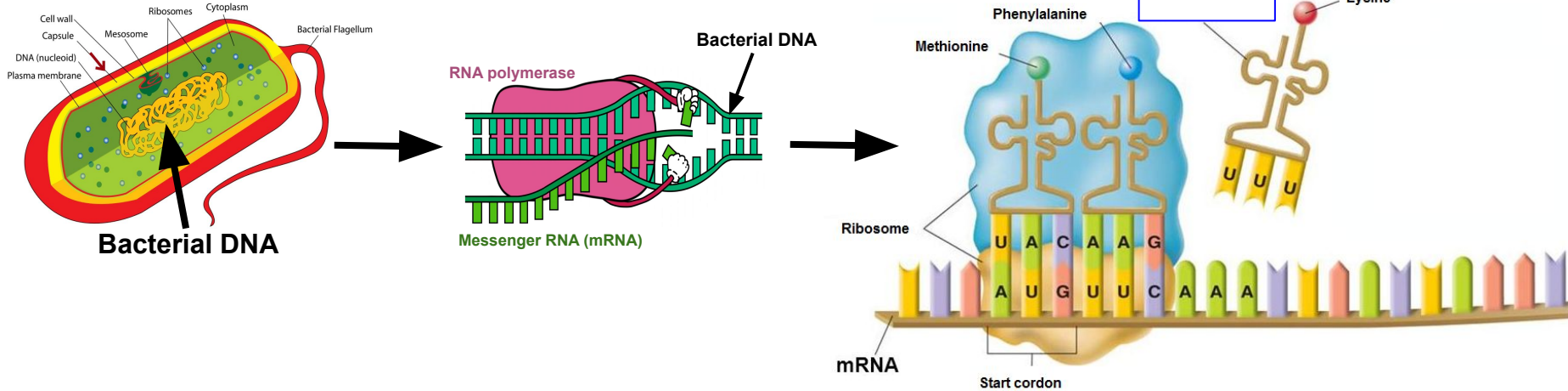


Bacterial DNA



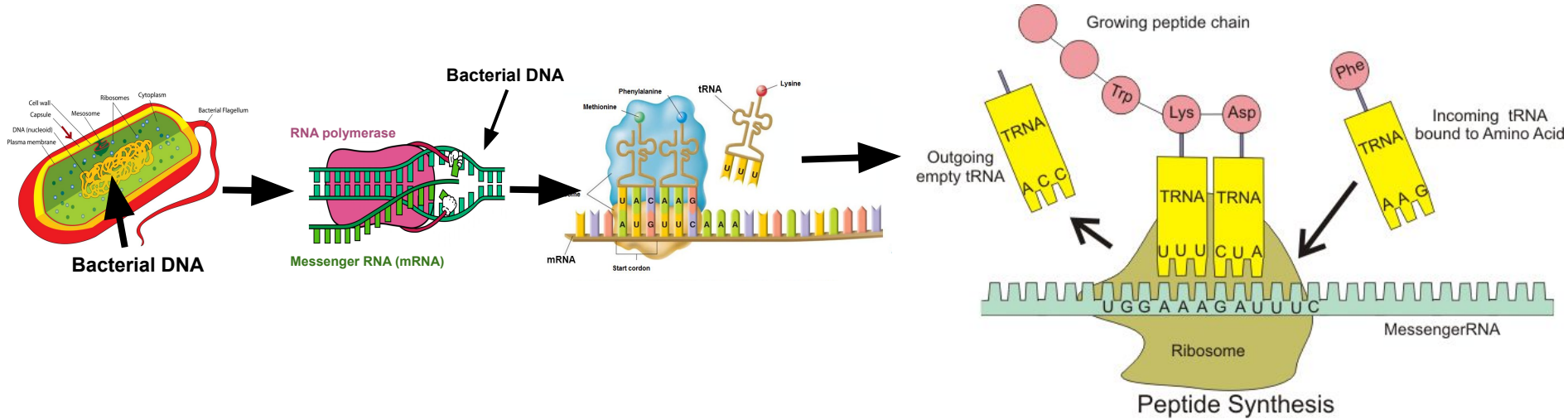
RNA polymerase makes **mRNA** using **DNA**

Mini crash course/ biology refresher



mRNA is read by **transfer RNA (tRNA)** that brings along amino acids (ex. Lysine, methionine, etc). The ribosome is what binds the **mRNA** and **tRNA** together.

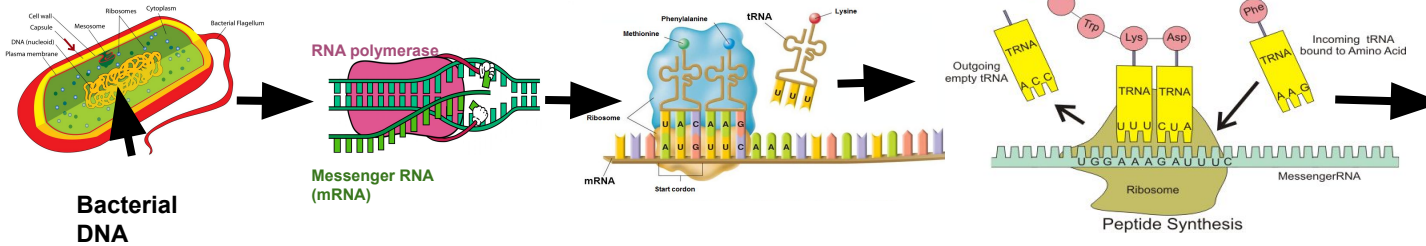
Mini crash course/ biology refresher



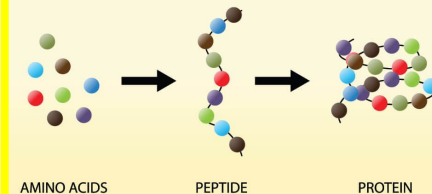
These amino acids grow into longer peptide chains as the ribosome continues to 'read' the **mRNA**.

Mini crash course/ biology refresher

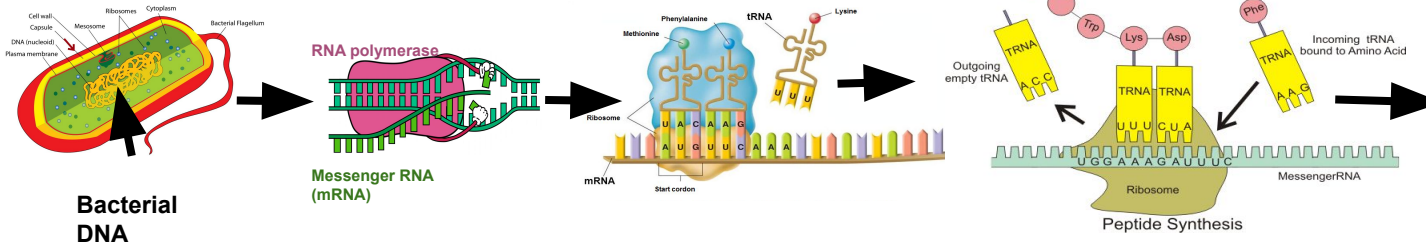
REMEMBER: these amino acids have abbreviations and when you put them together to make peptide chains and proteins you get many letters in a row.



Amino Acid	3-Letters	1-Letter
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Cysteine	Cys	C
Glutamic acid	Glu	E
Glutamine	Gln	Q
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

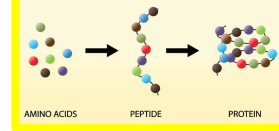


Mini crash course/ biology refresher



REMEMBER: these amino acids have abbreviations and when you put them together to make peptide chains and proteins you get many letters in a row.

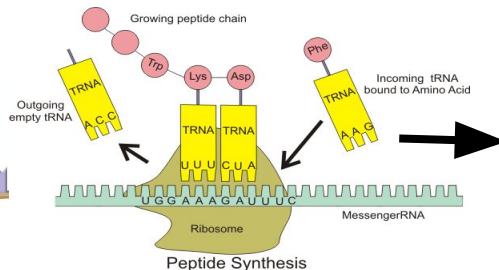
Amino Acid	3-Letters	1-Letter
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Cysteine	Cys	C
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Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V



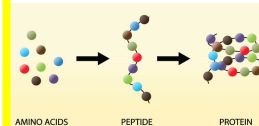
For example, one (small) protein sequence:

YLMKKFYVWHGHHEQRNDCCCHHGILKILKILK

Bacterial DNA



Amino Acid	3-Letters	1-Letter
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Cysteine	Cys	C
Glutamic acid	Glu	E
Glutamine	Gln	Q
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
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Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V



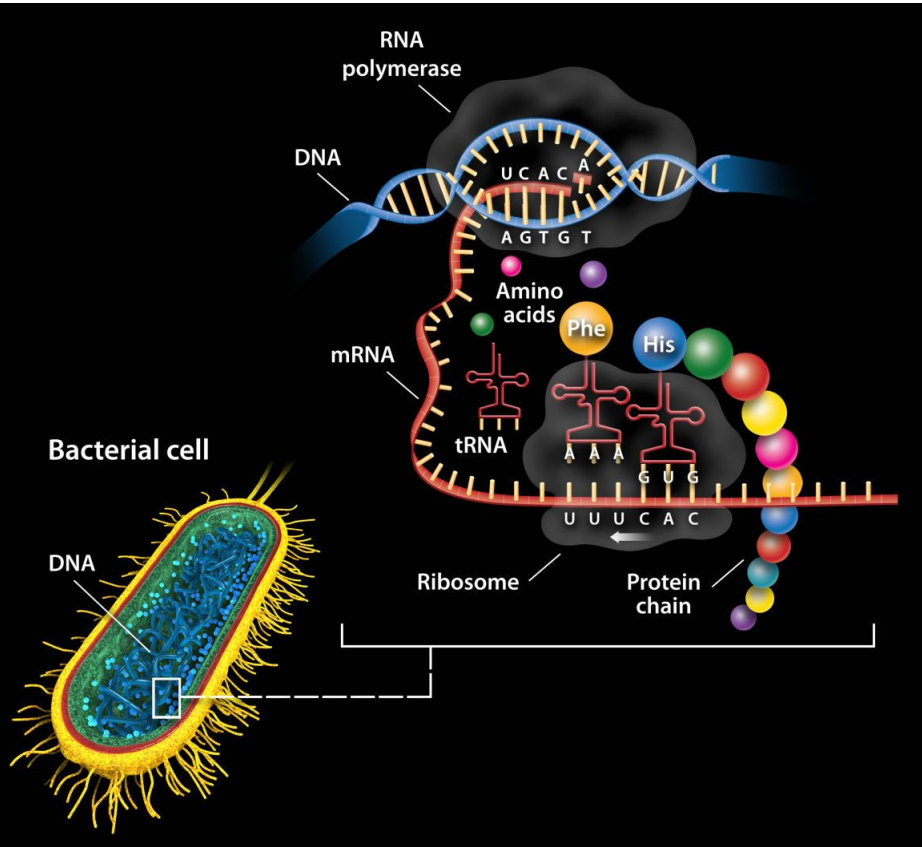
BUT a whole translated genome will have millions of amino acids! Ex:

[illegible]

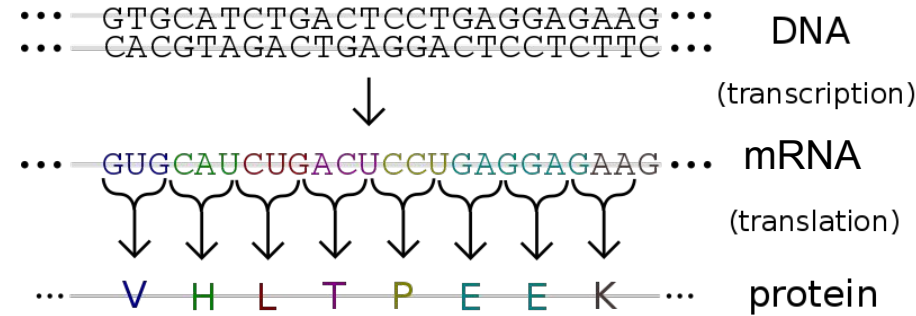
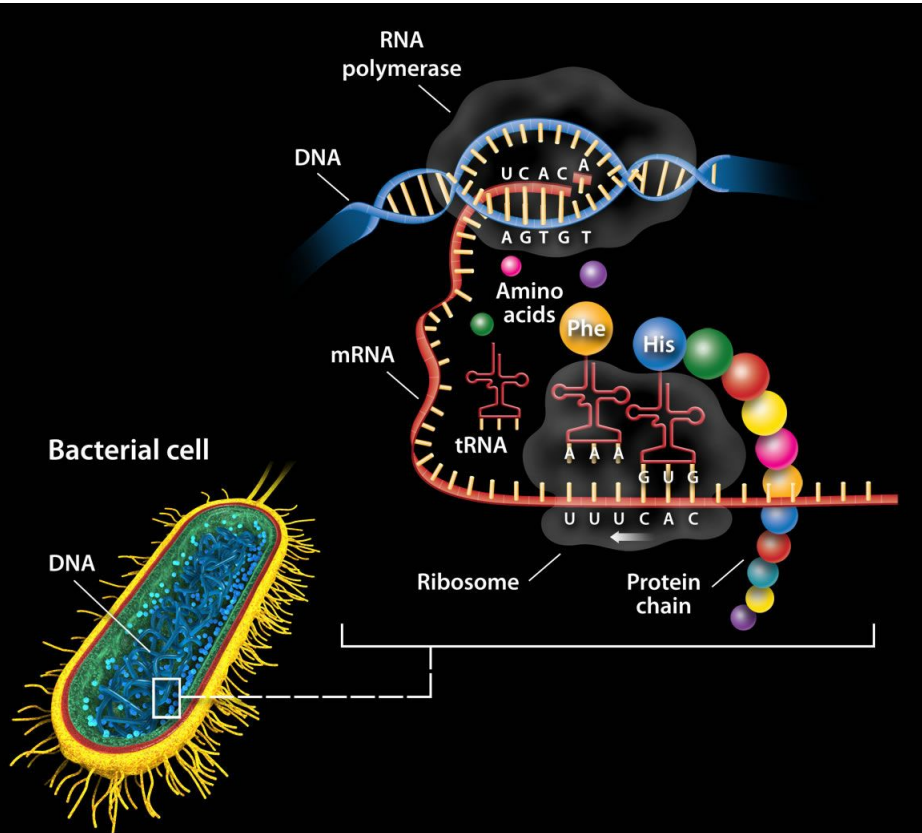
For example, one (small) protein sequence:

YLMKKFYVWHGHHEQRNDCCCHHGILKILKILK

RECAP: Mini crash course/ biology refresher



RECAP: Mini crash course/ biology refresher



Bacterial DNA

Cell wall, Capsule, Ribosomes, Cytoplasm, Bacterial flagellum, DNA (nucleoid), Plasma membrane

RNA polymerase

Messenger RNA (mRNA)

tRNA

Methionine, Phenylalanine, Lysine

Peptide Synthesis

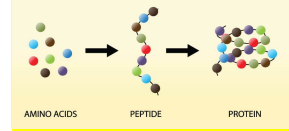
Growing peptide chain

Outgoing empty tRNA

Incoming tRNA bound to Amino Acid

Peptide Synthesis

Amino Acid	3-Letters	1-Letter
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Cysteine	Cys	C
Glutamic acid	Glu	E
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Glycine	Gly	G
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Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V



BUT a whole translated genome will have millions of amino acids! Ex:

[illegible]

Bacterial DNA

Cell wall, Capsule, Mesosome, Ribosomes, Cytoplasm, Bacterial flagellum, DNA (nucleoid), no membrane

RNA polymerase

Messenger RNA (mRNA)

Ribosome

mRNA

tRNA

Phenylalanine

Methionine

Lysine

Start codon

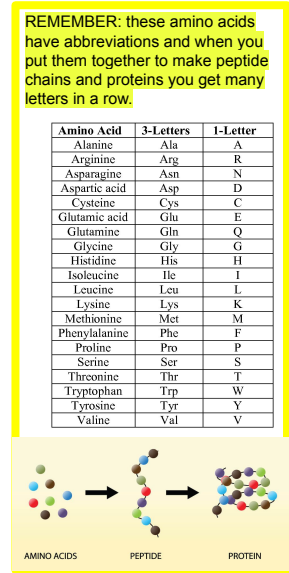
Outgoing empty tRNA

Incoming tRNA bound to Amino Acid

Peptide Synthesis

Ribosome

MessengerRNA

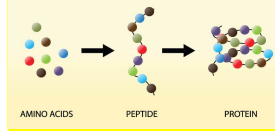


BUT a whole translated genome will have millions of amino acids! Ex:

[illegible]

The diagram illustrates the process of protein synthesis in a bacterial cell. It begins with **Bacterial DNA**, which is transcribed into **Messenger RNA (mRNA)** by **RNA polymerase**. The mRNA then moves to a **Ribosome**, where **tRNA** molecules (carrying amino acids like Methionine, Phenylalanine, and Lysine) assemble the growing peptide chain. The final stage is **Peptide Synthesis**, showing the outgoing empty tRNA and the incoming tRNA bound to an amino acid (Phe) as the chain grows.

Amino Acid	3-Letters	1-Letter
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Cysteine	Cys	C
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Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V



Extract DNA (lab work!)



BUT a whole translated genome will have millions of amino acids! Ex:

[illegible]

Bacterial DNA

Cell wall, Capsule, Mesosome, Ribosomes, Cytoplasm, Bacterial flagellum, DNA (nucleoid), Plasma membrane

RNA polymerase

Messenger RNA (mRNA)

Phenylalanine, **Lysine**, **Methionine**

tRNA

UAC, **CAU**, **AAA**, **UUA**, **CUA**, **AAA**

mRNA

Start codon

Growing peptide chain

Outgoing empty tRNA

Trp, **Lys**, **Asp**, **Phe**

Incoming tRNA bound to Amino Acid

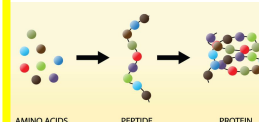
Peptide Synthesis

Ribosome

MessengerRNA

U G G A A A G A U U C

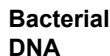
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Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V



ACTGGTCGCTACGATCGT
CAGCTAGCTAGTCAGTCG
ATAGCTAATCGATCGGCC
CCATCGATAA...

[illegible]

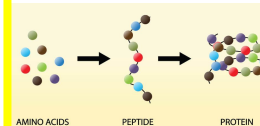
A detailed diagram of a bacterial cell. The cell is oval-shaped with a thick red outer layer labeled 'Cell wall' and a thinner yellow inner layer labeled 'Plasma membrane'. Inside the cell, there is a large, yellow, tangled mass labeled 'DNA (nucleoid)'. Small blue dots are labeled 'Ribosomes'. A circular structure is labeled 'Mesosome'. The fluid-filled interior is labeled 'Cytoplasm'. A long, wavy red line extending from the cell is labeled 'Bacterial flagellum'. A black arrow points to the DNA (nucleoid) region.



ACTGGTCGCTACGATCGTCAGCTAGCTAGTCAGTCGA
TAGCTAACTCGATCGGCCCATCGATAAAGTGGTCGT
ACGATCGTCAGCTAGCTAGCTAGTCAGTACGTAATCG
ATCGGCCCATCGATAAAGTGGTCGTACGATCGTCA
GCTAGCTAGTCAGTCGATAGCTAATCGATCGGCCCA
TCGATAAAGTGGTCGATACGATCGTCAGCTAGCTAGT
GCTCGATAGCTAATCGATCGGCCCATCGATAA

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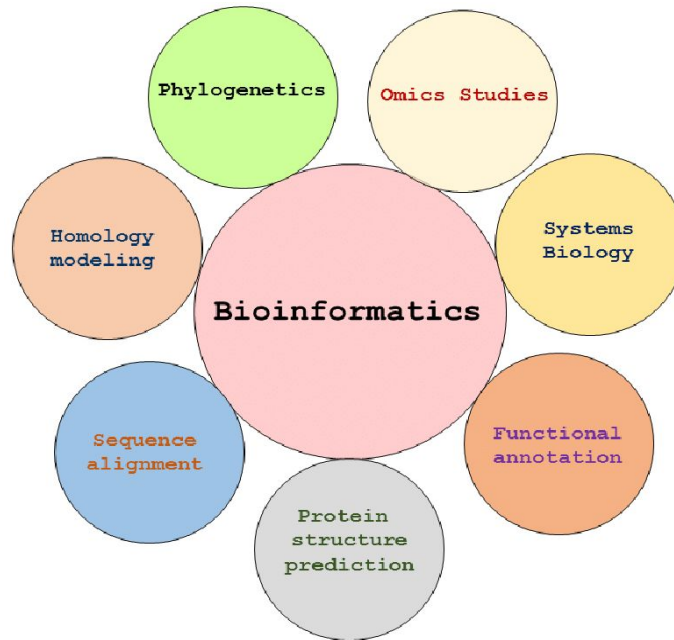


T a whole translated genome will have millions of amino acids! Ex:

[illegible]

What is bioinformatics?

- Combines biology and computer science to **interpret biological data**

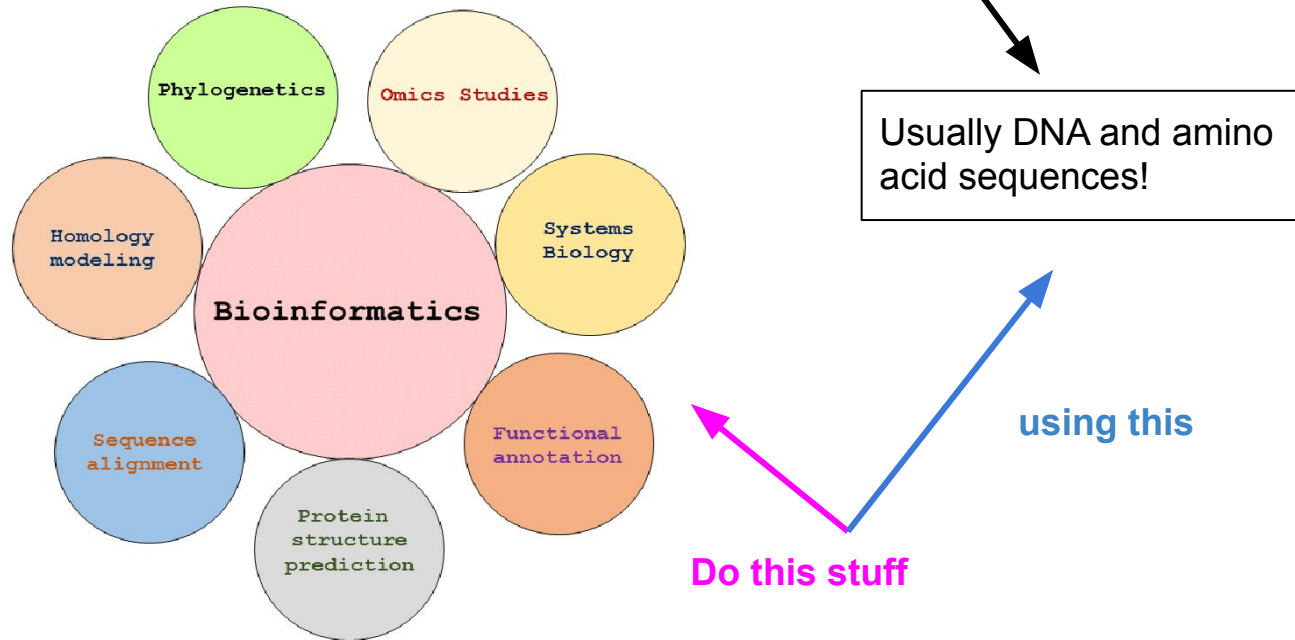


Usually DNA and amino acid sequences!

Do this stuff

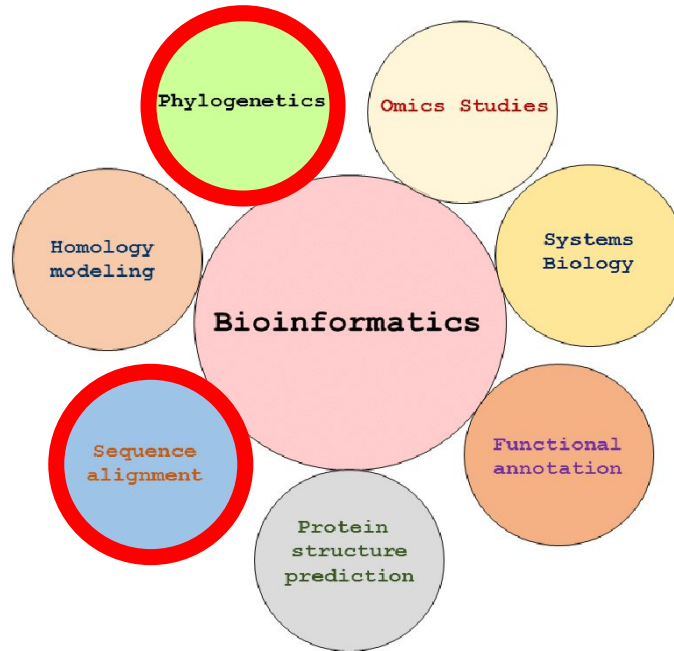
What is bioinformatics?

- Combines biology and computer science to **interpret biological data**



What is bioinformatics?

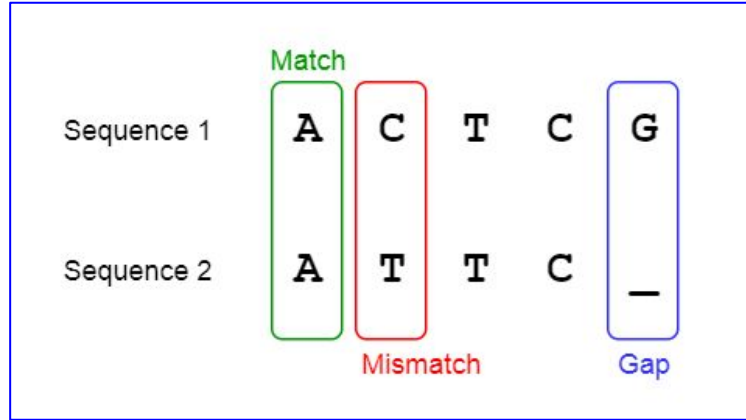
- Combines biology and computer science to **interpret biological data**



Usually DNA and amino acid sequences!

Sequence alignment and phylogenetics

Nucleotide sequences (DNA)



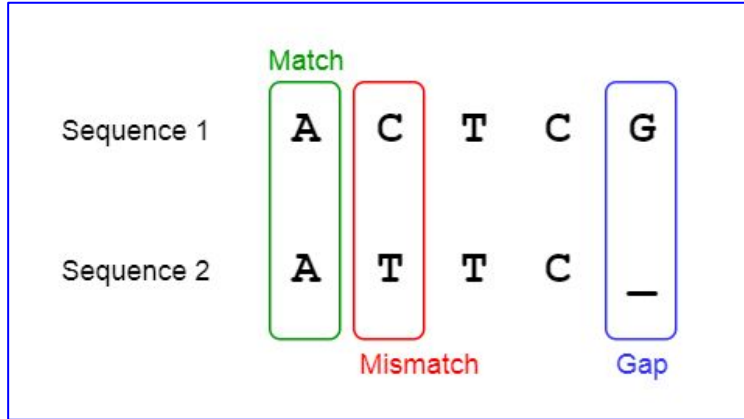
Amino acid sequences (protein)

position 12	helix H0	sheet
↓	oooooooo	
R Y D S R T T I F S P . .	E G R L Y Q V E Y A M E A I G N A .	G S A I G I L S
R Y D S R T T I F S P L R	E G R L Y Q V E Y A M E A I S H A .	G T C L G I L S
R Y D S R T T I F S P . .	E G R L Y Q V E Y A Q E A I S N A .	G T A I G I L S
R Y D S R T T I F S P . .	E G R L Y Q V E Y A M E A I S H A .	G T C L G I L A
R Y D S R T T I F S P . .	E G R L Y Q V E Y A M E A I G H A .	G T C L G I L A
R Y D S R T T I F S P . .	E G R L Y Q V E Y A M E A I G N A .	G S A L G V L A
R Y D S R T T T F S P . .	E G R L Y Q V E Y A L E A I N N A .	S I T I G L I T
S Y D S R T T I F S P . .	E G R L Y Q V E Y A L E A I N H A .	G V A L G I V A

Align sequences from different organisms (can see mismatches, gaps, insertions, deletions, regions of similarity, etc)

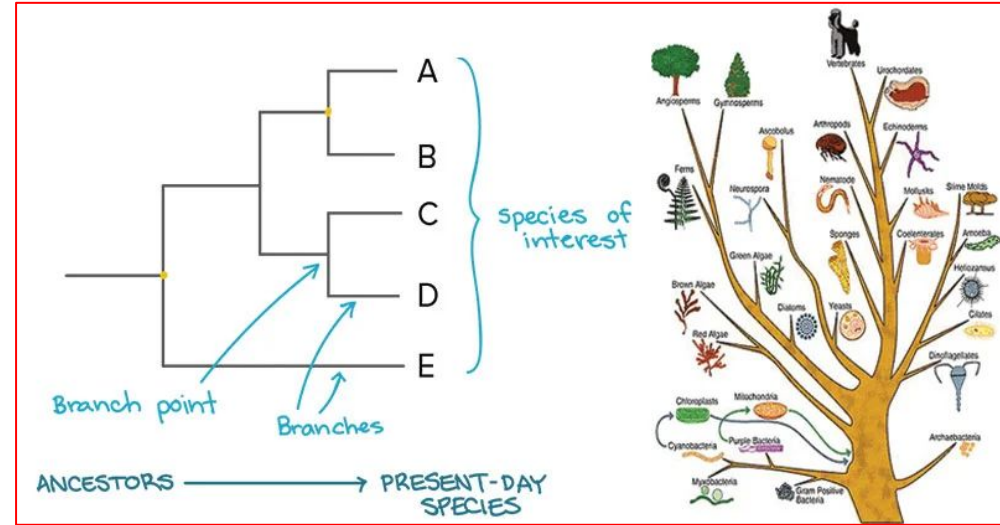
Sequence alignment and phylogenetics

Nucleotide sequences (DNA)



Amino acid sequences (protein)

position 12	helix H0	sheet
↓	oooooooo	
RYDSRRTTIFSP..	EGRLYQVEYAMEAIGNA.	GSATGILS
RYDSRRTTIFSP.LR	EGRLYQVEYAMEAISHA.	GTCLGILS
RYDSRRTTIFSP..	EGRLYQVEYAQAIGNA.	GTAIGILS
RYDSRRTTIFSP..	EGRLYQVEYAMEAISHA.	GTCLGILA
RYDSRRTTIFSP..	EGRLYQVEYAMEAIGHA.	GTCLGILA
RYDSRRTTIFSP..	EGRLYQVEYAMEAIGNA.	GSALGVLA
RYDSRRTTIFSP..	EGRLYQVEYALEAINNA.	SITIGLIT
SYDSRRTTIFSP..	EGRLYQVEYALEAINHA.	GVALGIVA

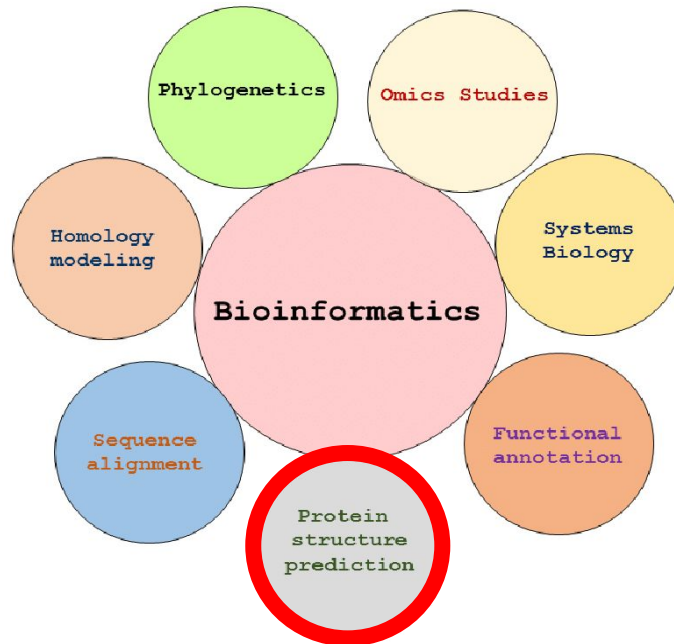


Align sequences from different organisms (can see mismatches, gaps, insertions, deletions, regions of similarity, etc)

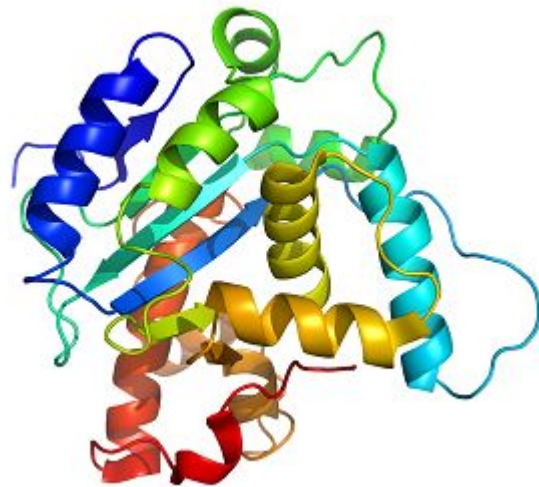
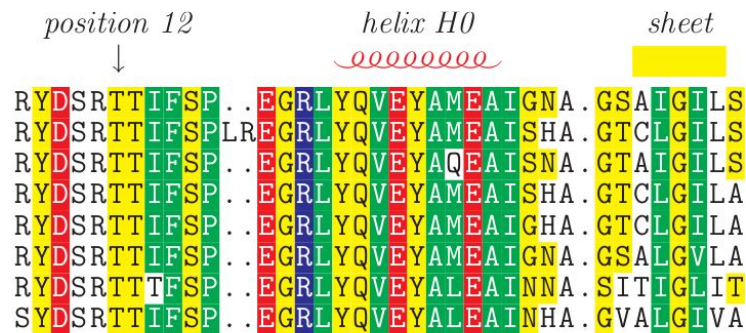
You can visually see sequence similarities by taking these sequences and making a phylogenetic tree (use a program to do this)

What is bioinformatics?

- Combines biology and computer science to **interpret biological data**



Protein structure prediction



Protein structure prediction

position 12
↓

helix H0
○○○○○○○○

sheet
■

R	Y	D	S	R	T	T	I	F	S	P	.	E	G	R	L	Y	Q	V	E	Y	A	M	E	A	I	G	N	A	.	G	S	A	I	G	I	L	S	
R	Y	D	S	R	T	T	I	F	S	P	L	R	E	G	R	L	Y	Q	V	E	Y	A	M	E	A	I	S	H	A	.	G	T	C	L	G	I	L	S
R	Y	D	S	R	T	T	I	F	S	P	.	.	E	G	R	L	Y	Q	V	E	Y	A	M	E	A	I	S	N	A	.	G	T	A	I	G	I	L	S
R	Y	D	S	R	T	T	I	F	S	P	.	.	E	G	R	L	Y	Q	V	E	Y	A	M	E	A	I	S	H	A	.	G	T	C	L	G	I	L	A
R	Y	D	S	R	T	T	I	F	S	P	.	.	E	G	R	L	Y	Q	V	E	Y	A	M	E	A	I	G	H	A	.	G	T	C	L	G	I	L	A
R	Y	D	S	R	T	T	I	F	S	P	.	.	E	G	R	L	Y	Q	V	E	Y	A	M	E	A	I	G	N	A	.	G	S	A	L	G	V	L	A
R	Y	D	S	R	T	T	I	F	S	P	.	.	E	G	R	L	Y	Q	V	E	Y	A	L	E	A	I	N	N	A	.	S	I	T	I	G	L	I	T
S	Y	D	S	R	T	T	I	F	S	P	.	.	E	G	R	L	Y	Q	V	E	Y	A	L	E	A	I	N	H	A	.	G	V	A	L	G	I	V	A



Use sequences to predict protein structure

Protein structure prediction

Protein PFF0165c

MSNKKRSKNENDESTSLPENSELLIEYIHNLSCLNVYRREIQEKNKYISIIKNDLSFHEC
ILTNVNVVWSVFNNDDLNLNLCNNEQKEEGEEIIKQRNIGDEINEYNNLTKLQNDENIKNNNM
IKEDLEDDANQNILMKSPYYNIENFLQVFLKYINKKKKKVKVKVDEGKKEKIEDKKYEQDD
EEENEEEEEEEEEGEENKEDEEFFKTFVSFNLYHNNNEKNISYDKNLVKQENDNKDEAR
GNDNMGNYDIHNERGEMLDKGKSYSGDEKINTSDNAKSCSGDEKQVITSDNGKSYDYVKNES
EEQEEKENMLNNKKRSLECNPNKAKKICFSLEEKIGTVQSVKLKEYNELSKENIEKNKHDDN
NICNYLSHNEGENVIEREDKLPNKLNNKNYRNEEEKKNQINFDYLKKKIKNNQDVFEETIQ
KCFILNLKKTTLNLINKIMYLNVEFRKYNLDYIRKINYEKCFYKNIYIDIKKKISELQKDNE
SLKIQVDRLEKKKATLIYKLNNDNIRKHILDNNIKDYQNGIDNSKVSFYFDEGENPYNRNNKN
YRTDNKNSDDNNNNNNYYNNYNSDDNYSNEDNEYNNGNYRFRNNYKDSLNEDDVKKNPLK
VCHKINSDSNIFVNFENIITQNIHSEPPFRNLLKESNELYITLKEKEKENIILKNEILKME
NKKDEEYEHLLNNTIEDKKELTRSIKELEINMMTCNMEKDKISNKVNTLEYEINVLKNIDKN
QTMQLQOKENDILKMKLYIEKLLSEKNLKDKIILLENKDKMLSGIHIKDNSFNEEKSEE
GKIQLRDIQNDNDEKYDDEKKRFKELFIENQKLKEELNKKRNVEEELHSLRKNYNIINEEIE
EITKEFEKKQEVDDEMILQIKNKELELLDKFNNKMNAVEEKLKELKNTYEEKMKHINNIY
KKHDDFVNIYLNLFQARKNAILSDSQREEQMNLFIKLDKYDIIFQKKIELTDILKNVYDC
NKKLIGHCQDLEKENSTLQNKLSNEIKNSKMLSKNLSKNSDDHLLIEENNELRRRLICSVCM
ENFRNYIIKCGHIYCNCIFNNLKTRNRKCPQCKVPFDKKDLQKIFLD

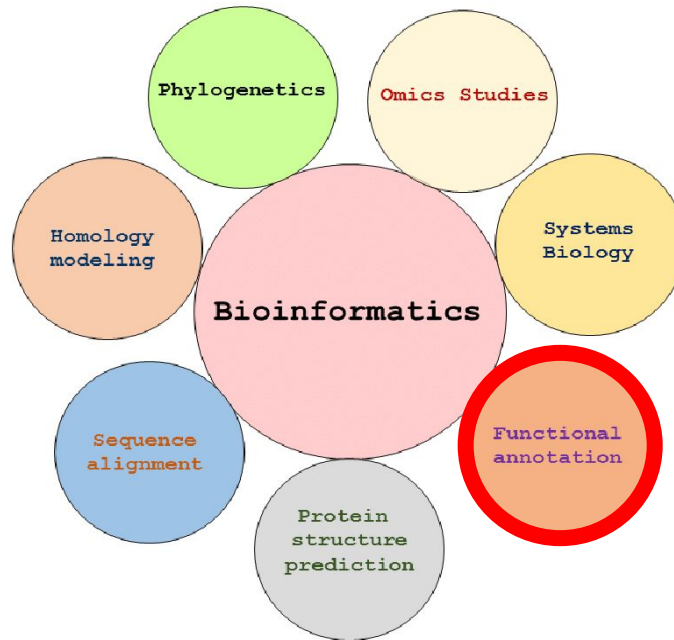
Schematic Representation



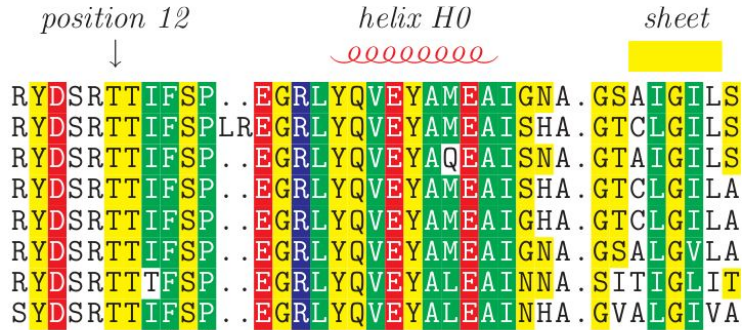
Use sequences to predict protein structure

What is bioinformatics?

- Combines biology and computer science to **interpret biological data**

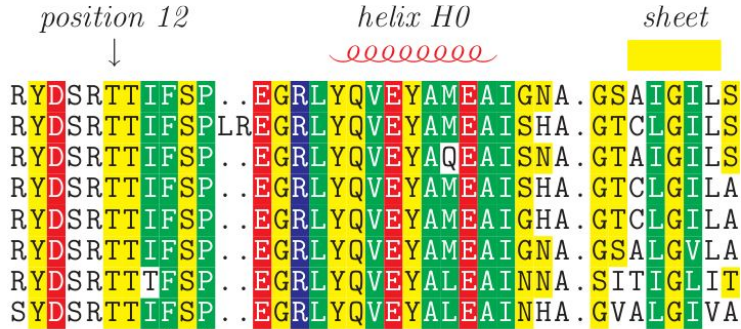


Functional annotation (aka labeling a protein's function)



Take protein sequence OR entire
genome (many many protein
sequences) of interest

Functional annotation (aka labeling a protein's function)



one protein sequence

BLAST - blastn suite - results for NM_001275.Homo sapiens chromogranin A (CHGA)

Job Title: NM_001275.Homo sapiens chromogranin A (CHGA)...

Database: refseq_mrna

Query ID: NM_001275.4

Description: Homo sapiens chromogranin A (CHGA), transcript variant 1, mRNA

Molecule type: nucleic acid

Query Length: 1985

Other reports: Distance tree of results MSA viewer

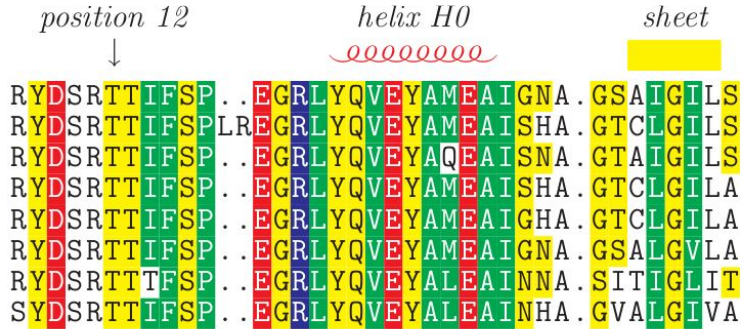
Sequences producing significant alignments

Accession	Score	Expect	Identities	Positives	Gaps	Frame	Accession
NM_001275450.1	3081	0.00	94.77%	3075	0.00	0.00	Mus musculus chromogranin A (CHGA) mRNA
NM_001310860.1	3075	0.00	94.72%	3070	0.00	0.00	Mus musculus chromogranin A (CHGA) mRNA
NM_001081812.2	1626	1626	80%	1626	0.00	0.00	Caenorhabditis elegans chromogranin A (CHGA) mRNA
NM_001050502.2	1548	1548	80%	1548	0.00	0.00	Bos taurus chromogranin A (CHGA) mRNA
NM_001168025.2	1415	1415	80%	1415	0.00	0.00	Sus scrofa chromogranin A (CHGA) mRNA
NM_001365552.2	270	270	80%	46-72	80.24%	0.00	Rattus norvegicus chromogranin A (CHGA) mRNA
NM_001050502.2	170	170	11%	20-41	81.81%	0.00	Mus musculus chromogranin A (CHGA) mRNA

Stick it into NCBI BLAST (website) and find closest 'hit'. This may help tell you what this protein is. This might be more useful if looking at just one protein.

Take protein sequence OR entire genome (many many protein sequences) of interest

Functional annotation (aka labeling a protein's function)



one protein sequence

BLAST - blastn suite - results for RID-M3JFFUA010

Job Title: NM_001275:Homo sapiens chromogranin A (CHGA)...

Query ID: NM_001275

Query Length: 1985

Other reports: Distance tree of results MSA viewer

Sequences producing significant alignments

Description	Max Score	Total Score	Query %	E	Per. %	Accession
Mus musculus chromogranin A (CHGA) mRNA	3081	3075	99%	0.0	94.77%	NM_001275050.1
Mus musculus chromogranin A (CHGA) mRNA	3075	3075	99%	0.0	94.79%	NM_001310860.1
Caenorhabditis elegans chromogranin A (CHGA) mRNA	1626	1626	99%	0.0	83.09%	NM_001081810.2
Sus scrofa chromogranin A (CHGA) mRNA	1548	1548	99%	0.0	81.91%	NM_001050502.2
Sus scrofa chromogranin A (CHGA) mRNA	1415	1415	99%	0.0	83.09%	NM_001156025.2
Rattus norvegicus chromogranin A (CHGA) mRNA	270	270	99%	4e-72	80.94%	NM_001305502.2
Mus musculus chromogranin A (CHGA) mRNA	176	176	100%	2e-41	81.91%	NM_001050502.2

Stick it into NCBI BLAST (website) and find closest 'hit'. This may help tell you what this protein is. This might be more useful if looking at just one protein.

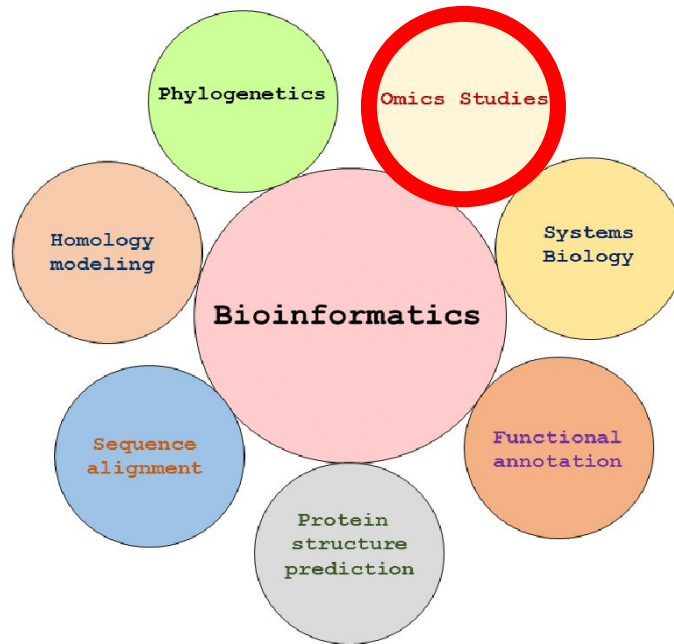
Take protein sequence OR entire genome (many many protein sequences) of interest

entire genome

BUT what we usually do when trying to determine what ALL of the proteins are in a genome is use a program to 'annotate' each gene and tell us what function it has. For example, it can tell us which protein is a photosystem I in our cyanobacteria, so now we know that this is likely a photosynthesizing organism.

What is bioinformatics?

- Combines biology and computer science to **interpret biological data**



'Omics studies

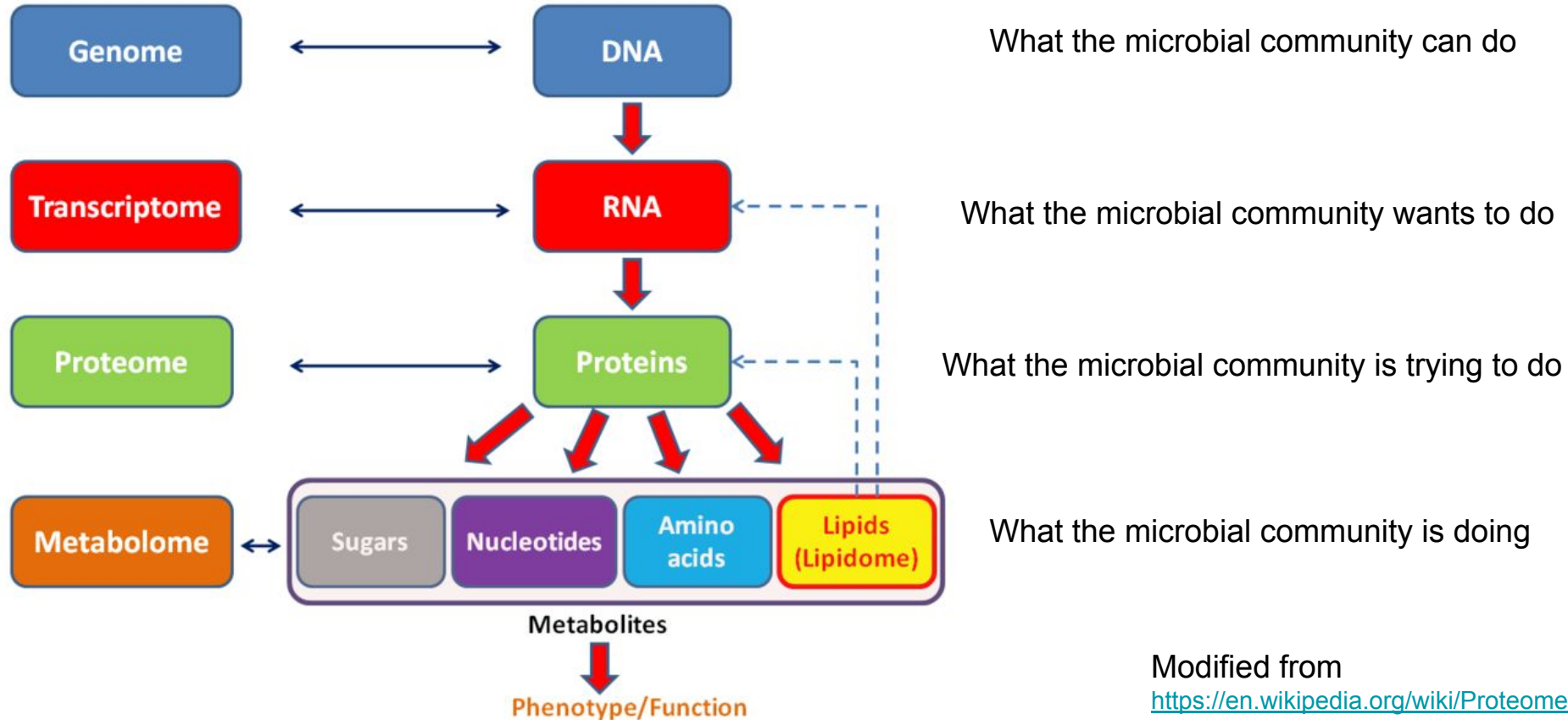
Types of 'omics studies:

- (Meta)genomics
- Transcriptomics
- Metabolomics
- Proteomics

Questions you can answer:

1. Who is there?
2. What might they be able to do?
3. Who is doing what?
4. How do these organisms or genes fit into the context of evolution?
5. And more!

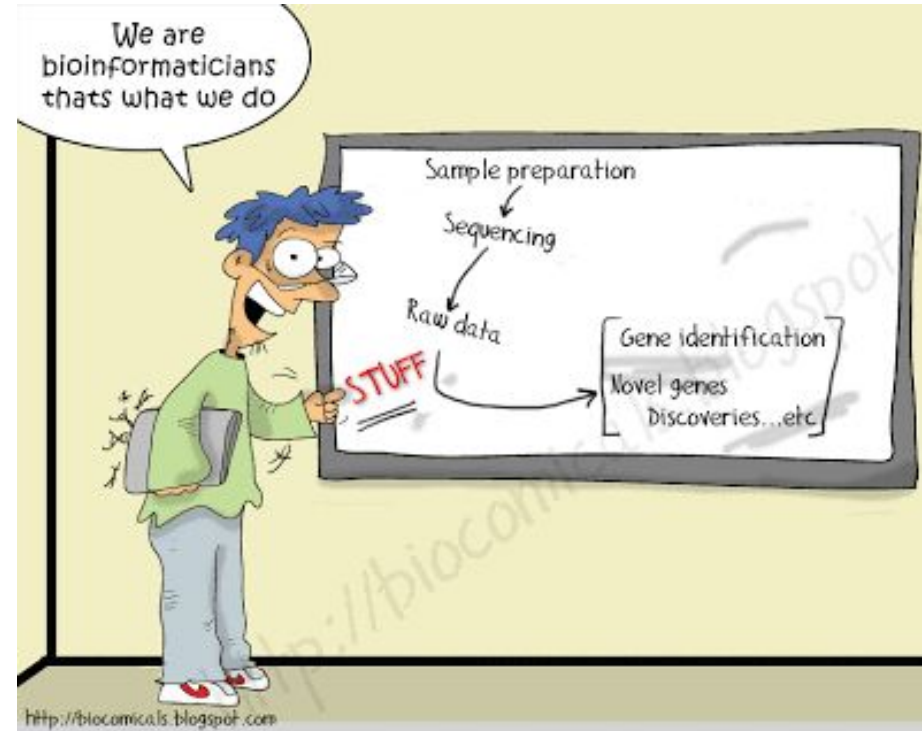
The omics cascade



Revisiting: What is bioinformatics?

- Bioinformatics is a subdiscipline of biology and computer science concerned with the acquisition, storage, analysis, and dissemination of biological data, most often DNA and amino acid sequences. Bioinformatics uses computer programs for a variety of applications, including determining gene and protein functions, establishing evolutionary relationships, and predicting the three-dimensional shapes of proteins.

Make more sense?!



Where do we do these bioinformatic analyses?

Locally (aka on your 'local' computer)

Pros:

- Anyone with a computer can perform basic bioinformatic tasks
- Don't need access to an HPC

Cons:

- Can do small amounts of computing
- Not good for large programs -installing takes a lot of space on your computer (this is where memory/ram and processors come into play)
- Not good for large datasets (memory and storage on your computer)

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Terms in case you are interested:

- **RAM (Random Access Memory):** used as a short-term memory storage space for the computer to place data it's currently working on so it's easily accessible. The more RAM a computer has, the more data it can usually juggle at any given moment.
- **CPU (Central Processing Unit):** provides the instructions and processing power the computer needs to do its work. The more powerful and updated your processor, the faster your computer can complete its tasks. By getting a more powerful processor, you can help your computer think and work faster.

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- Not good for large datasets (memory and storage on your computer)

HPC (aka cluster computing)

Pros:

- Can store and process lots of data much faster than your local computer

Cons:

- Need access to an HPC (\$\$)

What really is an HPC cluster?

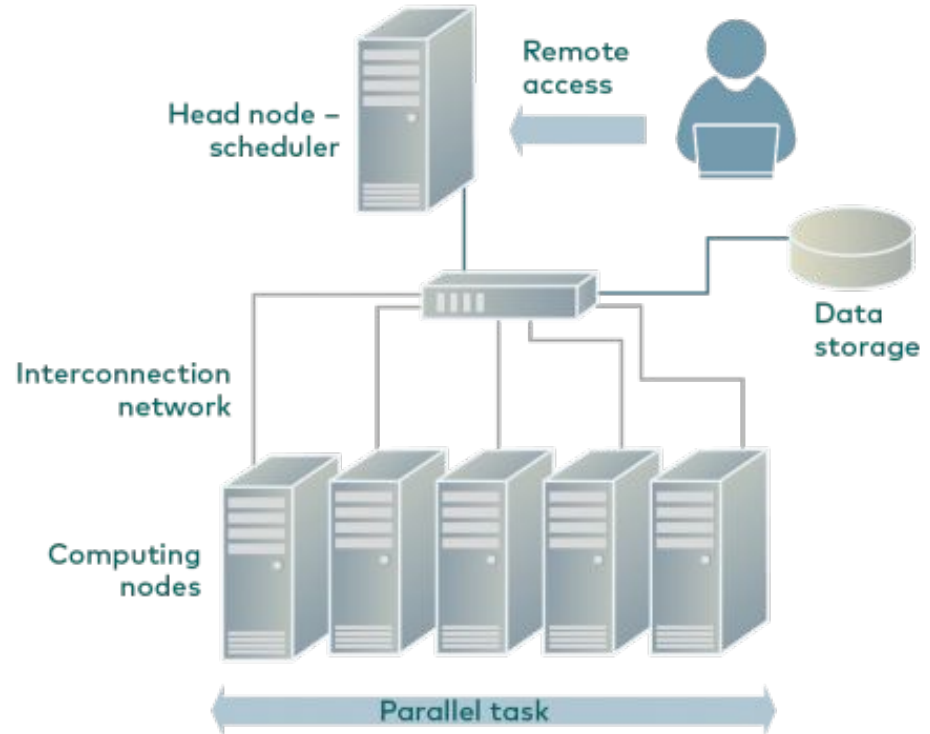


Less dramatically...



High performance computing (HPC) (cluster computing)

- An **HPC cluster** is a collection of many separate servers (computers), called **nodes**, which are connected with a fast interconnect.
- Each of the **HPC clusters** has a **headnode** or login node, where users log in and can schedule a task.
- When you schedule a task, you can ask for how many **nodes**, **cores**, and **threads** you need.



Nodes, cores, and threads

- A **node** is (typically) an individual computer, connected to others through a local network. A **node** contains (normally) a single **CPU** which contains one or more **cores**.
- **Cores** can implement hyper **threading**, allowing each core to handle the execution of several **threads**.
- If job is split between several processors, can perform many tasks *simultaneously* (faster).

