United Nations
Educational, Scientific and
Cultural Organization

UNESCO Chair on Adolescent Health Care
National and Kapodistrian University of Athens
Greece

UNIVERSITY
RESEARCH INSTITUTE
OF MATERNAL
AND CHILD HEALTH
& PRECISION MEDICINE

Open Science, Artificial Intelligence, Machine Learning, Precision Medicine, and Health

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Director, University Research Institute on Maternal and Child Health and Precision Medicine,

Holder, UNESCO Chair on Adolescent Health Care,

National and Kapodistrian University of Athens

Open Science = Knowledge for Everyone

Agora *vs.* Clergy

Ancient Greece *vs.* Ancient Egypt

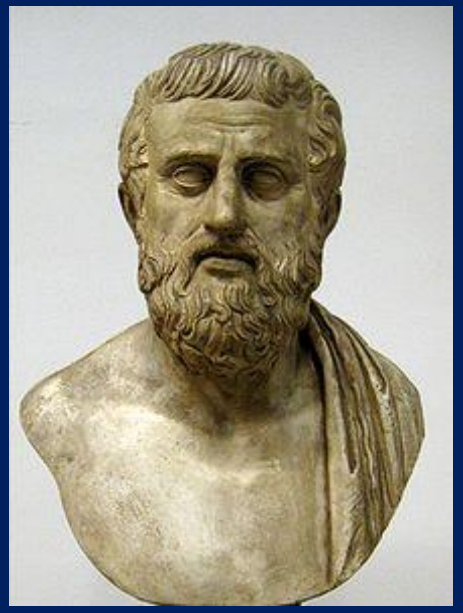
THE SCHOOL OF ATHENS: AGORA by Raphael


WHY
A.I.


What can the compurers
do that we can't?

Intelligence *vs.* Artificial Intelligence


WHAT
WENT
WRONG



“Πολλά τα δεινά κ’ουδέν ανθρώπου δεινότερον πέλλει.... ”

'There are many wonderful things and nothing is more wonderful than the human ... ”

Σοφοκλής

Sophocles

496-406 BCE

HUMAN COMPLEXITY: POST(EPI)GENOMIC ERA

Human genome:

About 3+3 billion bases, 98% formerly "junk DNA", 40-60% retroviral!
About 20 thousand protein-coding genes
About 24 thousand ncRNA-coding genes
About 16 thousand pseudogenes
About 100-140 thousand transcripts
(mRNAs, ncRNAs = miRNAs, lncRNAs, piRNAs, cRNAs, eRNAs)
About 200-260 thousand proteins

Single nucleotide polymorphisms (snp's or snv's),
microsatellites or copy number variants : **(91.1 *vs.* 0.9%)**

>25 million snp's (snv's), 1.5 million indels
About 20 million microsatellites
>5000 cnv's (many million bases), > 100 k disease-related mutations
>60% of promoters have CpG islands, >1 million reg. regions
Superenhancers

↓

EPIGENETICS (Epi)mutations

HUMAN COMPLEXITY: SOME HUMAN BRAIN NUMBERS

~ 100 billion neurons ($100x10^{12}$) x >10.000 synapses per neuron
= >10^{18} synapses)
~ 100.000 km of fibers
~ 1 trillion or more glial cells
~ 1.25 terabytes (recalculated ~1.4 petabytes)
~ 15 Watt lamp (2% of BW uses 20% energy)

↓

Plasticity

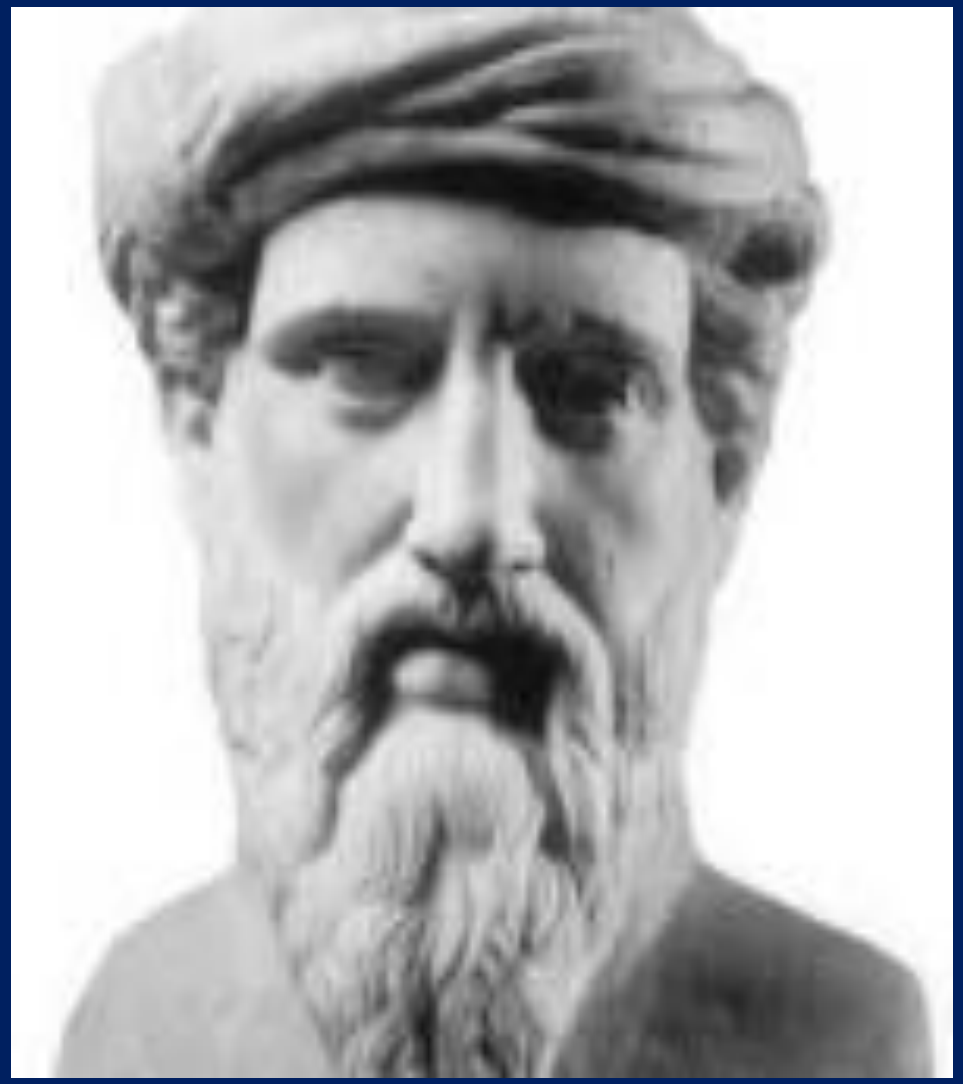
Complex Systems

- **Multiple interactants**
- **Self-organizing**
- **Adapting through feedback loops**
- **Resilient to perturbations**
- **Emergent properties**

Emergent Properties

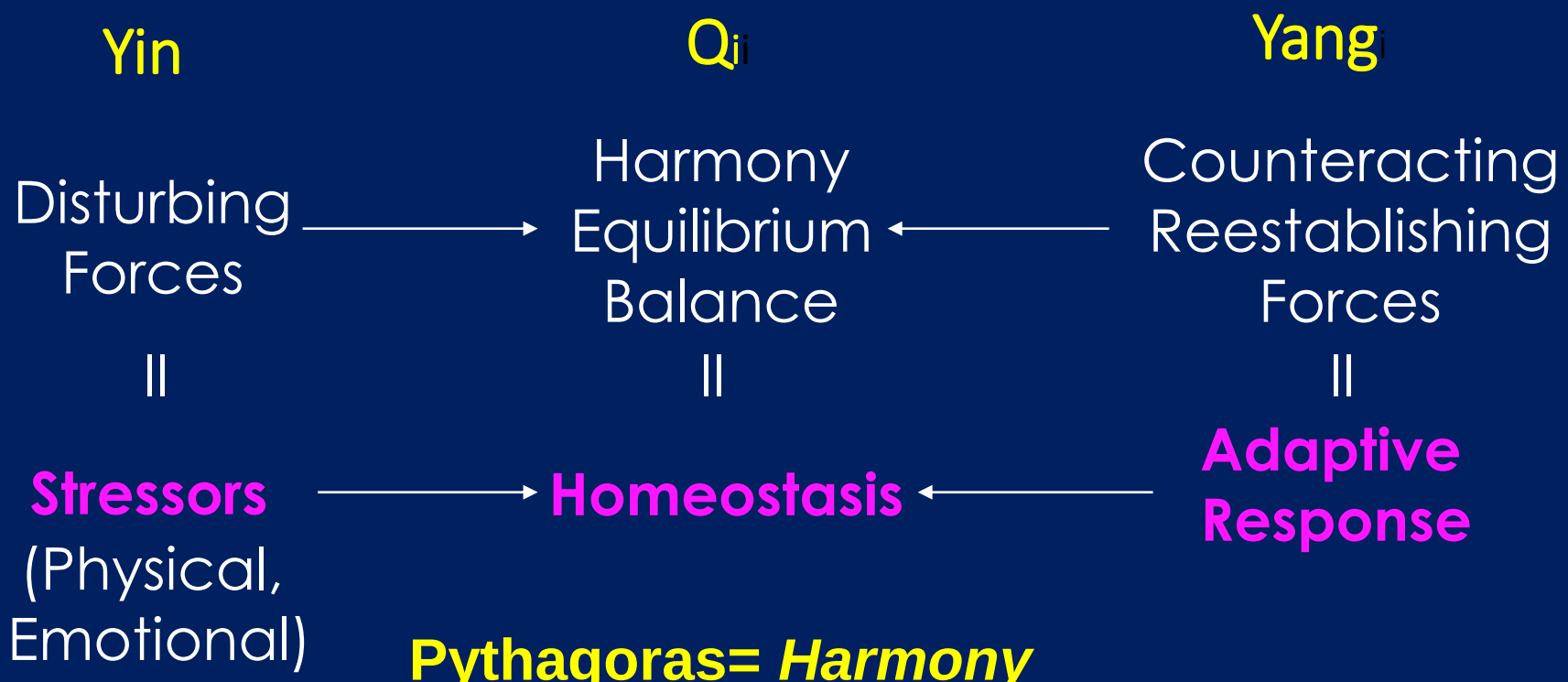
- **Earth Ecosystem**
- **Earth Life (Biosphere)**
- **Human beings**
- **Human intellect/soul**
- **Human civilization**

COMPLEXITY



Pythagoras 6th century BCE

Complex Systems Theory



Pythagoras= *Harmony*
Alcmaeon=*Iso-nomia*
Hippocrates= Eucrasia
Epicurus= Eustatheia
Walter Cannon= Homeostasis

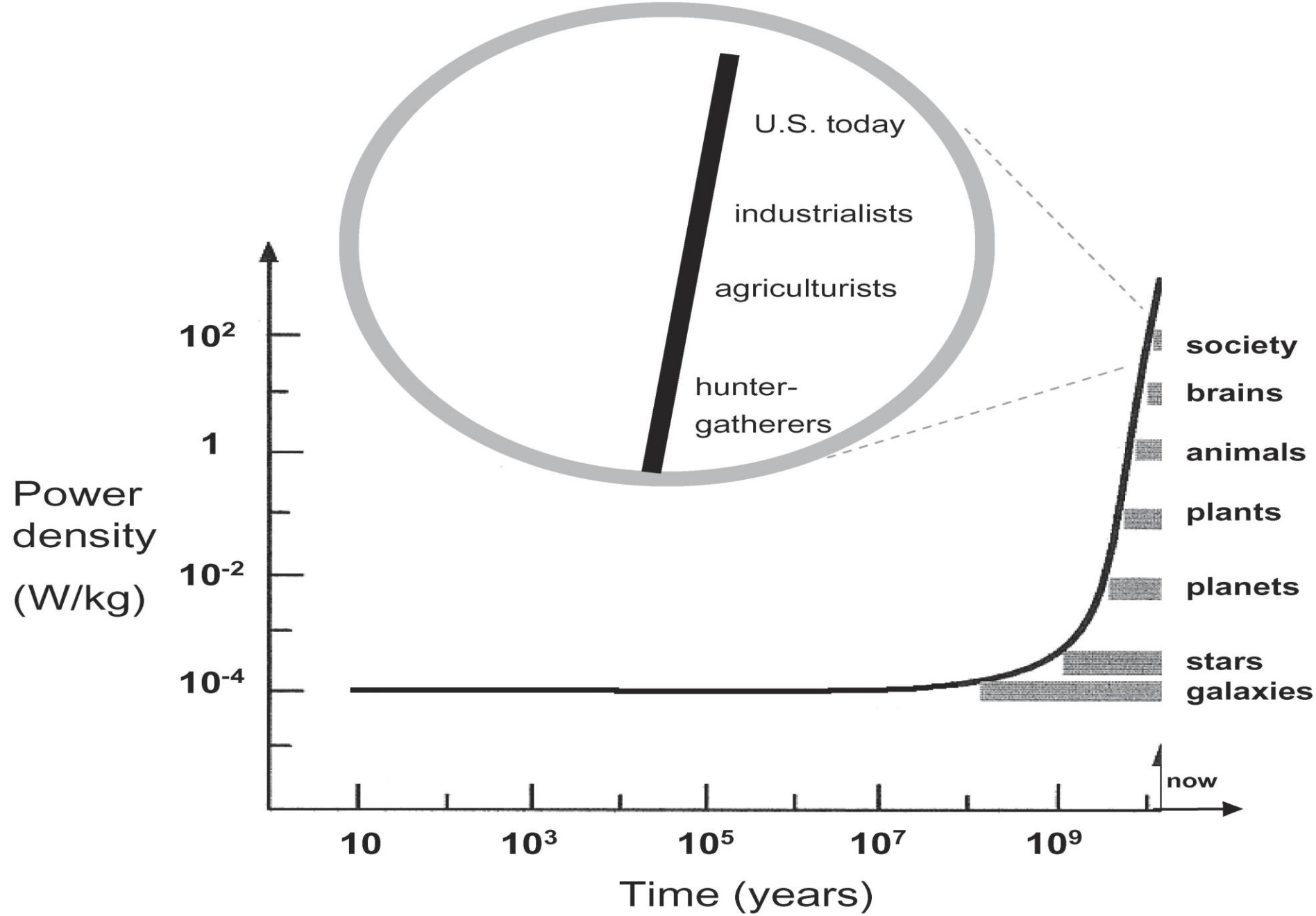
Complex Systems

“Αρμονία δ’εστί πολυμιγέων ένωσις και δίχα φρονεόντων συμφρόνησις”

“Harmony is the union of multiple mixed components and the agreement of the opposites”

Αλκμαίων Κροτωνιάτης
Almaeon of Croton

Stress is the State of Threatened (or Perceived as Threatened for us Humɑns) Homeostasis for any Complex System

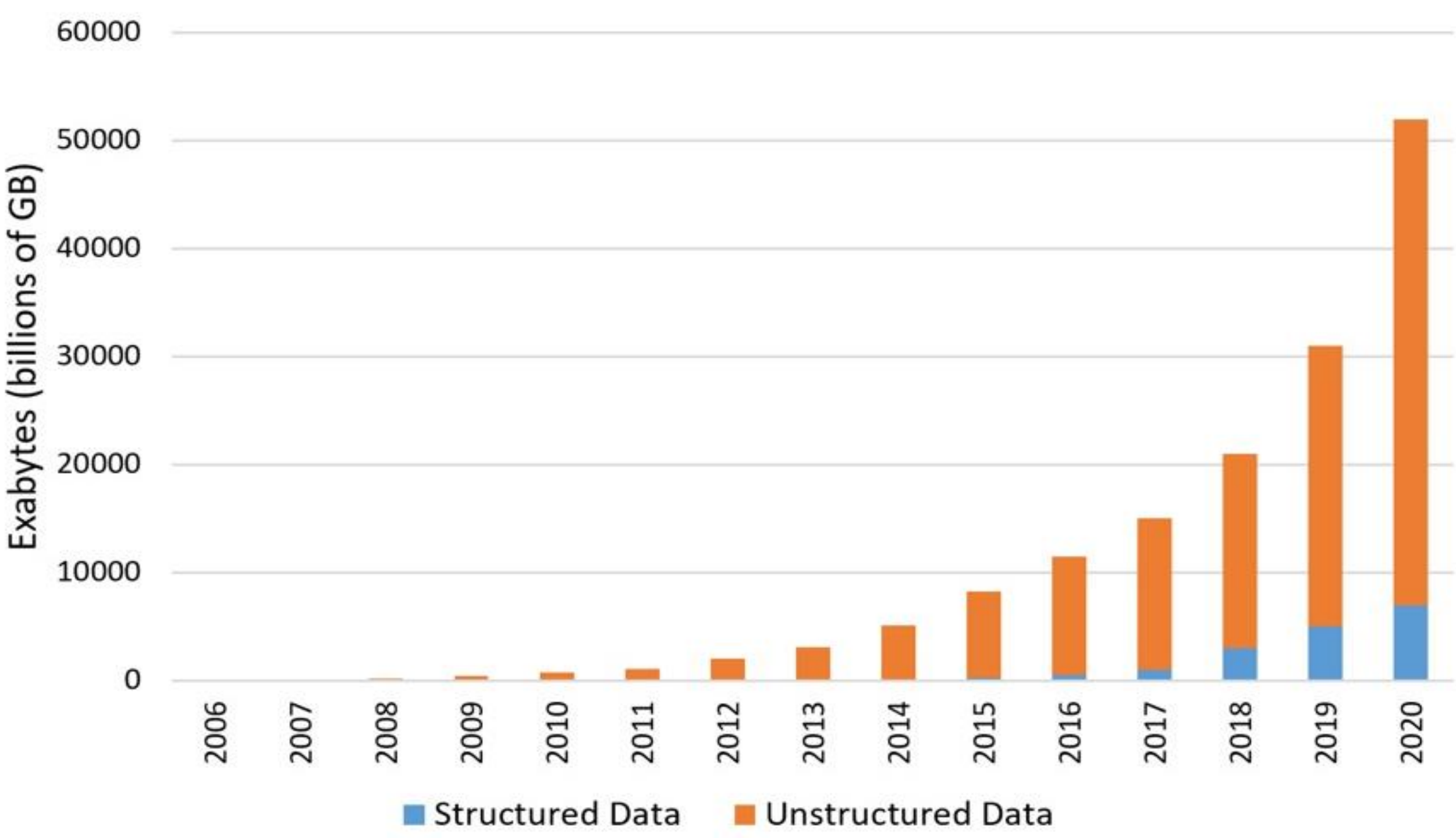

U.S. today
industrialists
agriculturists
hunter-
gatherers
Power
density
(W/kg)
10²
1
10⁻²
10⁻⁴
society
brains
animals
plants
planets
stars
galaxies
now
10
10³
10⁵
10⁷
10⁹
Time (years)

Man and his/her civilization are of unique complexity in the known universe.

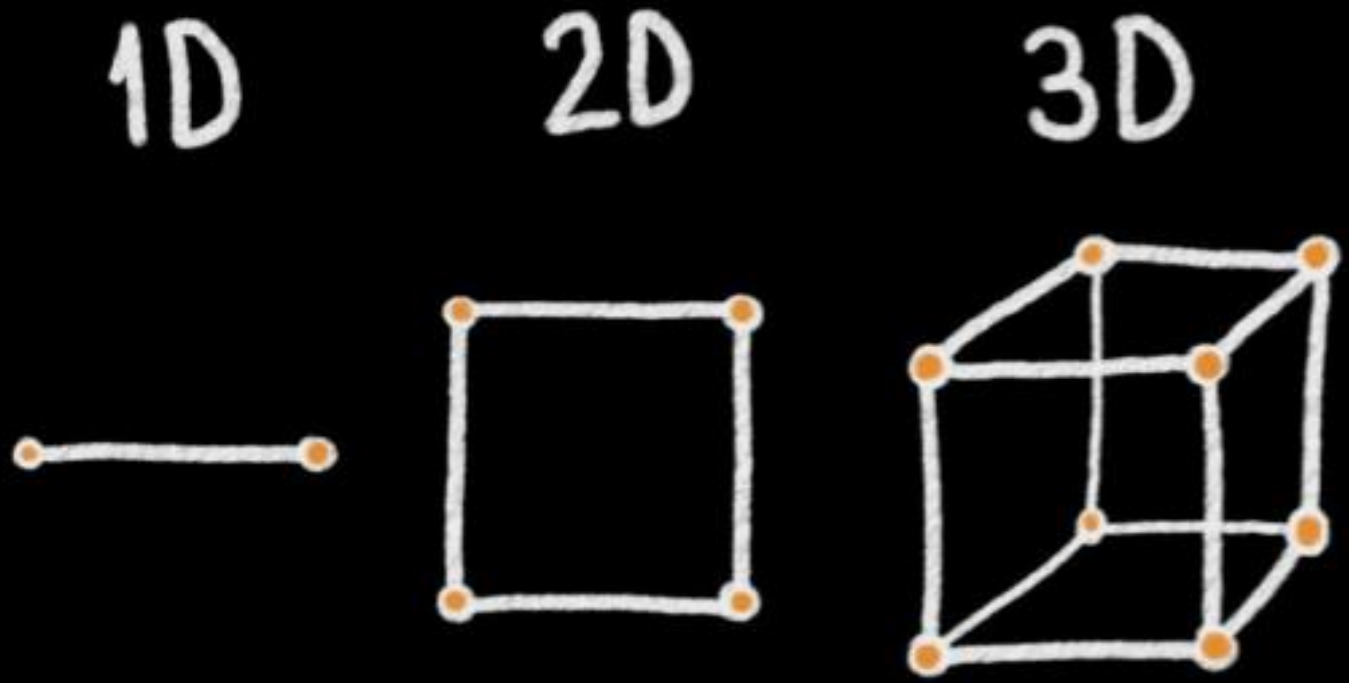
Complex systems are in a dynamic disequilibrium that requires energy to be sustained.

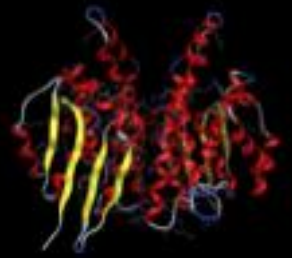
Complex systems have organizing principles and follow mathematic rules.

SYSTEMS BIOLOGY, SYSTEMS MEDICINE
NARRATIVE AND PRECISION MEDICINE
P4 MEDICINE (predictive, personalized, preventive, participatory)


60000
50000
40000
30000
20000
10000
0
Exabytes (billions of GB)
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
Structured Data
Unstructured Data

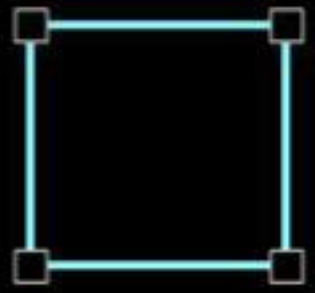
Why do we need artificial intelligence?



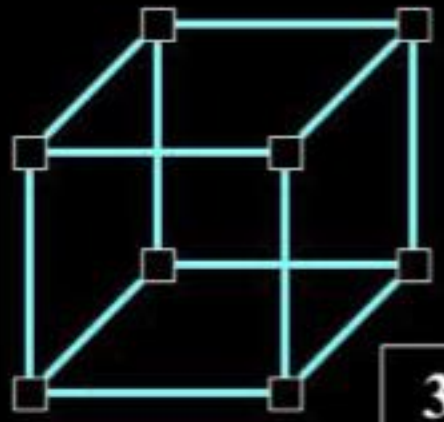


Let us add another dimension….

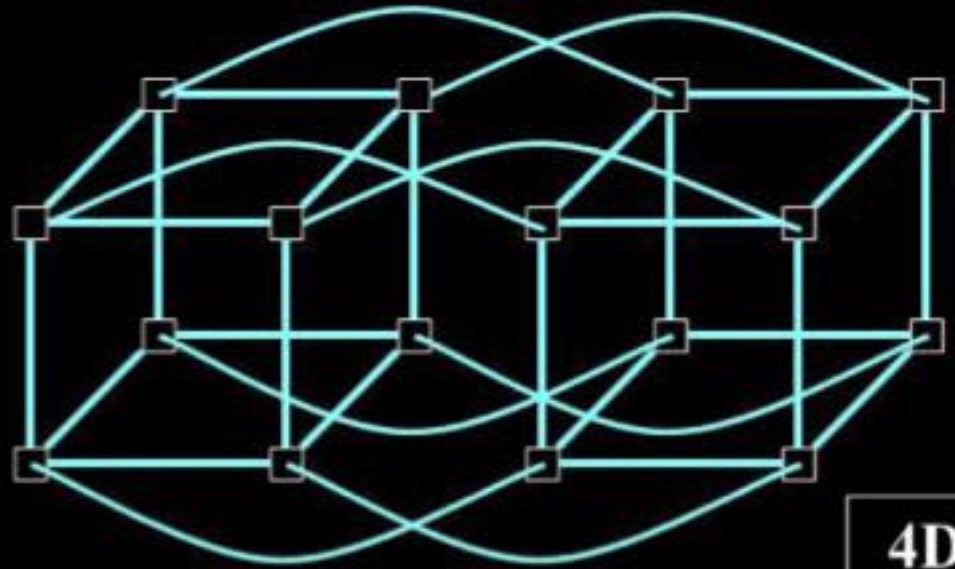
1D



2D



3D



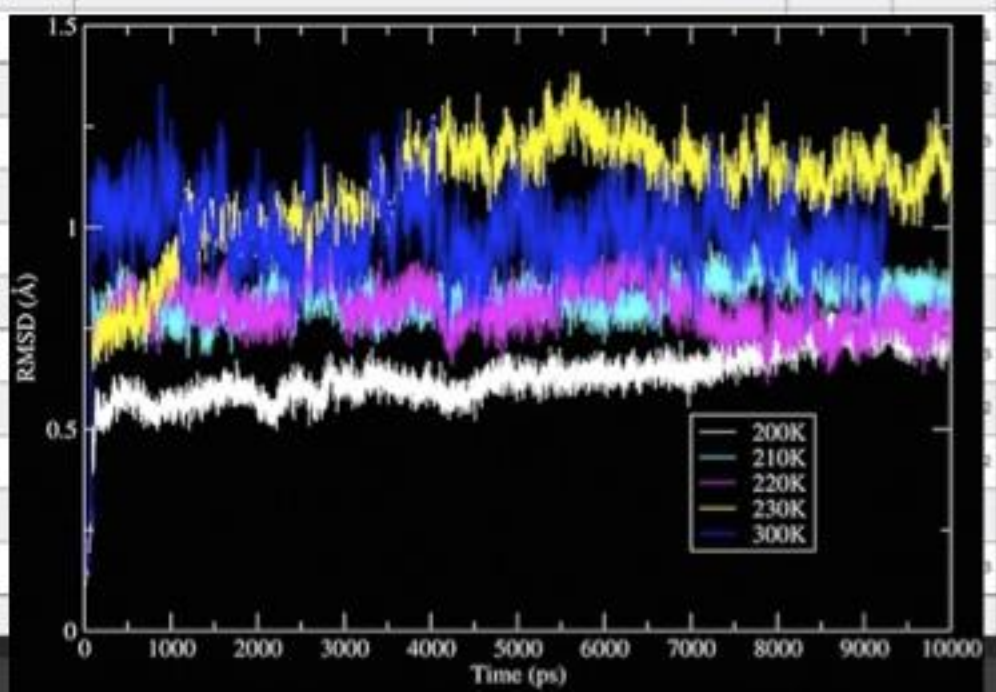
4D

aarhdna.gr

File Edit Display Compute Window Help

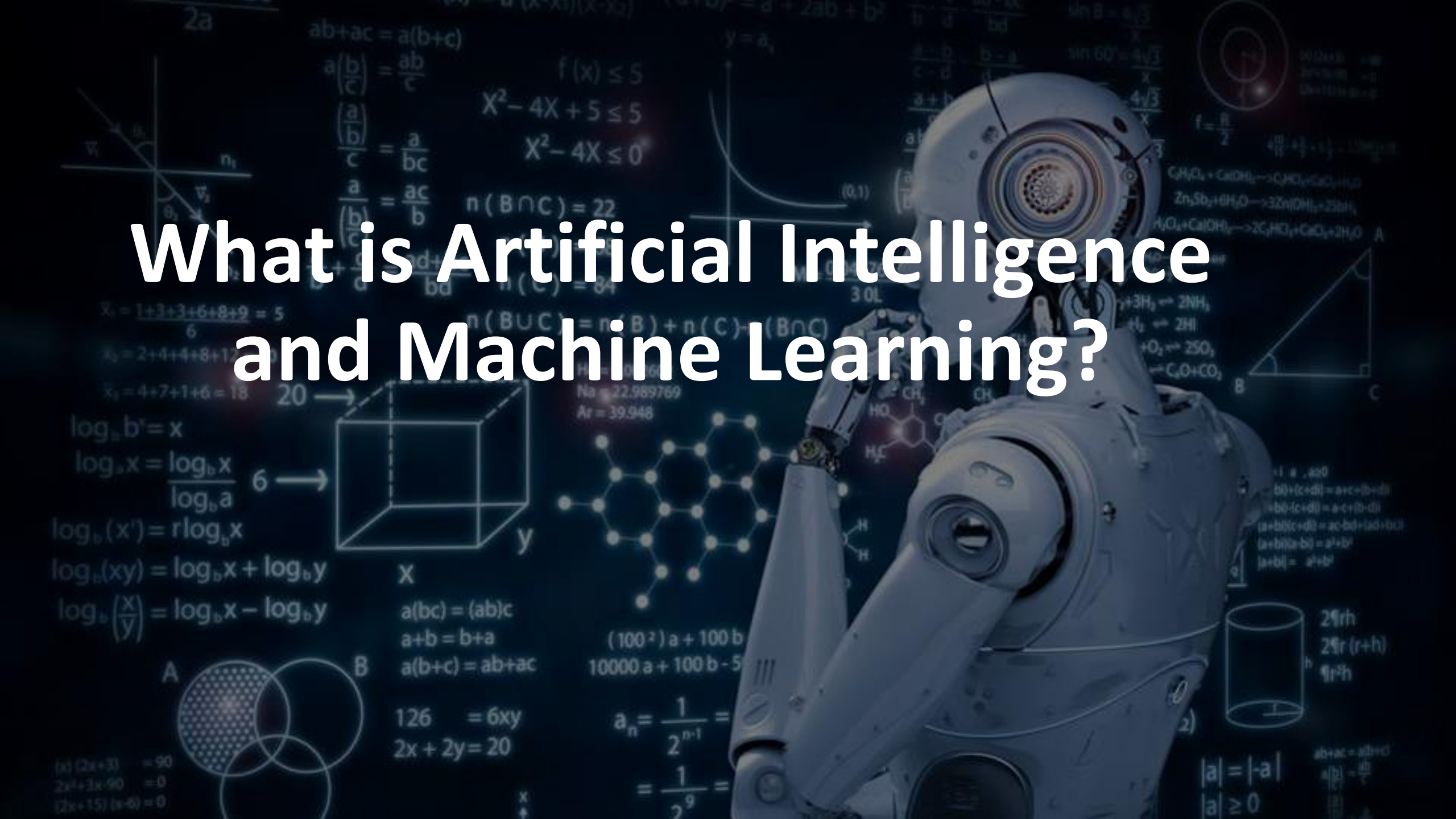
SVL DBV MOE Cancel

	mol	chain	_	domains	score	aligned	percent_identity	rmsd	suboptimal	mol:SSINFO	N	rpair	R	T	qm	AM1_dipole
2		2CLS.A	R	Ras (8.80035e-0	10.0000	168/177	44	1.2589	1	77 79 83 83 4 0 0 0 1 0 0 0 13 0 0 0 115 104 115 115 115 104 115 104 115 10	20	10 11 12 1	-0.0911 0.	-56.7336 -	0 2 3 4 5	0.0000
3		3RAP.B	P	Ras (2.49077e-0	9.6000	156/177	31	1.4283	1	77 79 83 83 4 0 0 0 1 0 0 0 12 0 0 0 115 104 115 115 115 104 115 104 115 10	18	2 3 4 5 6	-0.0815 0.	-56.7227 -	0 2 3 4 5	0.0000
4		2C5L.A	G	Ras (2.19980e-0	9.5000	158/177	31	1.3984	1	77 79 83 83 4 0 0 0 1 0 0 0 12 0 0 0 115 104 115 115 115 104 115 104 115 10	19	9 10 11 12	-0.0788 0.	-56.3822 -	0 2 3 4 5	0.0000
5		3REF.B	R	Ras (1e-047)	9.3000	161/177	41	1.2584	0	77 79 83 83 4 0 0 0 1 0 0 0 11 0 0 0 115 104 115 115 104 115 104 115 104 11	15	22 23 24 2	-0.0667 0.	-56.5721 -	0 2 0 0 4	0.0000
6		2W2V.A	R	Ras (1.20005e-0	9.0000	162/177	49	0.8813	1	77 79 83 83 4 0 0 0 1 0 0 0 13 0 0 0 115 104 115 115 104 115 104 104 115 10	15	9 10 11 12	-0.0937 0.	-56.5533 -	0 2 0 3 0	0.0000
7		5CH2.A	R	Ras (1.29987e-0	8.8000	157/177	29	1.6001	1	77 79 83 83 4 0 0 0 1 0 0 0 13 0 0 0 115 104 115 115 115 104 115 104 104 11	19	5 6 7 8 9	-0.1102 0.	-56.8583 -	0 2 3 4 5	0.0000
8		4CI2.A	R	Ras (7.29962e-0	8.8000	151/177	20	1.4692	1	77 79 83 83 4 0 0 0 1 0 0 0 12 0 0 0 115 104 115 115 115 115 104 115 104 10	16	29 30 31 3	-0.0753 0.	-56.2427 -	0 2 4 5 6	0.0000
9		4G01.B	R	Ras (1.39991e-0	8.6000	138/177	25	1.6208	0	77 79 83 83 4 0 0 0 1 0 0 0 11 0 0 0 115 104 115 115 115 104 115 104 104 11	13	11 12 13 1	0.0130 0.0	-93.6975 -	0 2 0 0 5	0.0000
10		1R2Q.A	R	Ras (2.49977e-0	7.9000	156/177	28	1.5849	1	77 79 83 83 4 0 0 0 1 0 0 0 12 0 0 0 115 104 115 115 104 115 104 115 104 10	17	5 6 7 8 9	-0.1254 0.	-56.9493 -	0 2 3 4 5	0.0000
11		1Z08.A	R	Ras (1.20005e-0	7.9000	158/177	24	1.6001	1	77 79 83 83 4 0 0 0 1 0 0 0 12 0 0 0 115 104 115 115 115 115 104 115 104 10	15	5 6 7 8 9	-0.1288 0.	-56.5491 -	0 2 4 5 6	0.0000
12		2IL1.A	R	Ras (1.69981e-0	7.8000	146/177	21	1.3303	1	77 79 83 83 4 0 0 0 1 0 0 0 12 0 0 0 115 104 115 115 104 115 104 104 115 10	18	25 26 27 2	-0.0719 0.	-56.2665 -	0 2 0 3 4	
13		3ICQ.B	G	Ras (2.09991e-0	7.7000	154/177	24	1.5559	1	77 79 83 83 4 0 0 0 1 0 0 0 10 0 0 0 115 104 115 115 115 115 104 115 115 10	15	3 4 5 6 7	-0.0662 0.	-56.1145 -	0 2 3 4 5	
14		3ESH.A	R	Ras (2.39994e-0	7.5000	155/177	27	1.3961	1	77 79 83 83 4 0 0 0 1 0 0 0 13 0 0 0 115 104 115 115 115 115 104 115 104 11	14	5 6 7 8 9	-0.0834 0.	-56.5194 -	0 2 4 5 6	
15		3BC1.A	R	Ras (1.99986e-0	7.4000	157/177	26	1.6369					-0.0665 0.	-56.7003 -	0 2 3 4 26	
16		1BYU.A	P	Ras (1.9002e-05	7.0000	139/177	21	1.6530					0.6366 -0.	-11.2738 3	0 2 0 5 6	
17		2J1L.A	R	Ras (5.40008e-0	6.6000	158/177	41	1.0635					0.9672 -0.	-98.7691 1	0 2 0 23 4	
18		2RHD.A	S	Ras (2.70023e-0	6.6000	145/177	25	1.3611					-0.0618 0.	-56.6260 -	0 2 0 0 5	
19		1RYF.A	R	Ras (6.09956e-0	6.5000	156/177	47	0.9504					-0.0955 -0	-27.1135 6	0 0 0 0 0	
20		1XTQ.A	G	Ras (4.79954e-0	6.5000	152/177	27	1.4516					-0.0704 0.	-56.6665 -	0 2 0 3 4	
21		2P5S.A	R	Ras (5.00035e-0	6.4000	142/177	25	1.3878					-0.0637 0.	-56.8873 -	0 2 0 0 4	
22		2BME.A	R	Ras (3.29989e-0	6.3000	161/177	28	1.3745					-0.0849 0.	-56.4731 -	0 2 3 4 5	
23		1Z06.A	R	Ras (4.70002e-0	6.3000	149/177	23	1.5831					-0.0852 0.	-56.3211 -	0 2 0 3 4	
24		2GF9.A	G	Ras (4.90004e-0	6.2000	136/177	22	1.5868					-0.0742 0.	-56.5143 -	0 2 0 0 5	
25		2ATV.A	R	Ras (5.30029e-0	5.8000	149/177	24	1.6478					-0.0944 0.	-56.4626 -	0 2 0 4 5	
26		2C3W.B	G	Ras (3.69999e-0	5.6000	141/177	23	1.5145					-0.0753 0.	-56.6864 -	0 2 0 0 4	

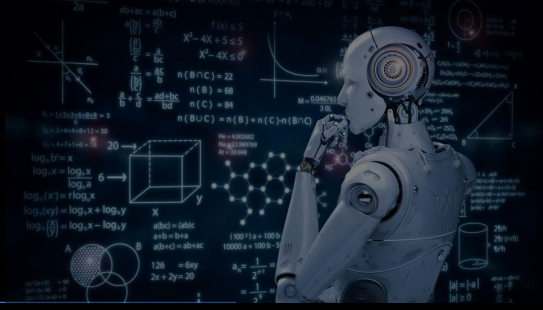


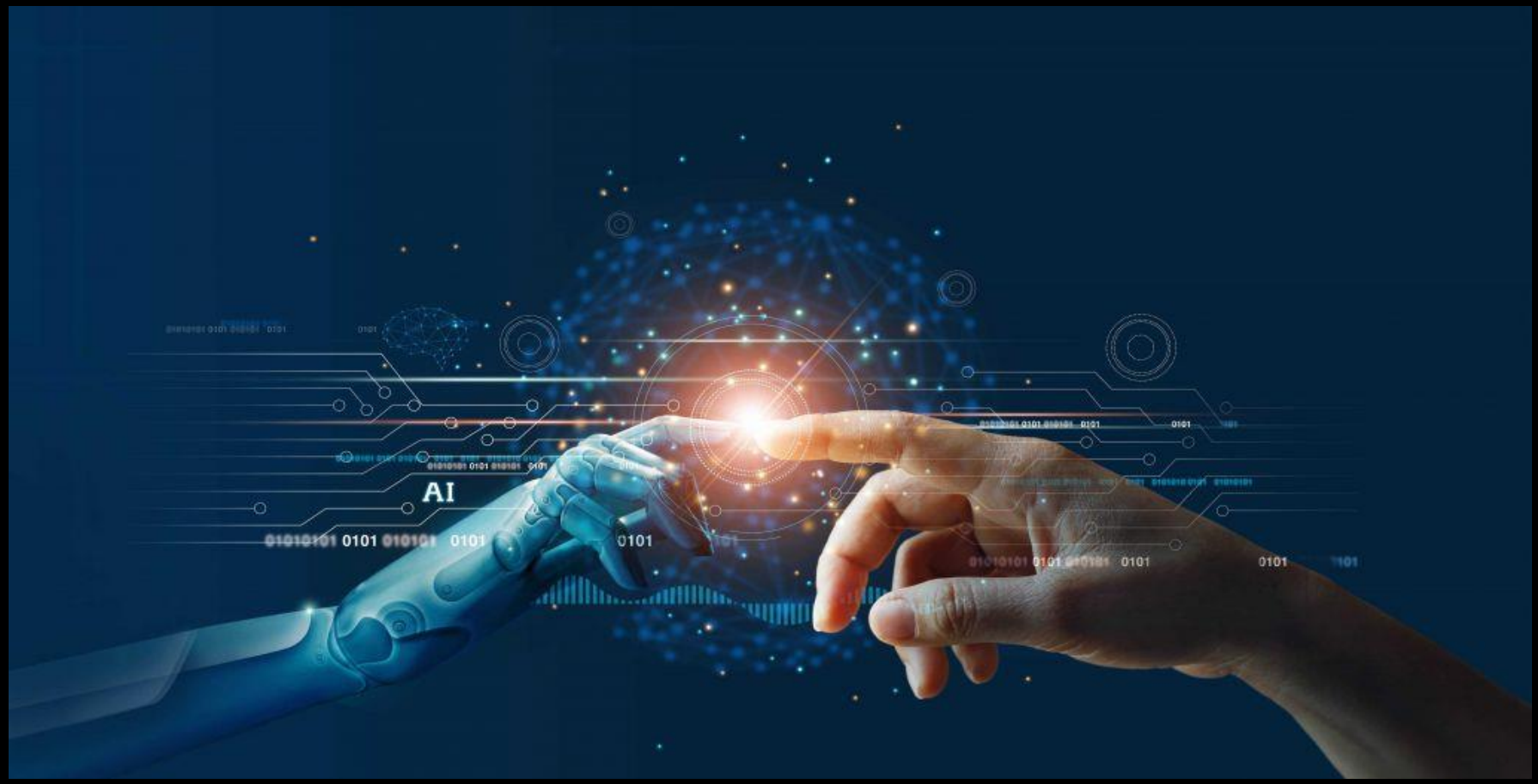
36 entries, 0 selected, all visible, 450 fields, 0 selected, all visible.

The problem of dimentionality…

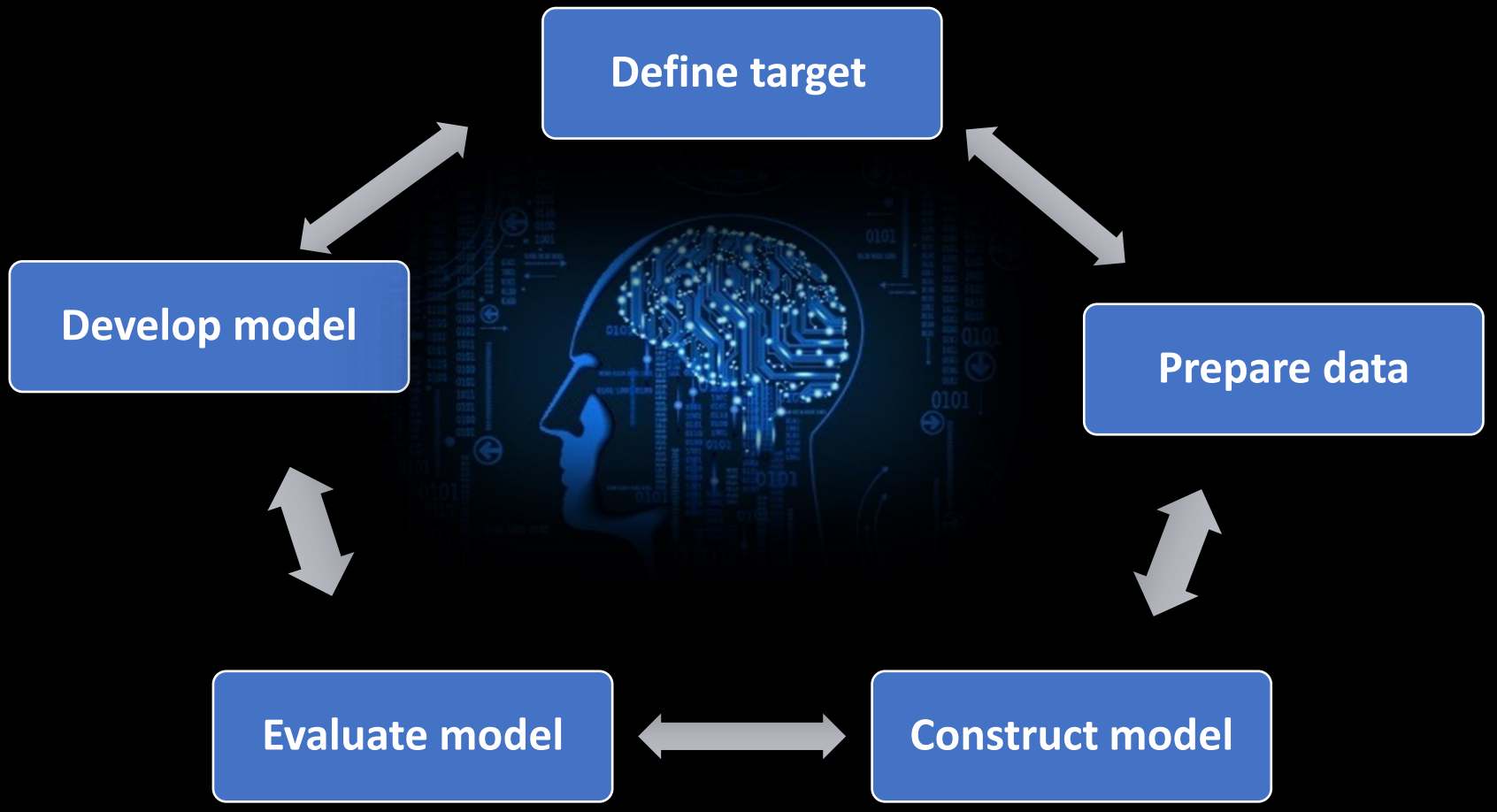

What is Artificial Intelligence and Machine Learning?

Artificial Intelligence…

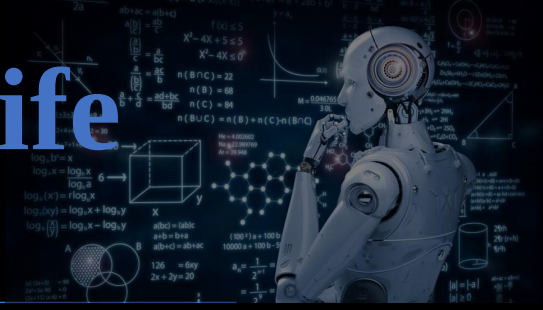




Machine Learning Process

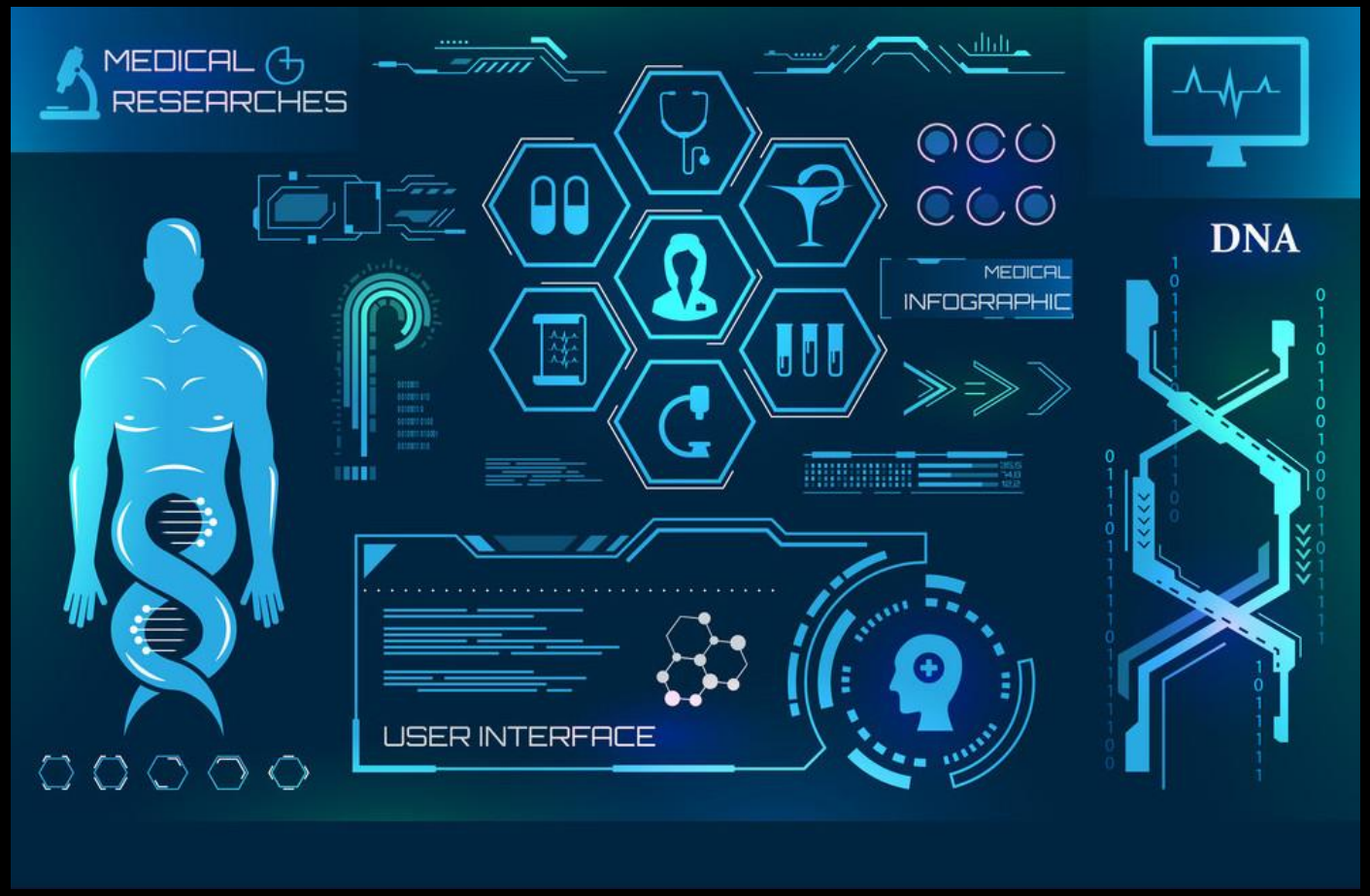


Applications of AI and ML in the Life Sciences

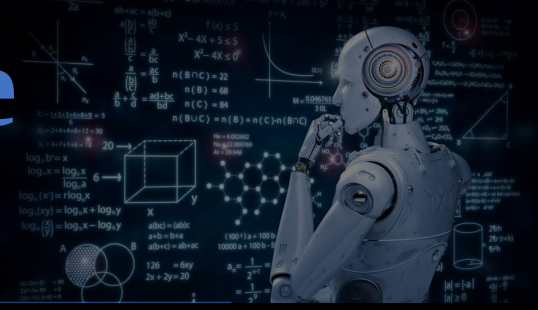


Precision Medicine:

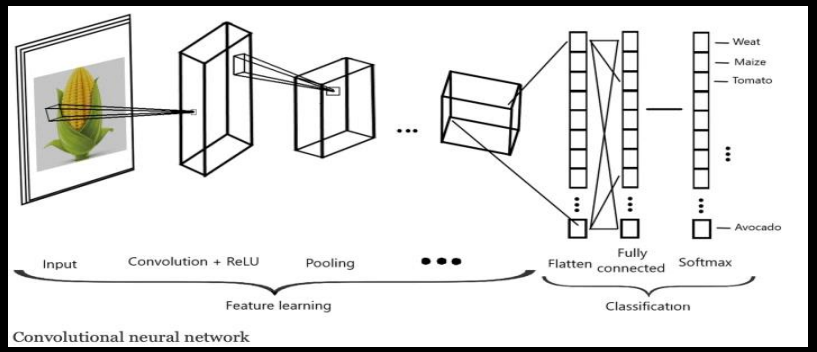
omics and clinical data used in the diagnosis, prevention, prognosis, and therapy of diseases



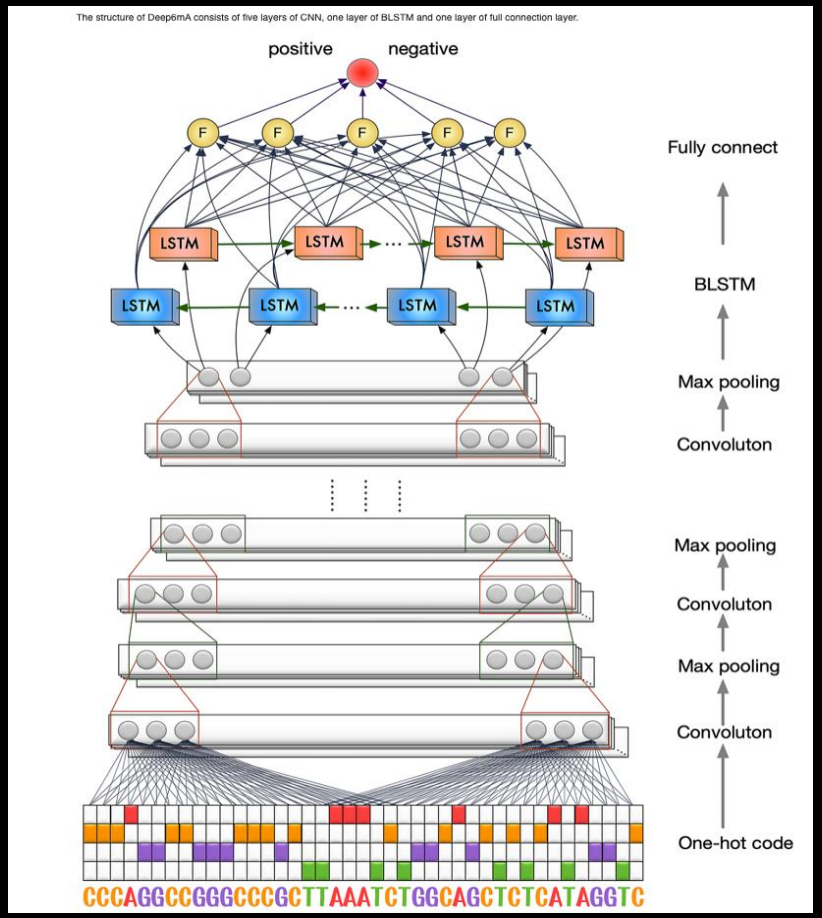
Applications of AI and ML in the Life Sciences



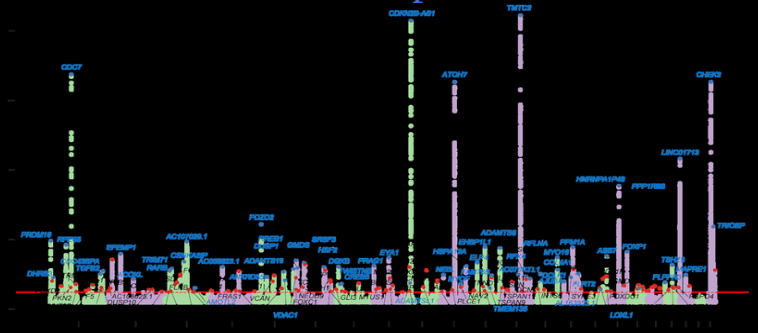
Genomics through image processing

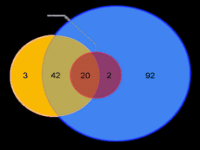


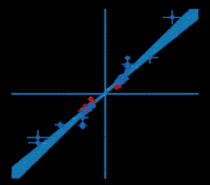
Model discovery on methylation



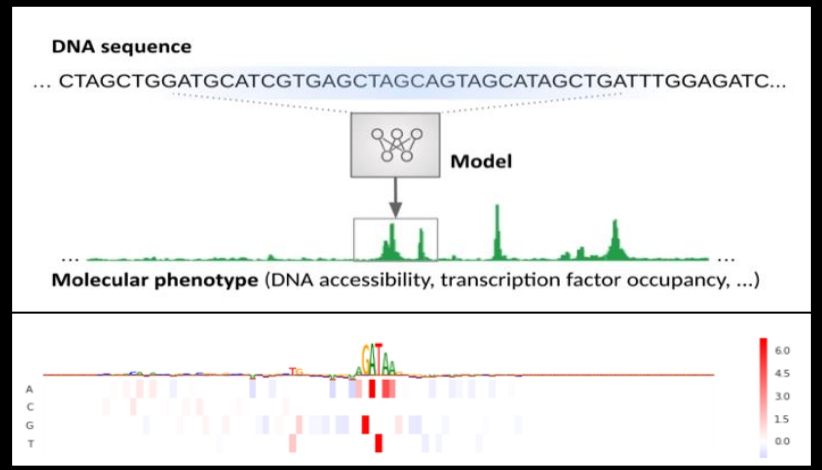
Genomic comparisons



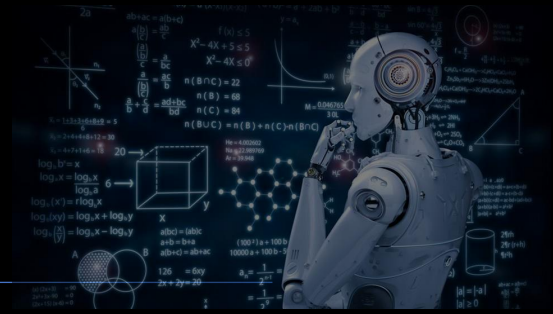




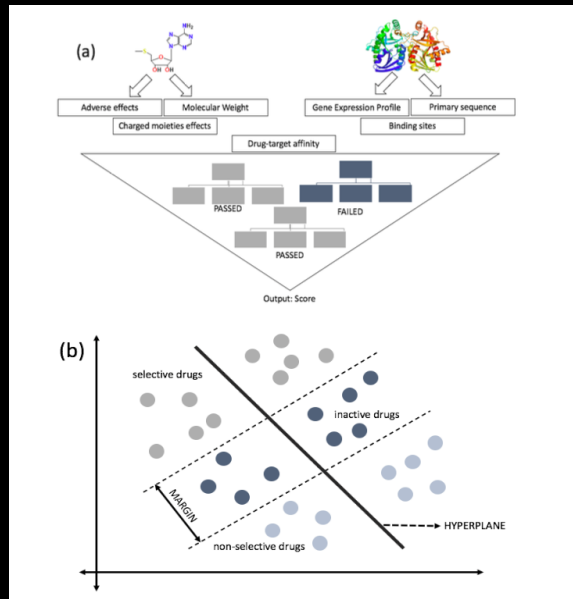
Transcriptional and posttranscriptional models of gene regulation

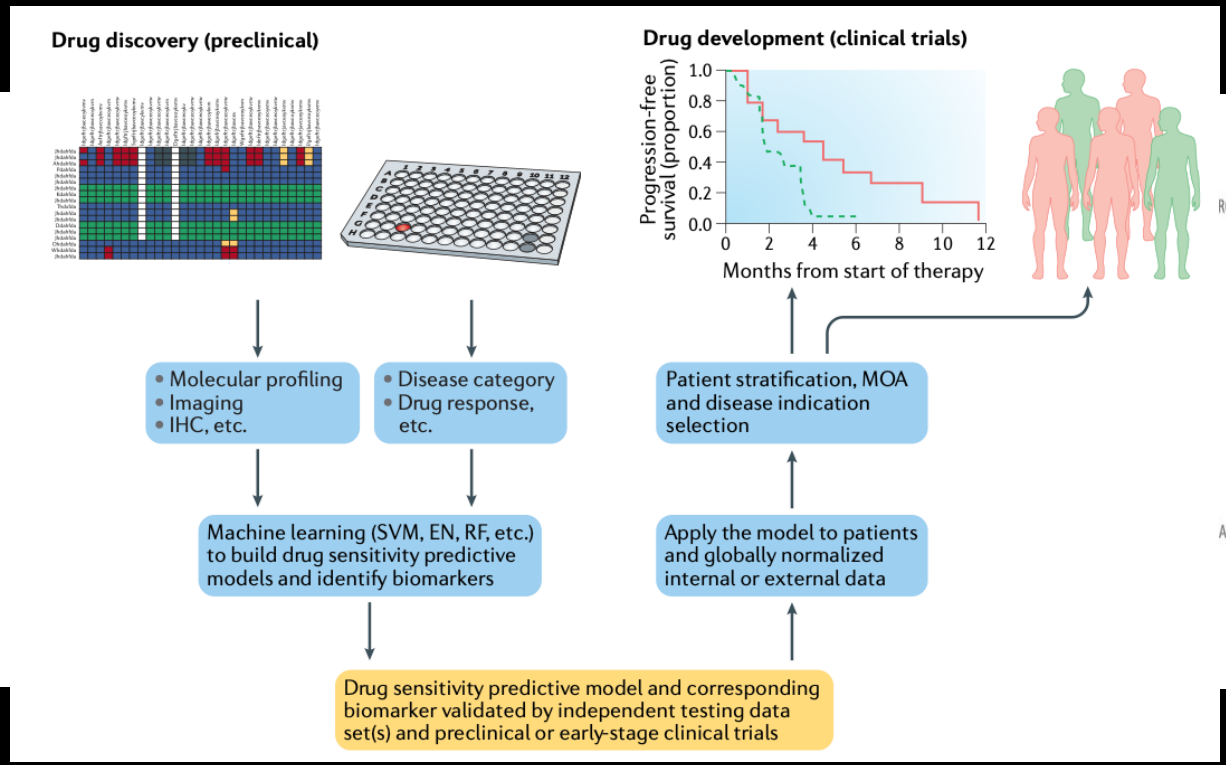


Applications of AI and ML in the Life Sciences

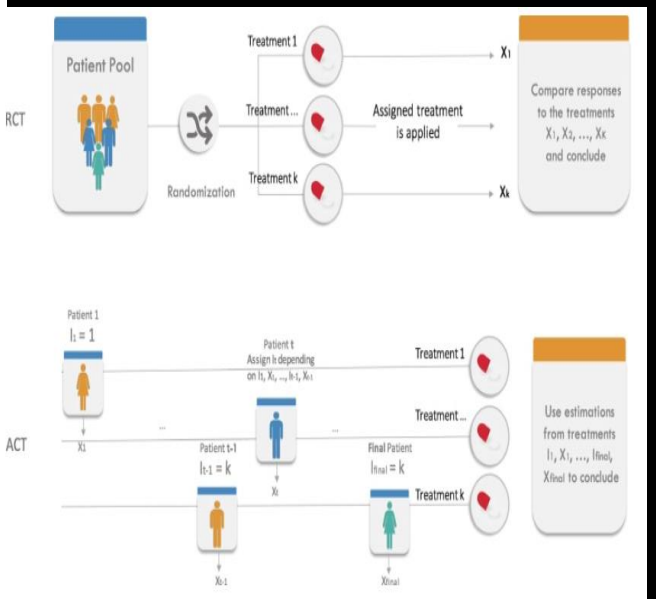


Drug Discovery





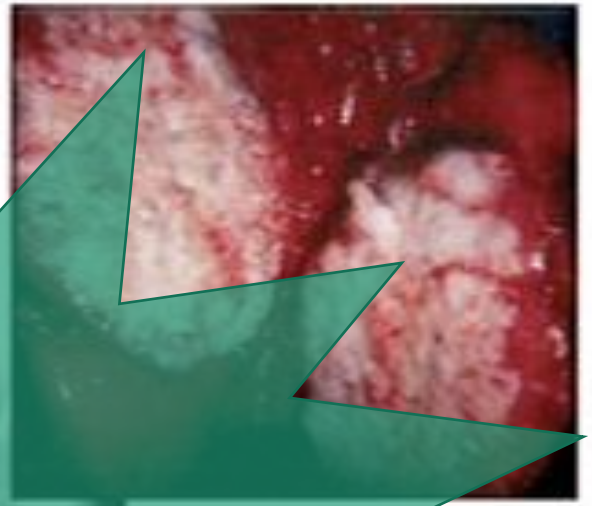
Clinical Trials



Development and Evaluation of Medicines

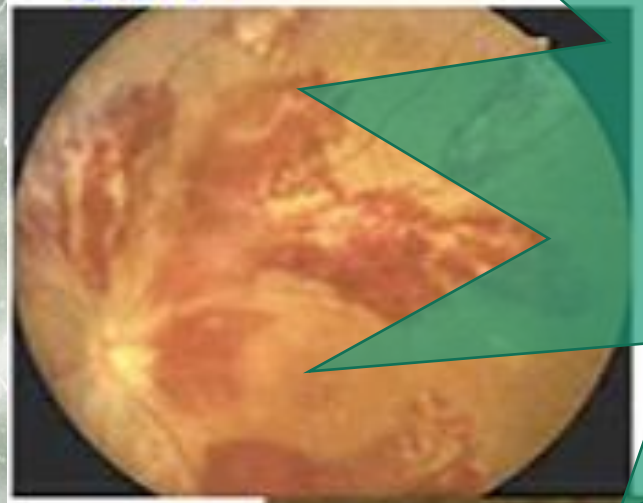
HSV

Cancer



flu

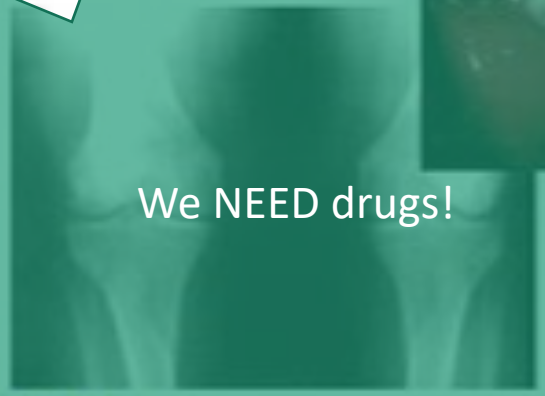
CMV



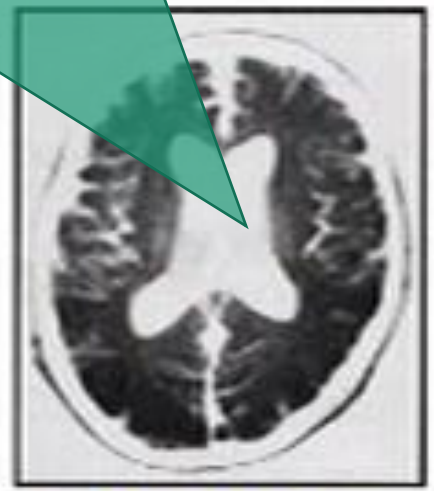
We NEED drugs!

VV/Smallpox

OA

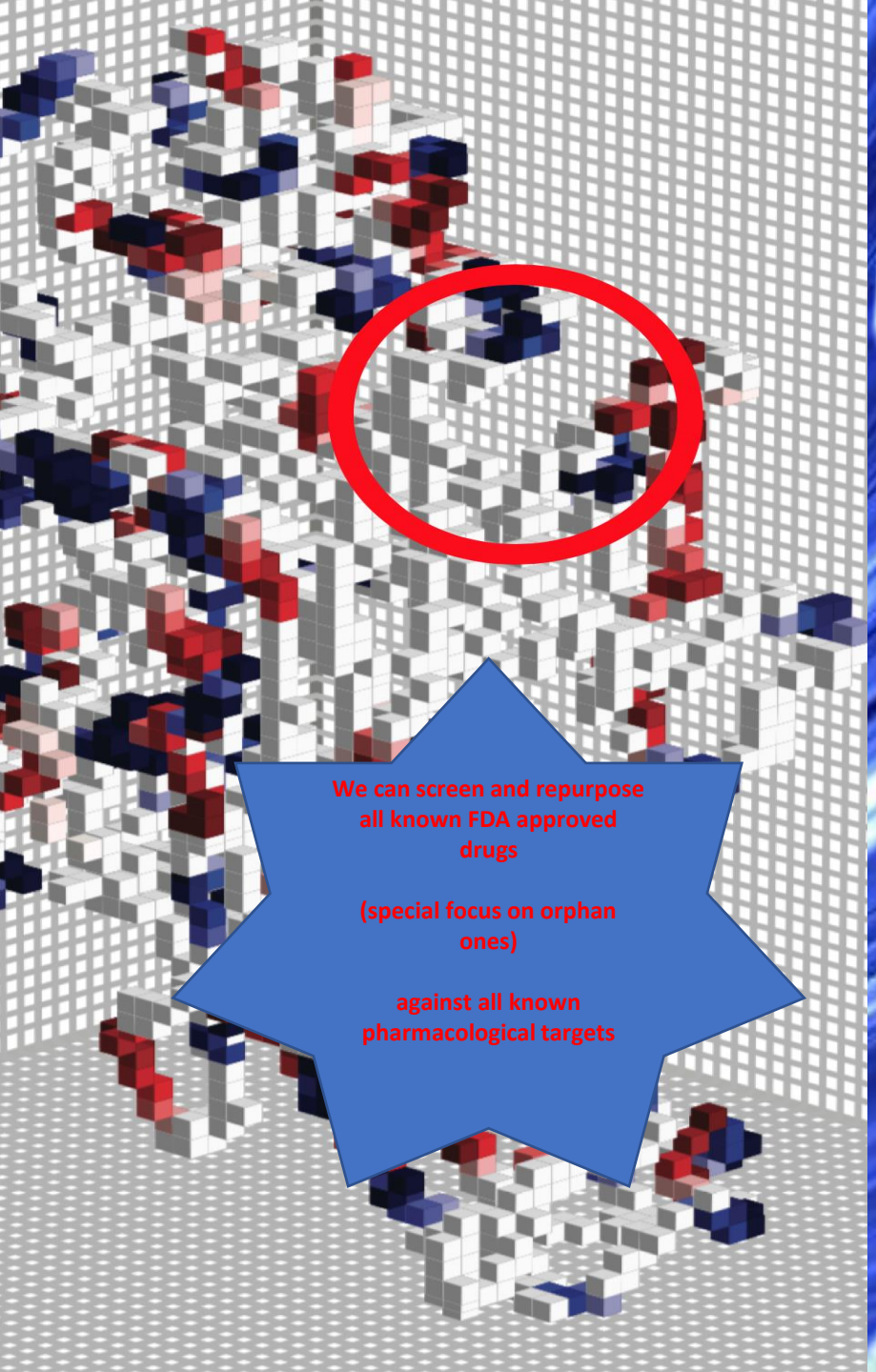


VZV



HIV/AIDS

Hepatitis B/C


We can screen and repurpose all known FDA approved drugs
(special focus on orphan ones)
against all known pharmacological targets


N
CHCH3
N
O
CH3
H3C
CH2
CH2

The Brave New World is Here !!