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Machine Learning in Bioinformatics

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Afiahayati, S.Kom., M.Cs., Ph.D

2004 – 2008 S.Kom, Universitas Gadjah Mada
2008 – 2010 M.Cs., Universitas Gadjah Mada
Oct 2010 Short Course of Computational Logic, TU Dresden
2011 – 2015 Ph.D, Keio University, Japan

Thesis :
2008 Multiple Sequence Alignment Using Hidden Markov Model (S.Kom)
2010 Multiple Sequence Alignment Using Hidden Markov Model With Augmented Set
And Its Influence On Phylogenetic Tree Accuracy (M.Cs)
2015 Development of *de novo* assemblers for metagenomic sequencing data (Ph.D)

Selected Awards :
1. Mahasiswa berprestasi UGM 2007
2. Accenture High Performer Scholarship 2007
3. Asea Uninet Scholarship 2009, On Place Master Program, funded by Austrian Gov.
4. Asia Development Scholarship 2011
5. Google Anita Borg Memorial Scholarhsip 2012
6. Schlumberger Faculty for The Future Fellowship Award 2013

Collaborations

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- Covid19 Genome Analysis : dr. Gunadi, Ph.D. (FKKMK UGM) , drh. Hendra Wibawa, DVM, MSc, PhD (Disease Investigation Center Wates)
- Cancer Analysis : Prof. Sofia Mubarika, Ph.D. (FKKMK UGM)
- GamaComet : drg. Ryna Y., Ph.D. (FKG UGM)
- Metagenomic Analysis : Prof. Sakakibara (Keio Univ, Japan)
- NGS analysis for Banana : Prof. Siti Subandiyah (Fac. of Agriculture, UGM)

Outlines

- Bioinformatics discipline
- Genetics Background
- Datasets
- Overview Machine Learning
- Genome Assembly
- Protein Secondary Structure Prediction
- GAMAComet
- Several potential research topics in Indonesia

Bioinformatics Discipline

Bioinformatics?

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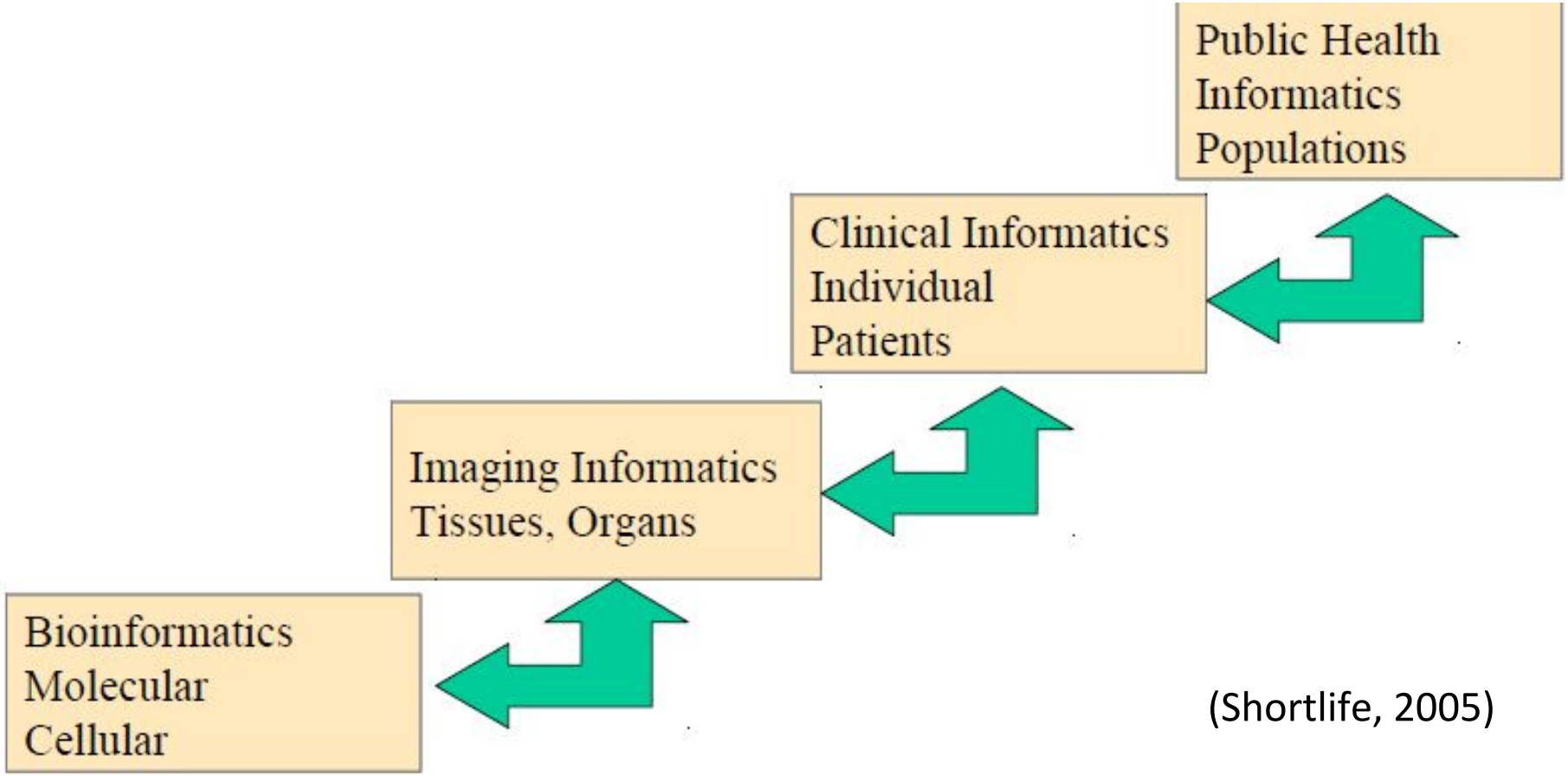
- You do not need A-level biology for the course
- We don’t have any background requirements

AI might help, databases might help…

Bioinformatics?

- An intersection of AI and genetics
  - Two very popular (most wanted) sciences
- An opportunity to:
  - Use some of the most interesting computational techniques to solve some of the most important and rewarding questions

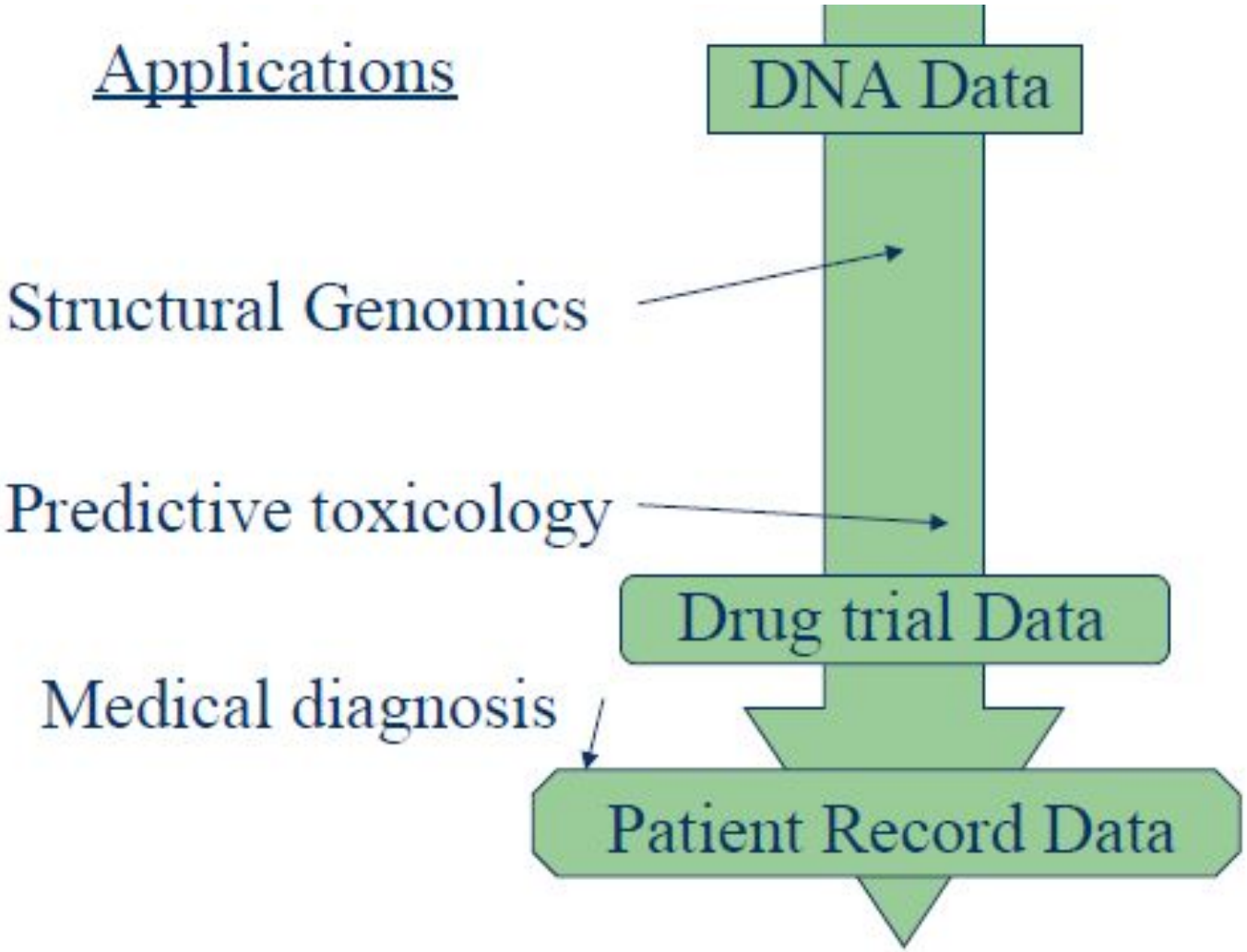
Health Information



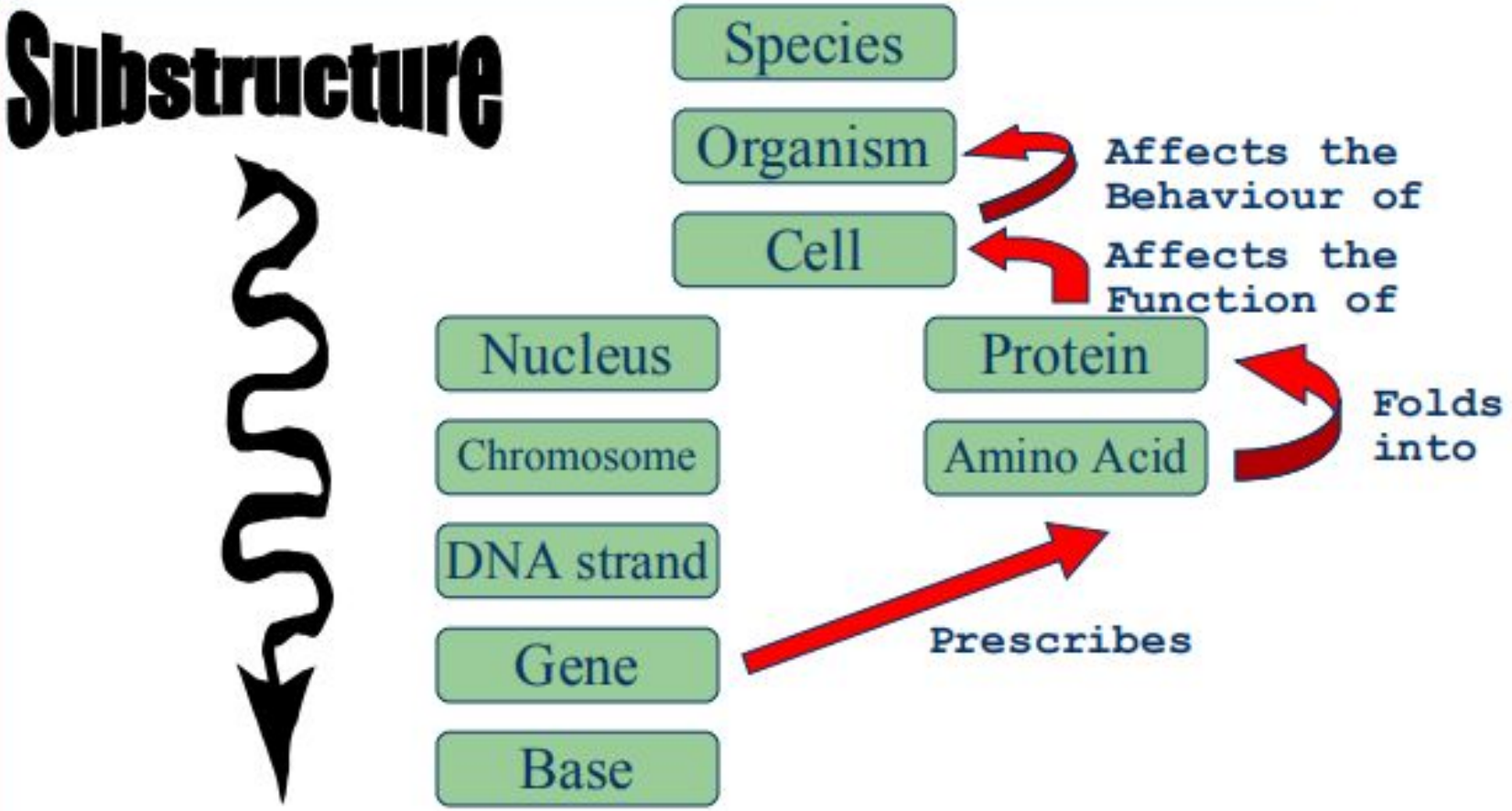
(Shortlife, 2005)

Genetic Backgrounds

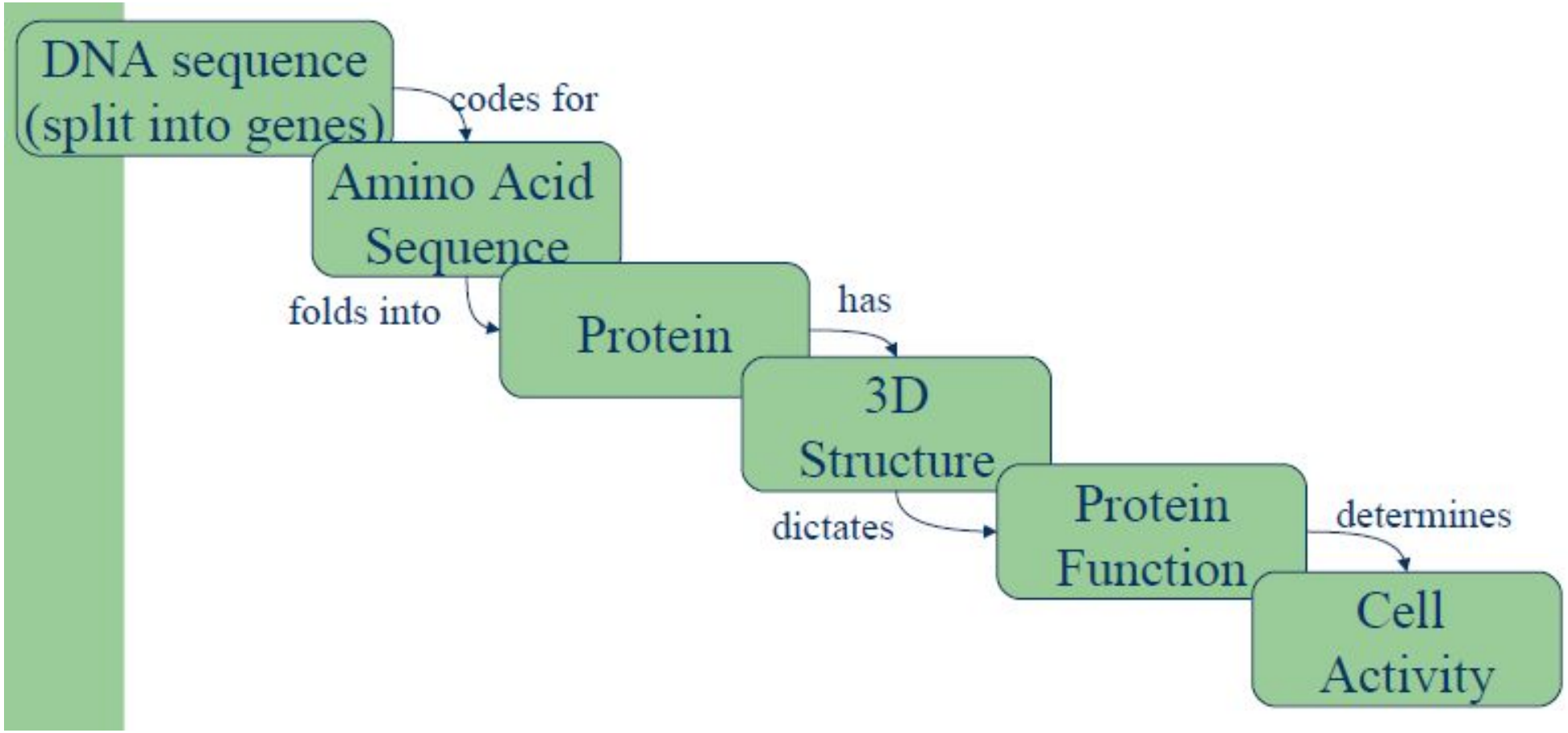
Bioinformatics Data



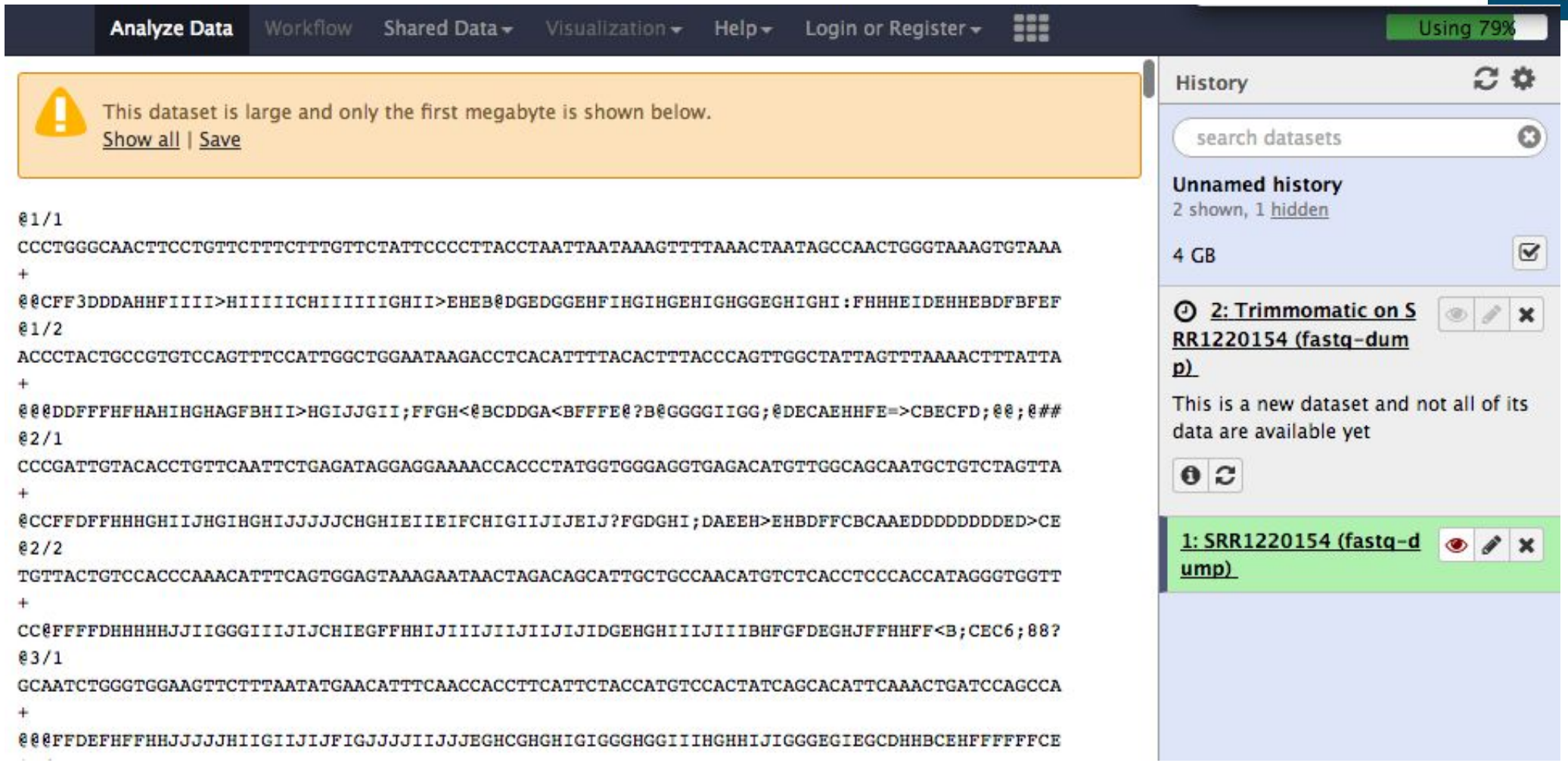
Substructure and Effect (Top Down/Bottom Up)



From DNA to Cell Function



DNA Sequence



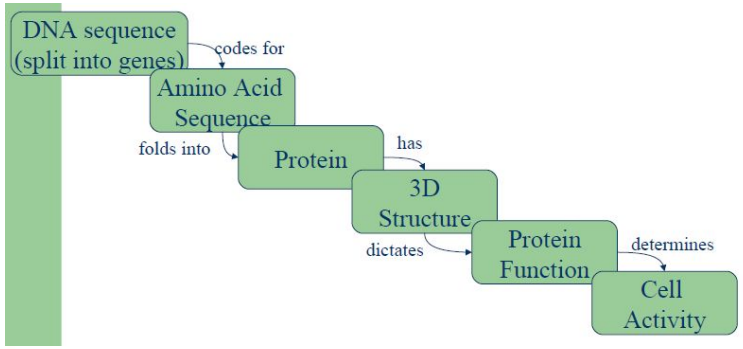
Amino Acids

Genetic Code

Second letter

First letter	U	C	A	G	Third letter
U	UUU, UUC Phe UUA, UUG Leu	UCU, UCC, UCA, UCG Ser	UAU, UAC Tyr UAA Stop UAG Stop	UGU, UGC Cys UGA Stop UGG Trp	U C A G
C	CUU, CUC, CUA, CUG Leu	CCU, CCC, CCA, CCG Pro	CAU, CAC His CAA, CAG Gln	CGU, CGC, CGA, CGG Arg	U C A G
A	AUU, AUC, AUA Ile AUG Met	ACU, ACC, ACA, ACG Thr	AAU, AAC Asn AAA, AAG Lys	AGU, AGC Ser AGA, AGG Arg	U C A G
G	GUU, GUC, GUA, GUG Val	GCU, GCC, GCA, GCG Ala	GAU, GAC Asp GAA, GAG Glu	GGU, GGC, GGA, GGG Gly	U C A G

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



Multiple Sequence Alignment

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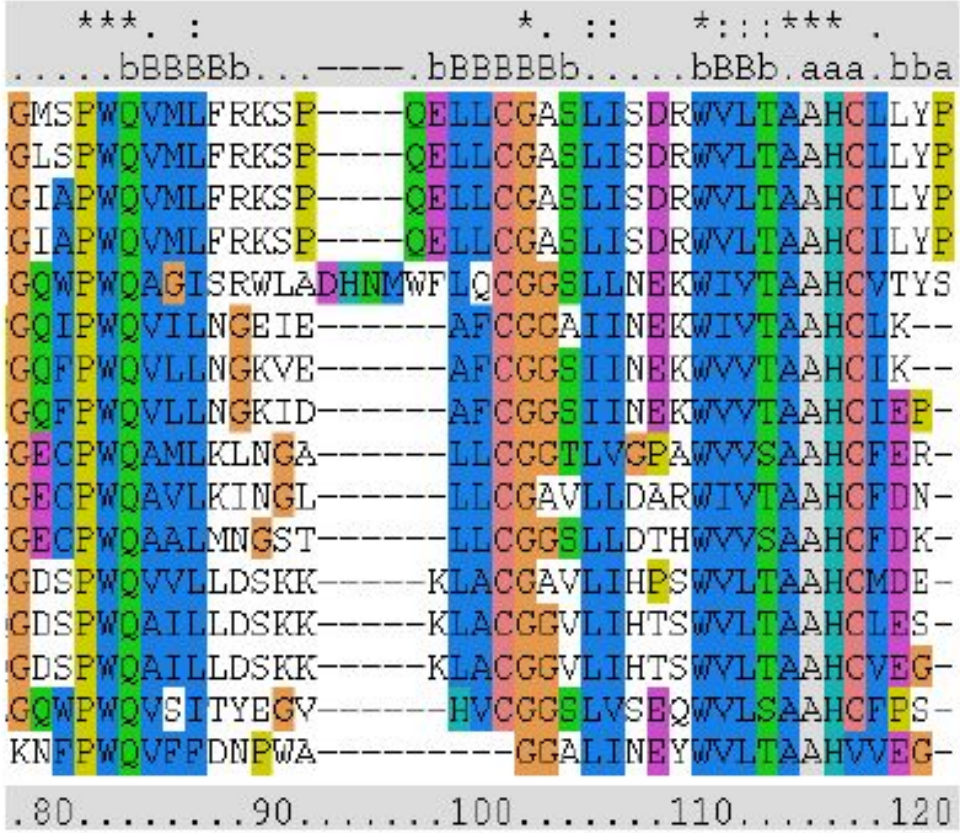
- Protein sequences form families
  - Learn much more about a gene by looking at its family

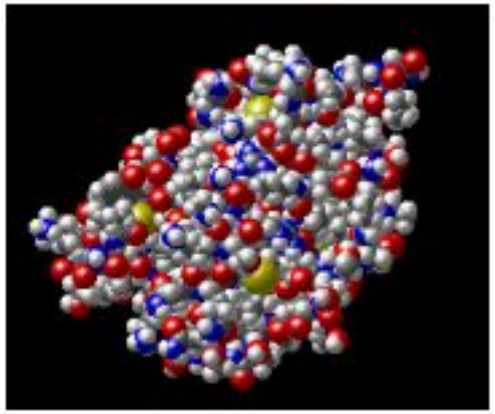
- Multiple sequence alignment algorithms
  - Profiles
  - PSI-BLAST

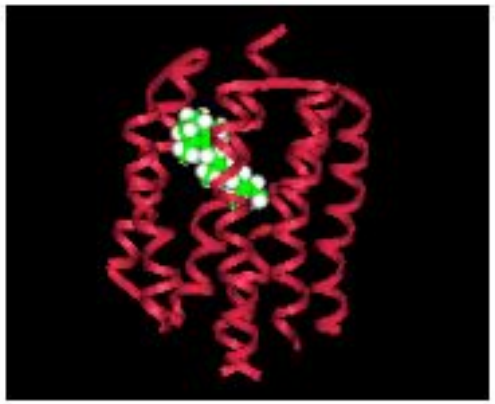


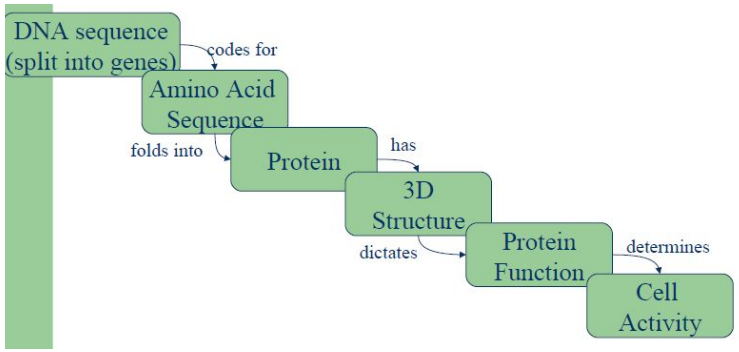
Proteins

Proteins

- DNA codes for
  - strings of amino acids
- Amino acids strings
  - Fold up into complex 3d molecule
  - 3d structures:conformations
  - Between 200 & 400 “residues”
  - Folds are proteins
- Residue sequences
  - Always fold to same conformation
- Proteins play a part
  - In almost every biological process







Datasets

Datasets

- Primary Datasets
  - Data acquisition : DNA sequence, Comet Assay
- Secondary Datasets, benchmarking datasets
  - NCBI (DNA sequence, protein, …)
  - RS126 (SSP)
  - CullPDB (SSP)
  - Cb513 (SSP)

Primary dataset : DNA Seq

Contents lists available at ScienceDirect

Data in brief

journal homepage: www.elsevier.com/locate/dib

Data Article

RNA-seq data of banana bunchy top virus (BBTV) viruliferous and non-viruliferous banana aphid (*Pentalonia nigronervosa*)

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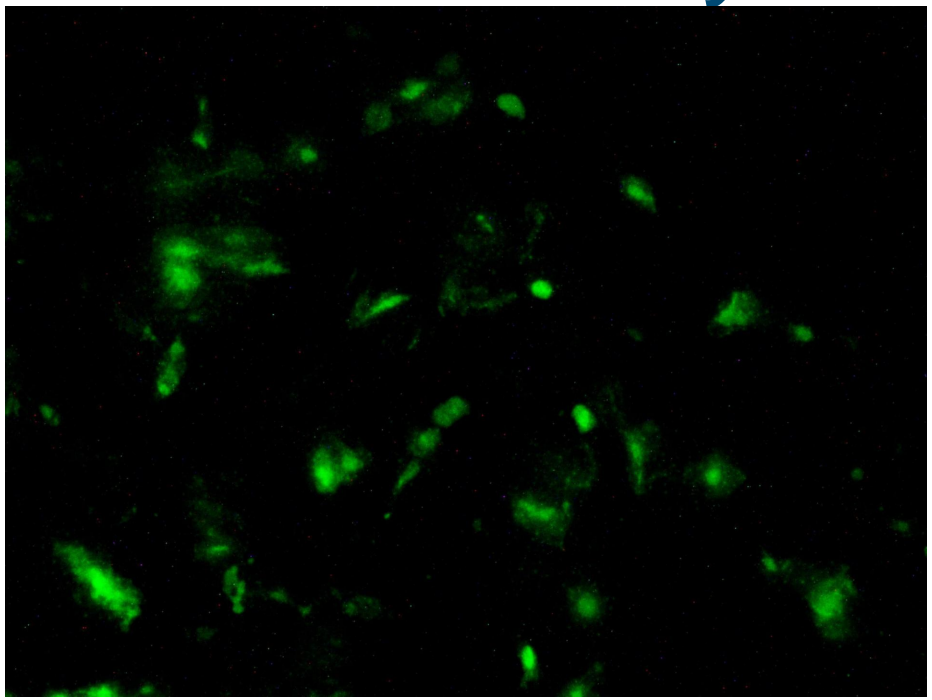
RNA-Seq

ABSTRACT

Banana bunchy top disease (BBT) is one of the most economically serious viral diseases of banana caused by banana bunchy top virus (BBTV: Nanoviridae: Babuvirus). BBTV is a circular, ssDNA virus which is suitable in the phloem tissue and currently only being transmitted by the banana aphid (*Pentalonia nigronervosa*) in a persistent, non-propagative, circulative manner. Interaction of BBTV and banana aphid had been studied in several ways, such as transmission and translocation of BBTV inside the banana aphid body at cellular level. However, the molecular mechanism underlying the interaction between BBTV and banana aphid have been poorly understood

Primary dataset : Comet Assay



Secondary Datasets

Benchmarking datasets :CullPDB, CB513

princeton.edu/~jzthree/datasets/ICML2014/

Index of /~jzthree/datasets/ICML2014

Name	Last modified	Size	Description
Parent Directory		-	
cb513+profile_split1.npy.gz	2014-01-21 00:49	9.3M	
cullpdb+profile_5926.npy.gz	2018-10-28 23:53	103M	
cullpdb+profile_5926_filtered.npy.gz	2018-10-28 23:53	95M	
cullpdb+profile_6133.npy.gz	2014-01-21 00:37	108M	
cullpdb+profile_6133_filtered.npy.gz	2014-01-21 00:37	100M	
cullpdb.tar.gz	2017-02-25 23:02	1.1G	
dataset_readme.txt	2018-10-28 23:53	2.7K	
slides.pdf	2015-10-01 21:16	822K	

Secondary Datasets

NCBI

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ncbi.nlm.nih.gov

NCBI Resources How To Sign in to NCBI

NCBI National Center for Biotechnology Information

All Databases | Search

COVID-19 is an emerging, rapidly evolving situation.
Get the latest public health information from CDC: https://www.coronavirus.gov .
Get the latest research from NIH: https://www.nih.gov/coronavirus.
Find NCBI SARS-CoV-2 literature, sequence, and clinical content: https://www.ncbi.nlm.nih.gov/sars-cov-2/.

- NCBI Home
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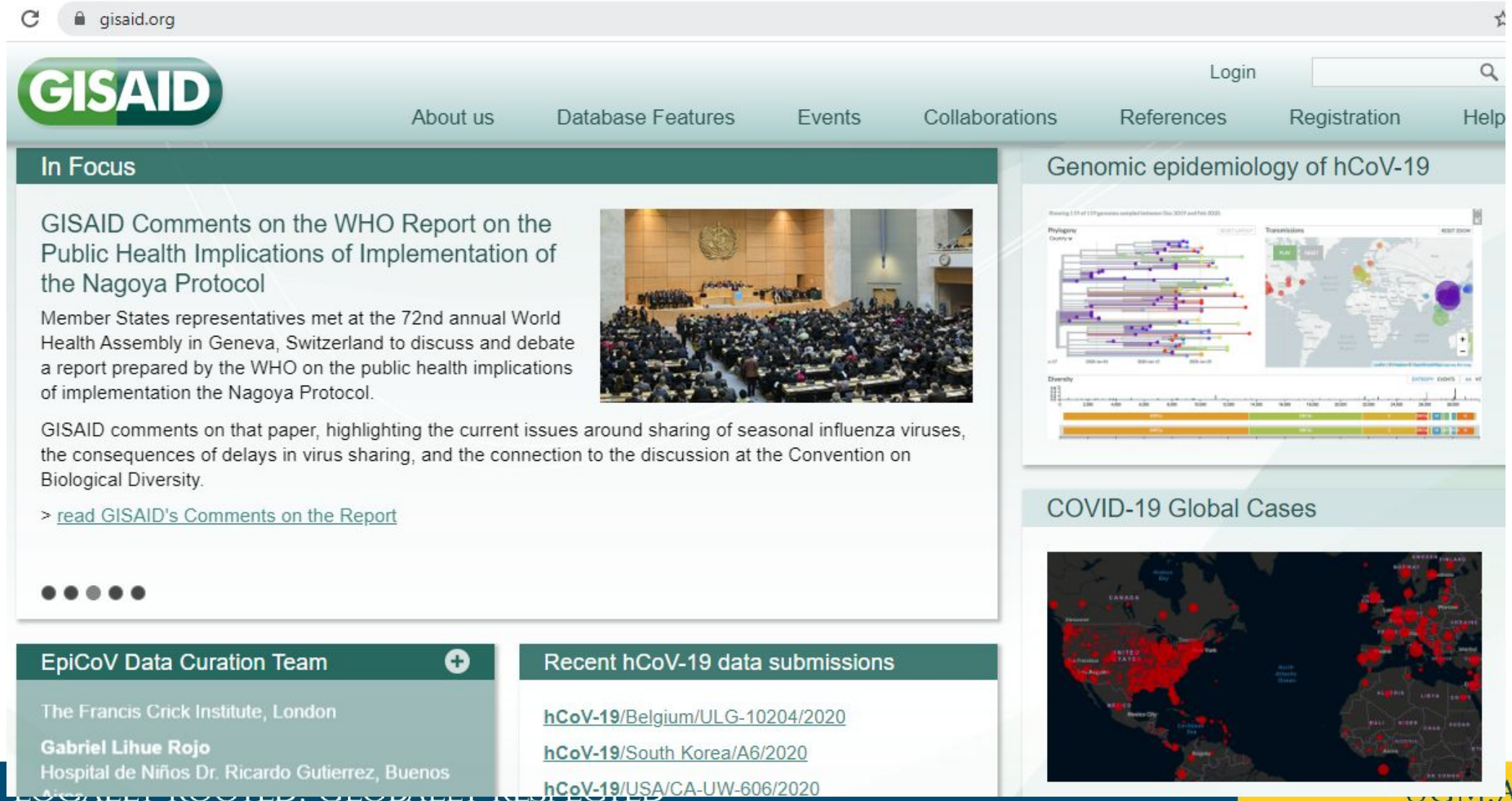
NCBI News & Blog
The BLAST Docker and databases are now ready to use on Google and Amazon clouds

Secondary Datasets

GISAID



Overview
Machine Learning

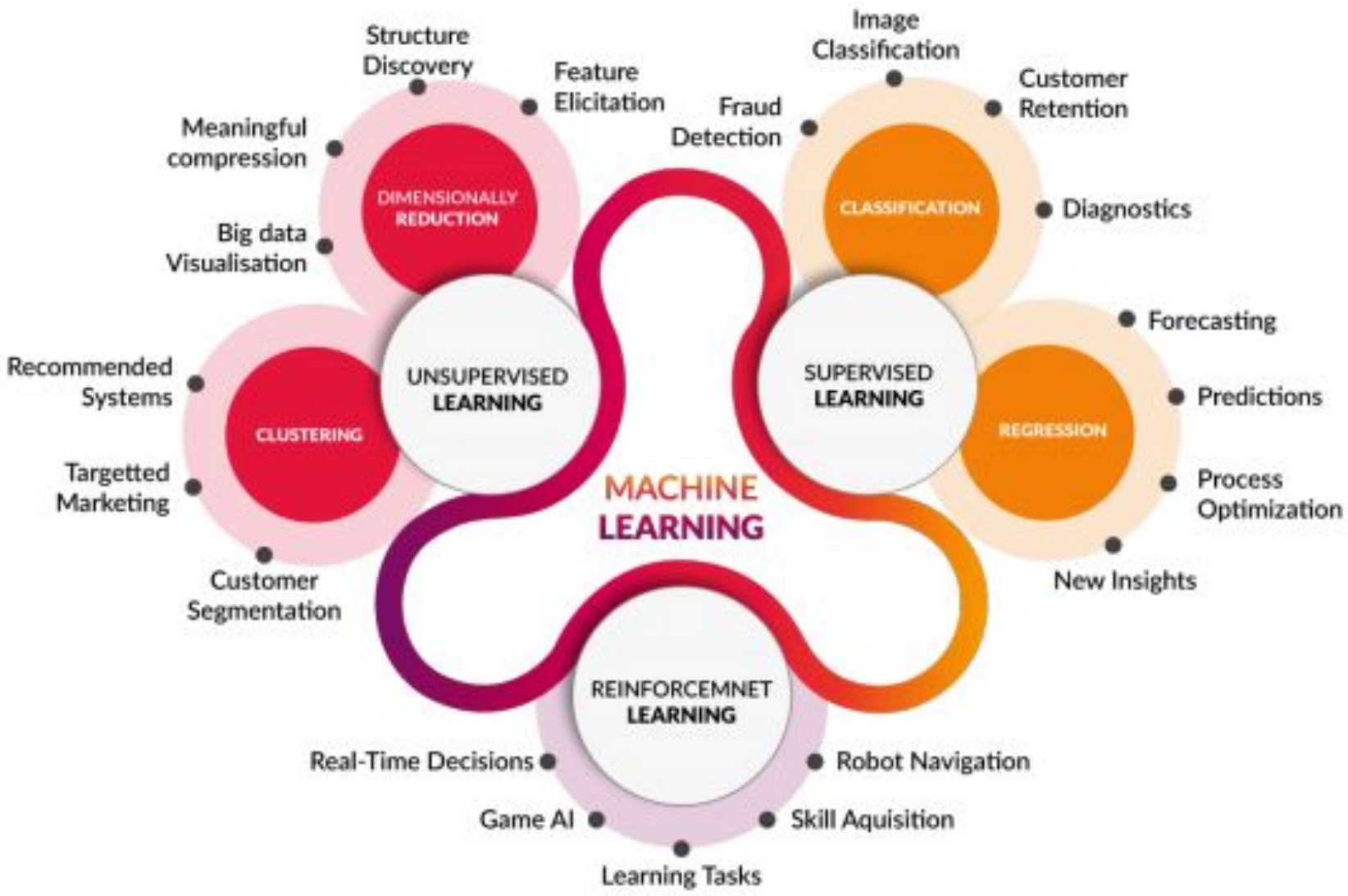
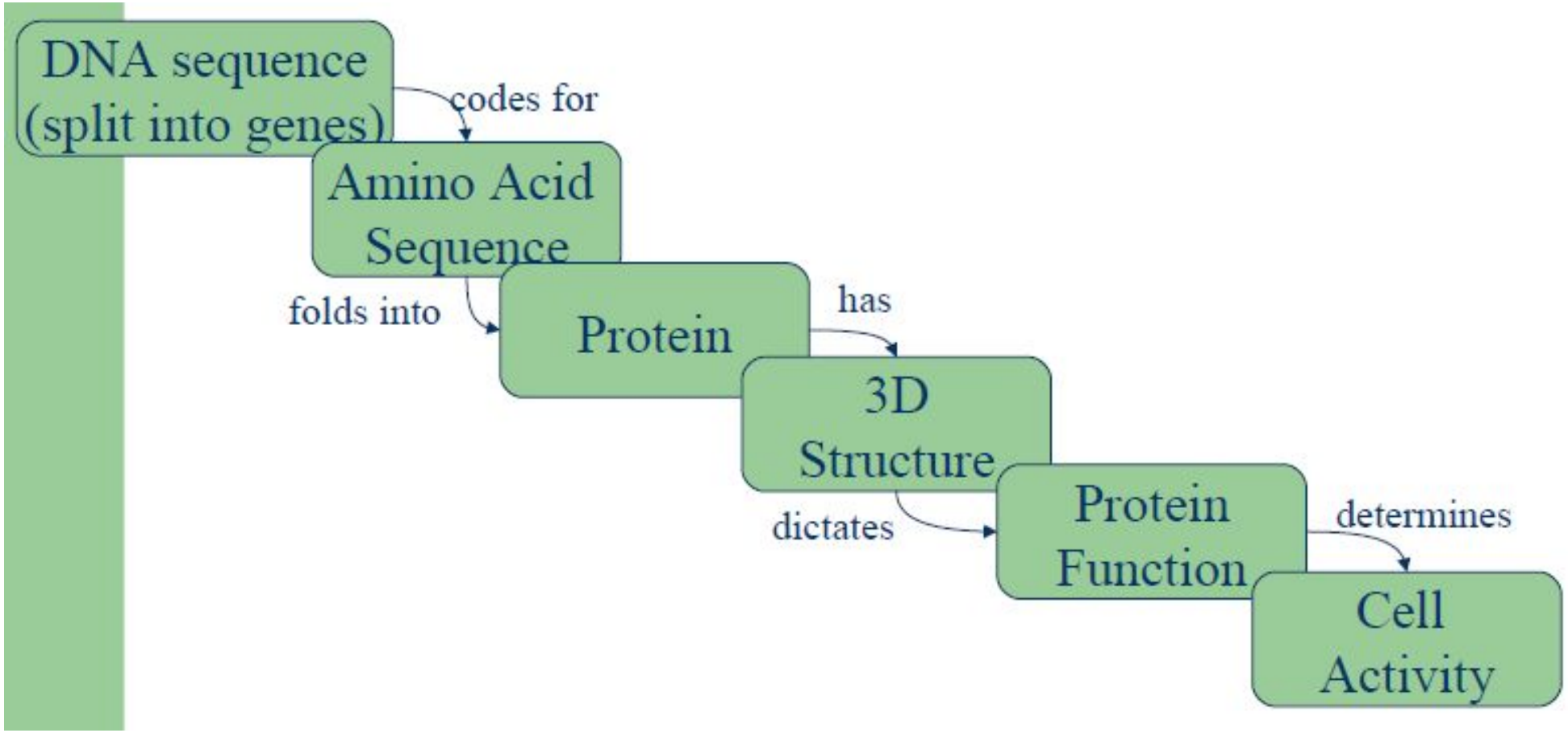


Figure: ML Map (Image source: http://www.cognub.com/index.php/cognitive-platform/)

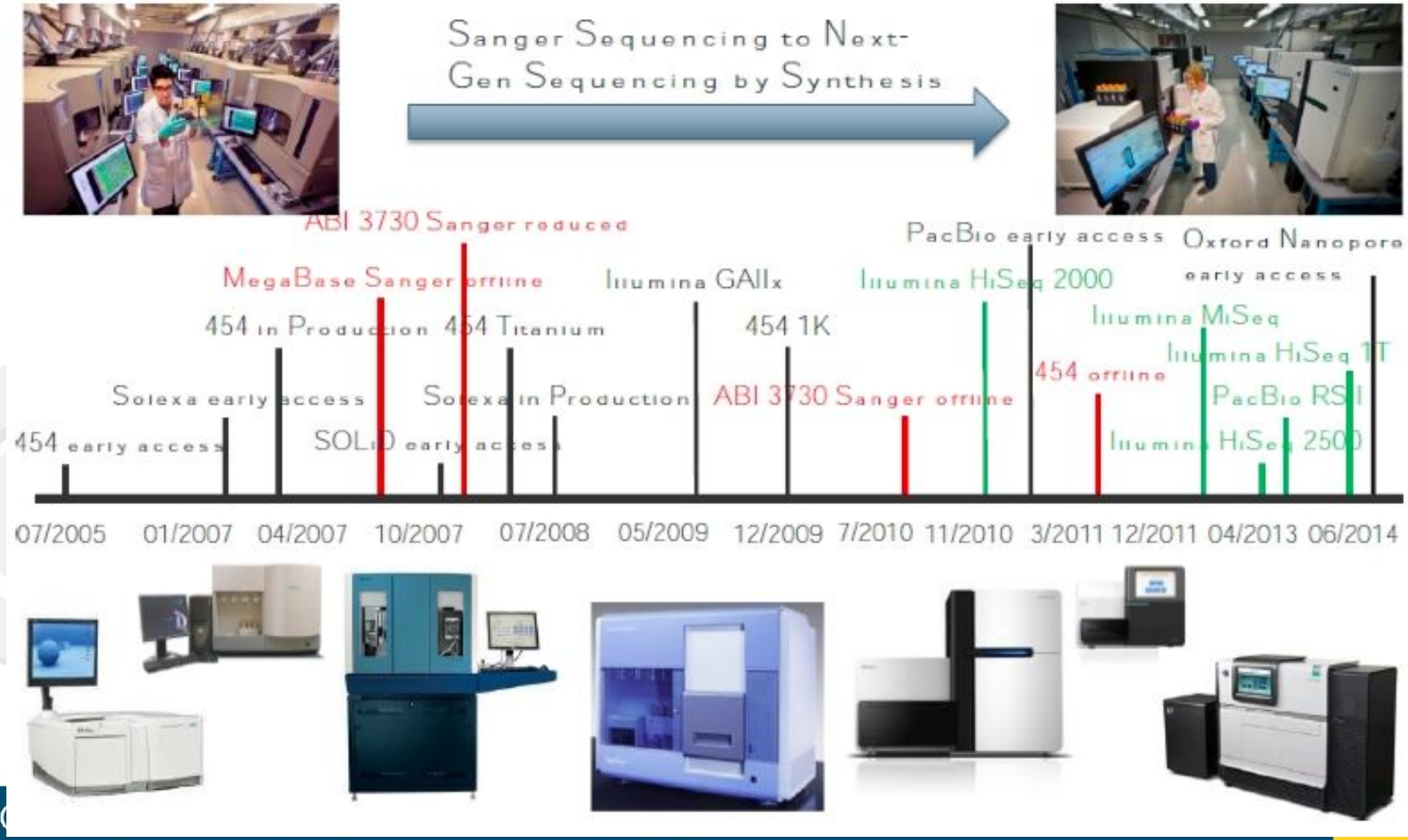
Machine Learning in Bioinformatics



Genome Assembly

DNA Data => Next Generation Sequencing

Staying state of the art



NGS Data

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Sequencing Platform




	Illumina HiSeq 1T	Illumina HiSeq 2500	Illumina HiSeq 2000	Illumina NextSeq 500	Illumina MiSeq	Pacific Biosciences RSII
Reads (Single-Read/Cluster)	>1,500 Million per Flowcell	200 Million per Flowcell	>1,000 Million per Flowcell	400 Million per Flowcell	>10 Million per Flowcell	0.06 Million per SMRT Cell
Readlength	2 X 150bp Max*	2 X 250bp Max	2 X 150bp Max*	2 X 150 Max	2 X 300bp Max	11,000bp Avg; 50,000bp Max
Total Bases	500 Gb per Flowcell	130 Gb per Flowcell	350 Gb per Flowcell	>100 Gb per Flowcell	5-20 Gb per Flowcell	>0.4 Gb per SMRT Cell
Run Time	7 Days for 2 X 150	4.5 Days for 2 X 250	16 Days for 2 X 150	1 Days for 2 X 150	2 Days for 2 X 300	0.08-0.12 Days (2-4 hours)
Applications	Primary Sequence Generator at JGI	Rapid output HiSeq	Supplement / Backup Platform	Development / Supplement	16s iTags, Library QC, R&D	Assembly improvement, de novo, SynBio validation, methylation/epigenome

NGS Data

genome.gov/human-genome-project

COVID-19 is an emerging, rapidly evolving situation. CDC health information NIH research information

NIH National Human Genome Research Institute

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What is the Human Genome Project?›

The Human Genome Project was the international research effort to determine the DNA sequence of the entire human genome.

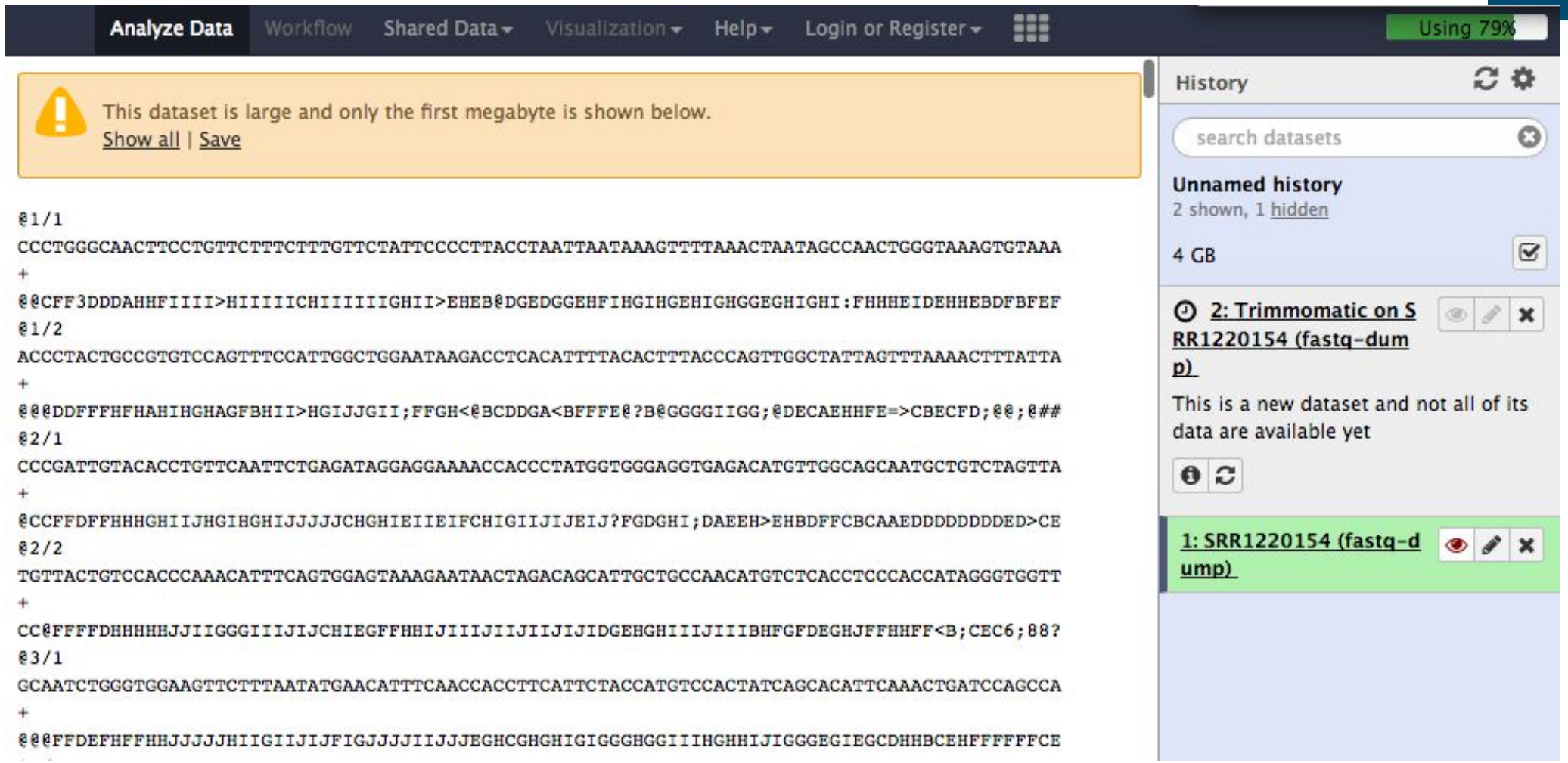
Human Genome Project Results›

In 2003, an accurate and complete human genome sequence was finished two years ahead of schedule and at a cost less than the original estimated budget.

Human Genome Project Timeline of Events›

Key moments and press releases from the history of the Human Genome Project.

DNA Sequences



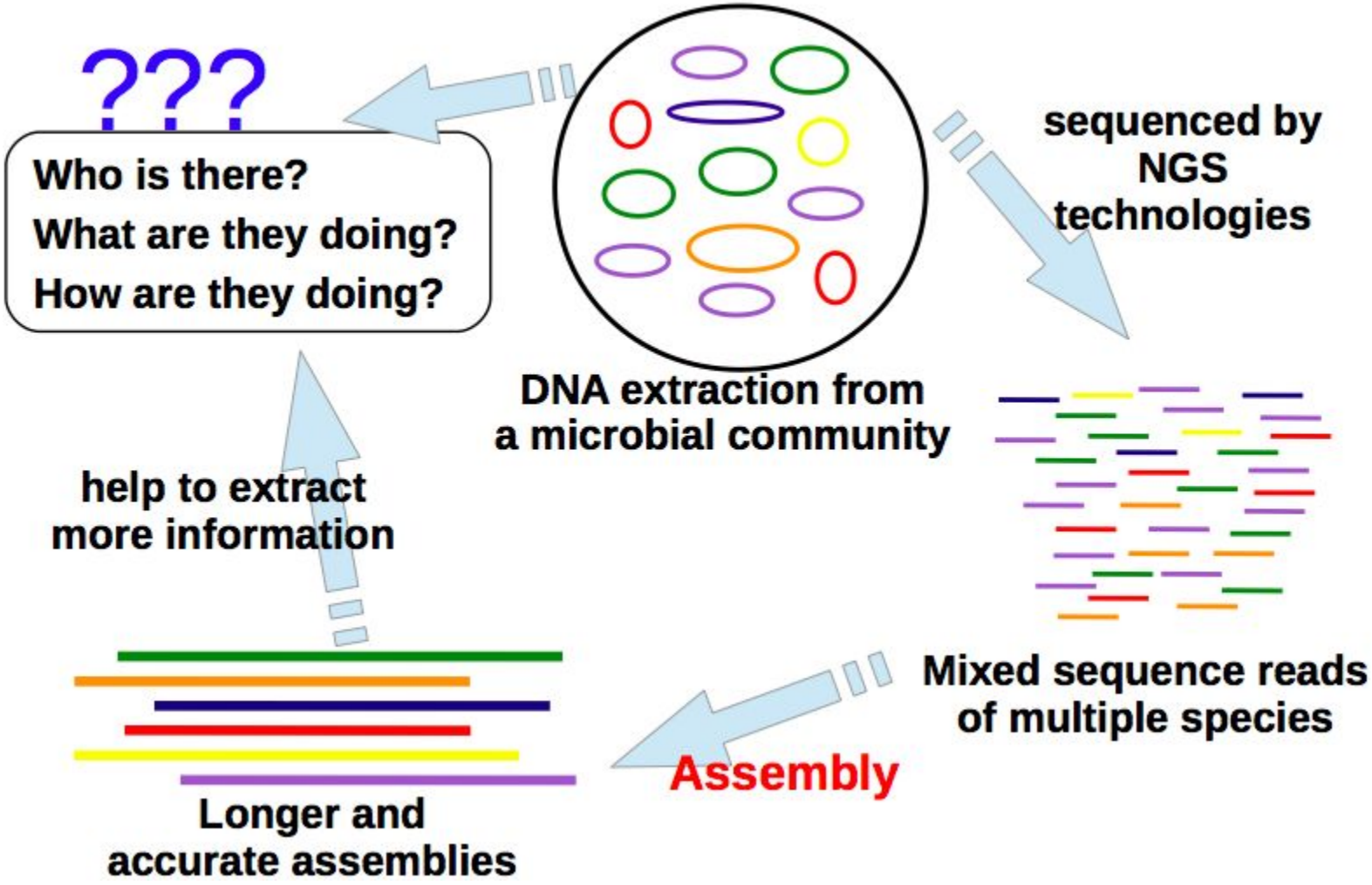
DNA data Sequence

Advantages :

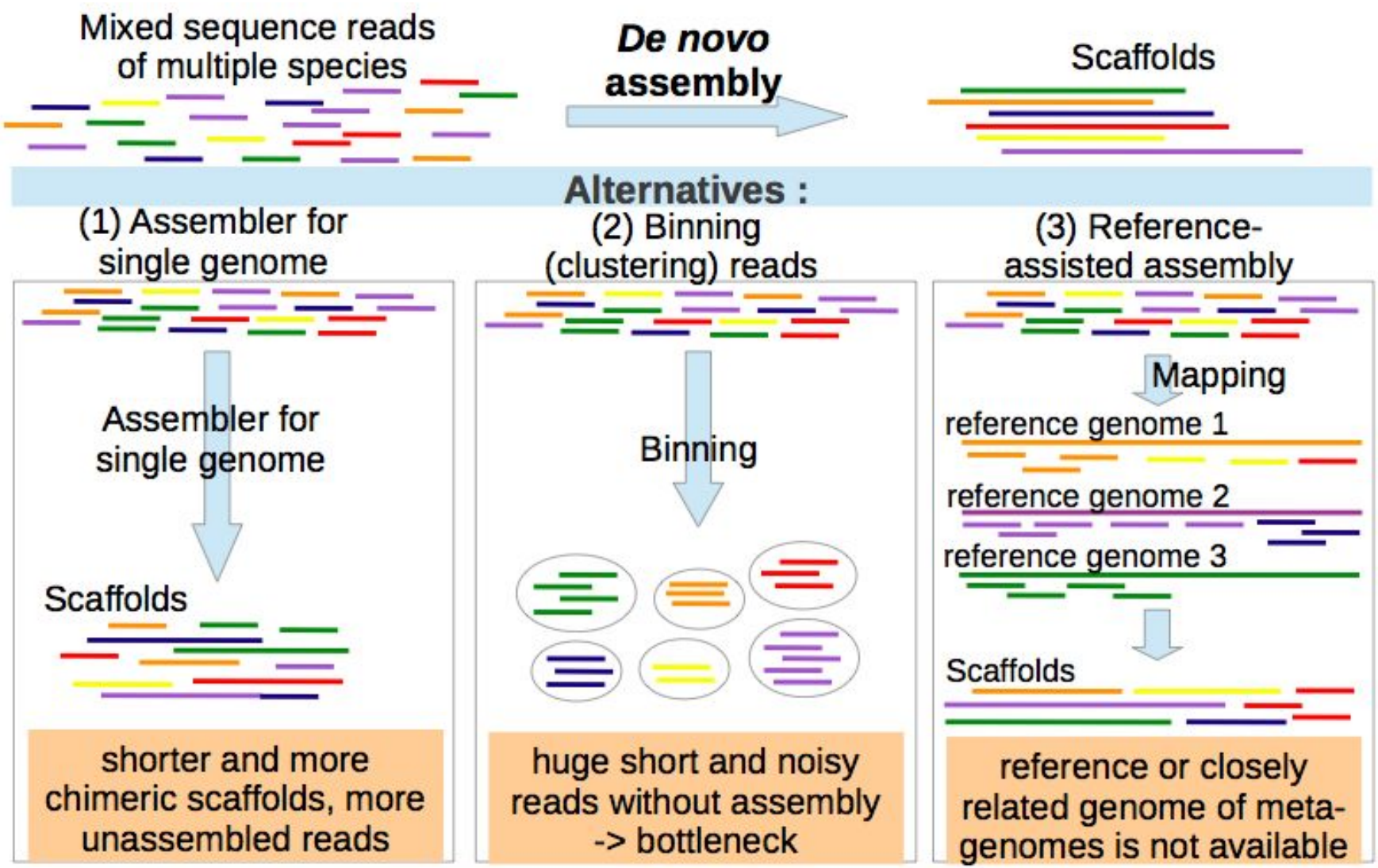
- Lower cost
- High troughput sequencing
- Deep sequencing

(Afiahayati et al., 2015)

Metagenomic Analysis



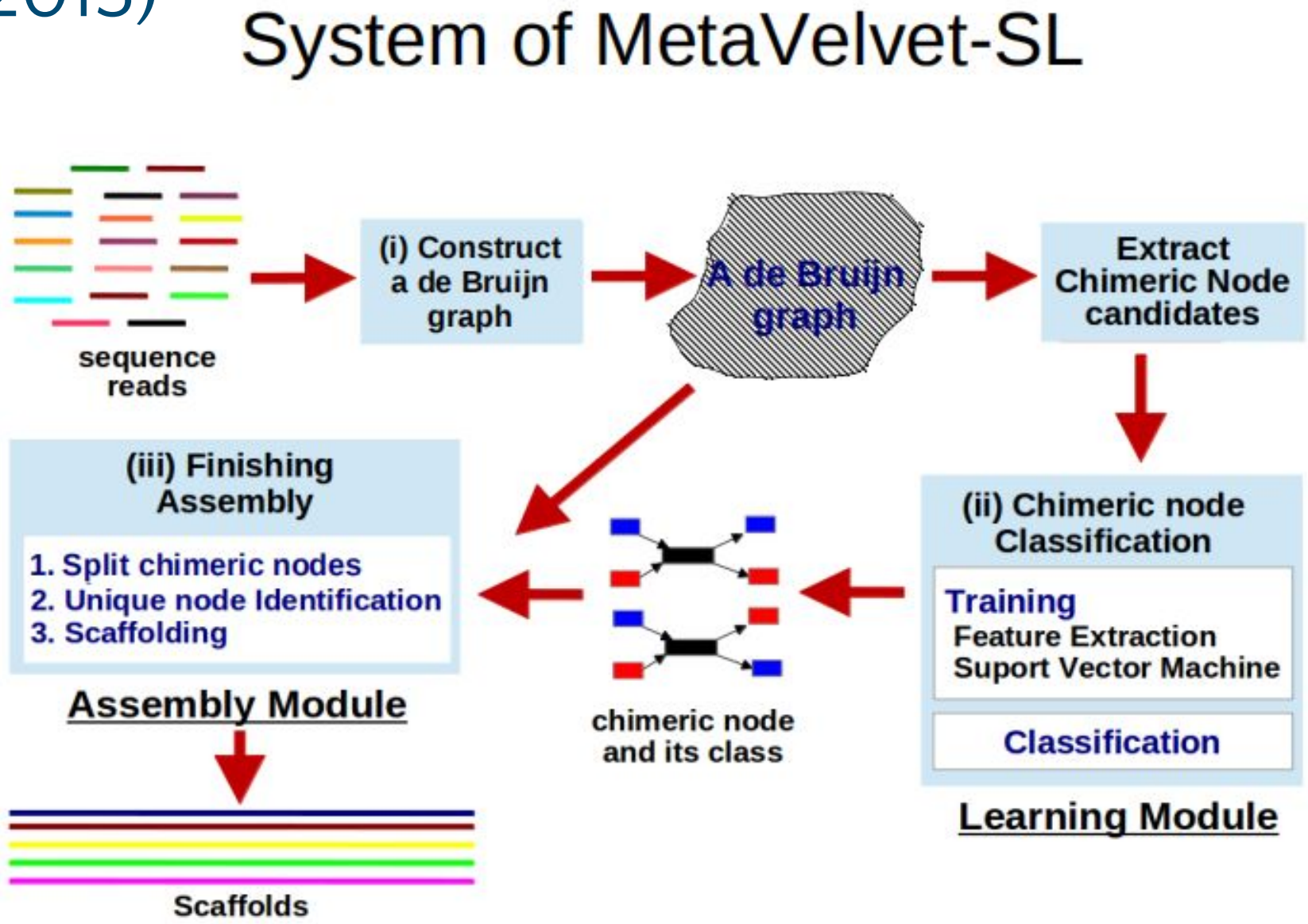
Metagenomic Analysis – Metagenomic Assembly



MetaVelvet-SL

http://metavelvet.dna.bio.keio.ac.jp/MSL.html

(Afiahayati et al., 2015)



Computational Infrastruture for Bioinformatics Analysis

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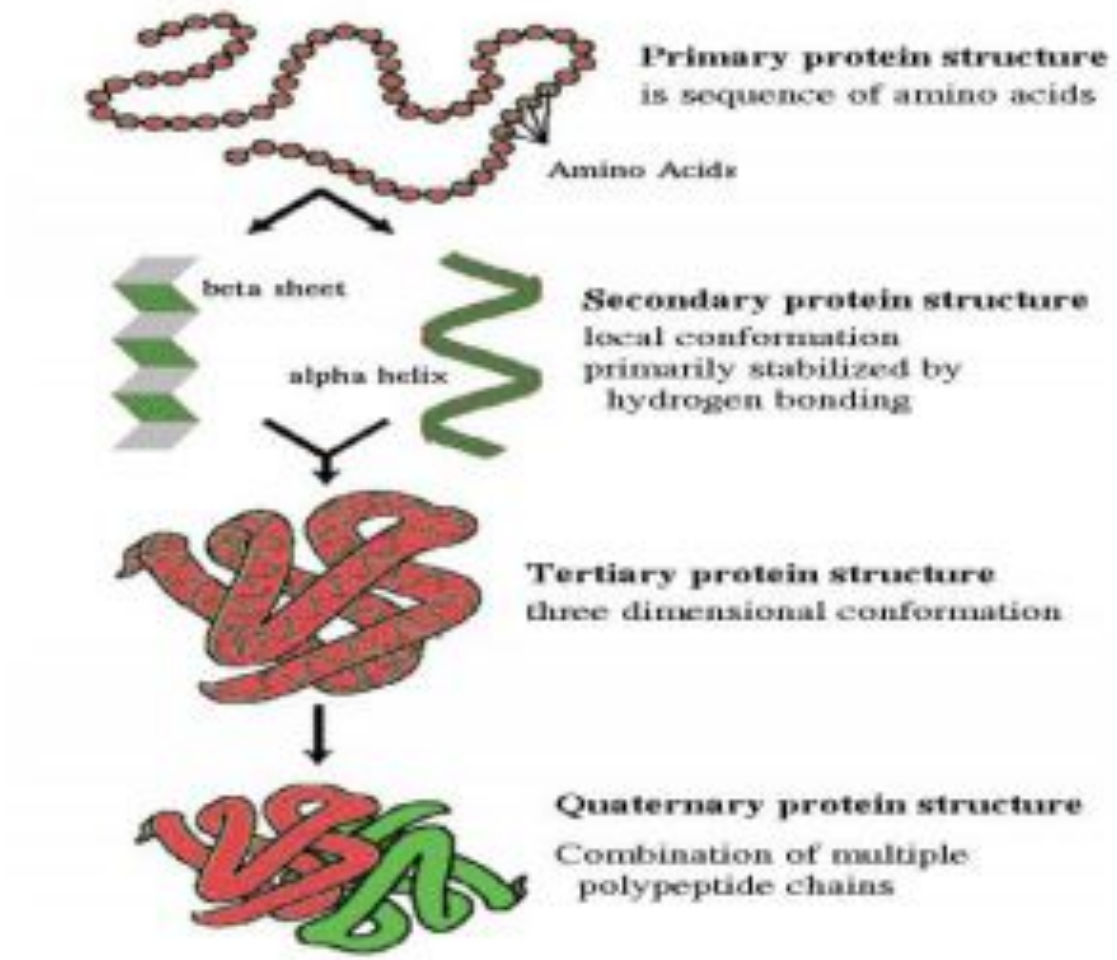
- NGS => Super Big data => super performance computing
- High performance computing infrastructure :
  - Computing cluster :
    - Multiple nodes(servers) with multiple cores
    - High computer memory (64 GB)
    - High performance storage(TB, PB level)
    - Fast networks(10Gb ethernet, infiniband)
  - Operating System : Unix based (Linux)
  - Server room
  - System admin

Protein Secondary Structure Prediction

Secondary Structure Prediction



Kelas DSSP	Simbol 8 Kelas	Simbol 3 Kelas	Nama Kelas
α-helix 3_{10}-helix	H G	H	*Helix*
B-Strand B-bridge	E B	E	*Sheet*
Loop/Irreguler B-Turn Bend π-helix	L T S I	C	*Coil / Loop*

Secondary Structure Prediction

Sekuens 1: Panjang sekuens = 67

SPP	VPSLATISLENSWSGLSKQIQLAQGNNGIFRTPIVLVDNKGNRVQITNV TSKVVTSNIQLLLNTRNI
SSP 3	CCCHHHHHHHHHHHHHHHHHHHHHHHCCCCCEEEEEEEECCCCCCCEEE EECCCHHHHHCECCECCHHHC
SSP 8	LLLHHHHHHHHHHHHHHHHHHHHHHTTTTEEEEEEEEELLSSSSLEEEEET TSHHHHHTBLLBLLGGGL
PSSP 3	CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC CCCCCCCCCCCCCCCCCC
PSSP 8	LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL LLLLL

Secondary Structure Prediction

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- Machine learning methods :
  - Multi Layer Perceptron
  - Support Vector Machine
  - Convolutional Neural Network
  - Recurrent Neural Network (as a sequence prediction)

Secondary Structure Prediction menggunakan CNN

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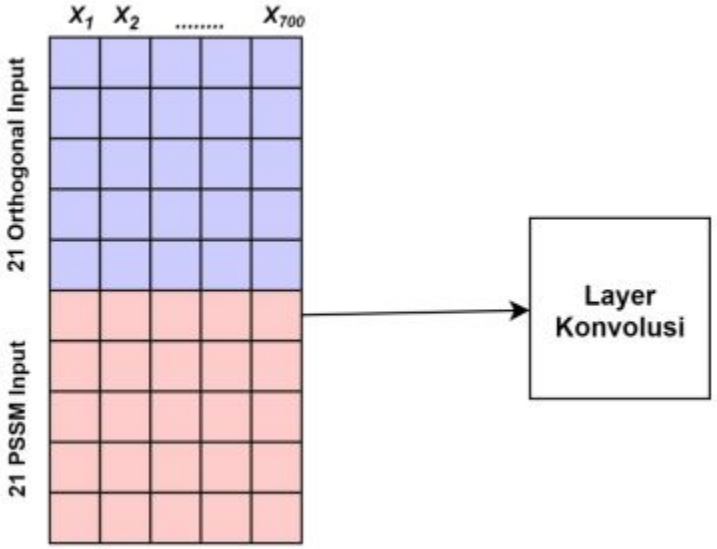
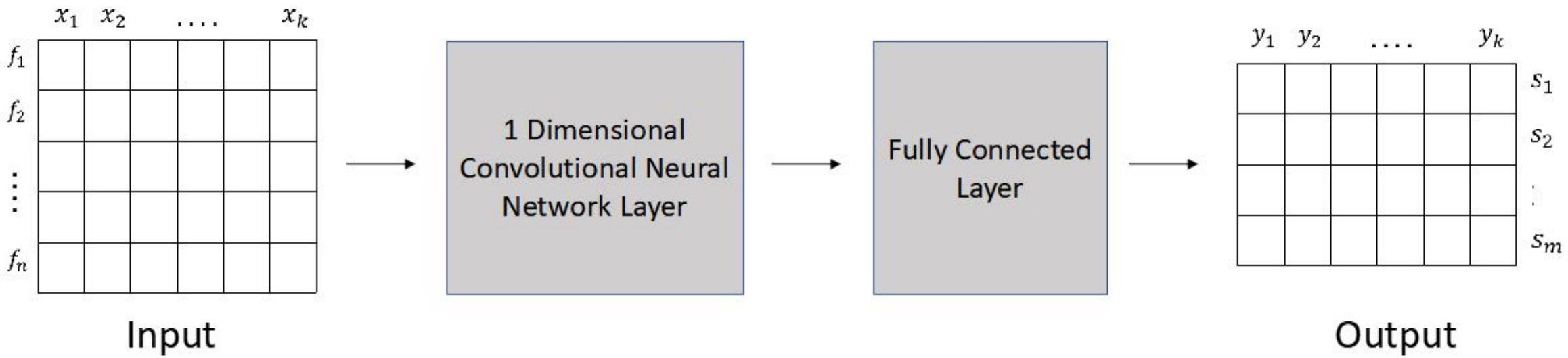
Orthogonal Encoding

	A	C	E
A	1	0	0
C	0	1	0
E	0	0	1
D	0	0	0
...	...	...	...
...	...	...	...
Y	0	0	0

Input Layer – Convolutional Layer



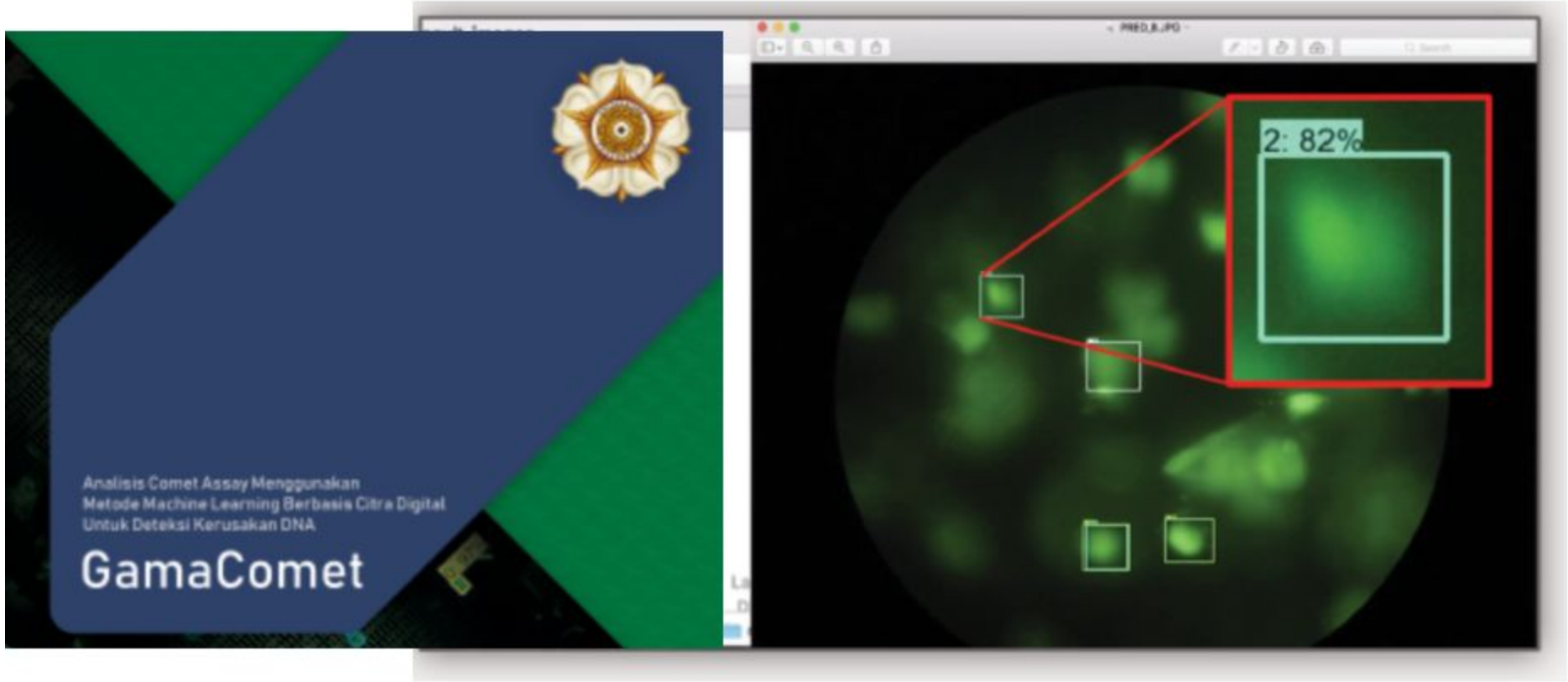
Secondary Structure Prediction menggunakan CNN



GAMAComet

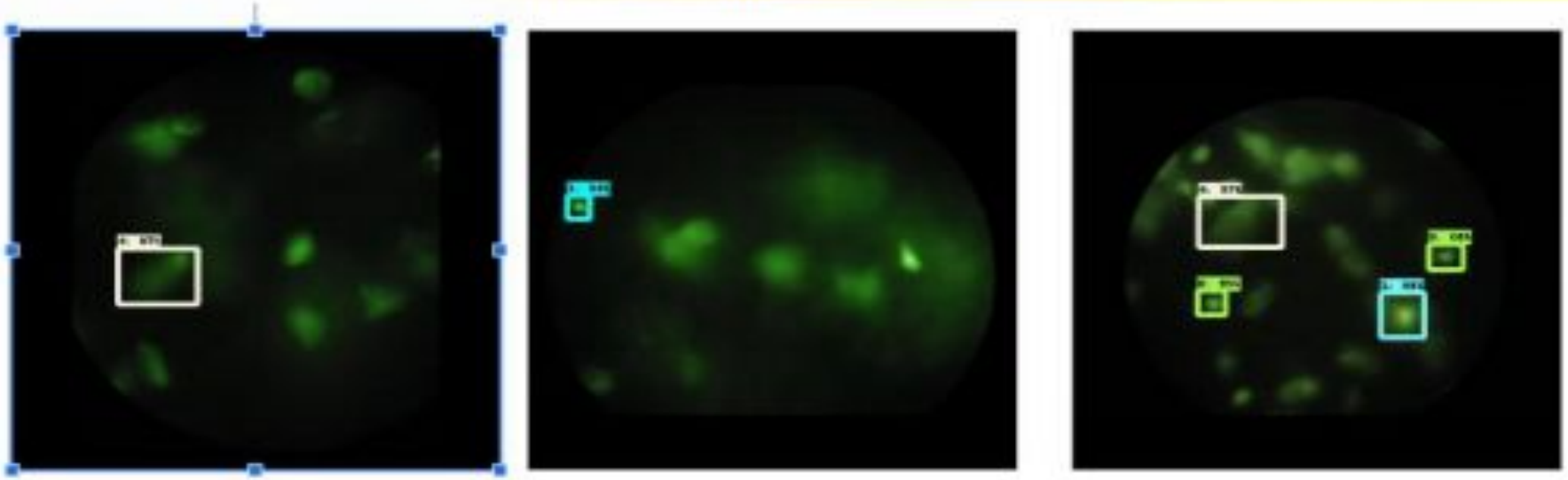
GAMAComet
(kerjasama dengan FKG UGM)

Hak Cipta : 000143480



GamaComet :

Analisis Comet Assay Menggunakan Machine Learning Untuk Deteksi Kerusakan DNA



- Done :
  - ✓ Classification using super tiny dataset and transfer learning
  - ✓ Automatic segmentation classification - FasterRCNN
- OnGoing :
  - ✓ Classification using ELM
  - ✓ Automatic segmentation - 2D Otsu Methods
- Next :
  - ✓ Data oversampling
  - ✓ Segmentation - using pixel classification

- GRANT :
  - ✓ PTUPT

link.springer.com/chapter/10.1007/978-3-030-14132-5_22

Springer Link

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Asian Conference on Intelligent Information and Database Systems
ACIIDS 2019: Intelligent Information and Database Systems: Recent Developments pp 279-289 | Cite as

Comet Assay Classification for Buccal Mucosa's DNA Damage Measurement with Super Tiny Dataset Using Transfer Learning

Authors | Authors and affiliations

Afiahayati, Edgar Anarossi, Ryna Dwi Yanuaryska, Fajar Ulin Nuha, Sri Mulyana

Chapter
First Online: 06 March 2019

Part of the Studies in Computational Intelligence book series (SCI, volume 830)

Abstract

Paper GamaComet (1)

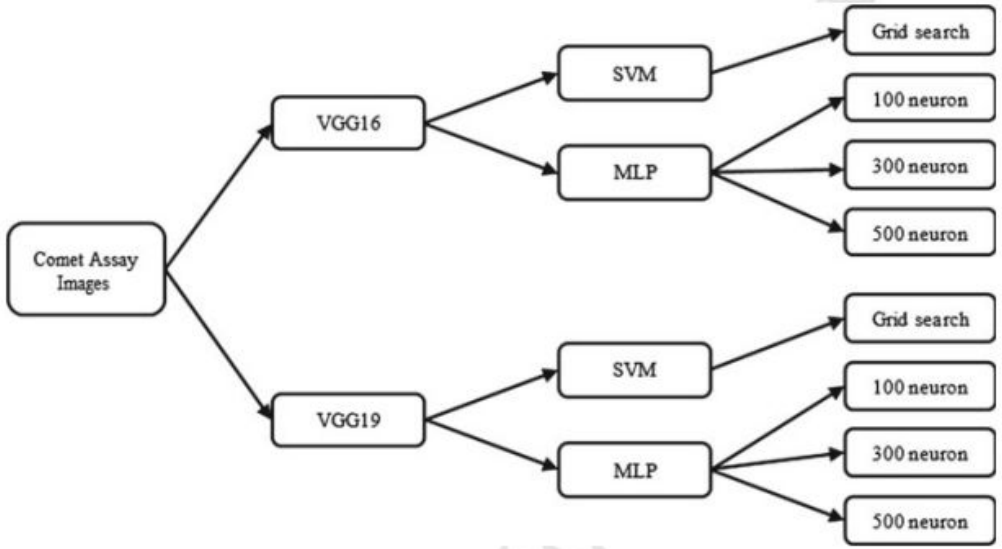

Fig. 5 Classification process using transfer learning

Table 6 Results of transfer learning using MLP and SVM as classification methods with VGG16 as a feature extractor

Data/architecture	SVM	MLP 100	MLP 300	MLP 500
No augmentation	0.6202	**0.7049**	**0.7049**	0.639
Augmented	0.6272	0.664	0.68	0.604

Table 7 Results of MLP and SVM classification with VGG19 as a feature extractor

Data/architecture	SVM	MLP 100	MLP 300	MLP 500
No augmentation	0.6238	0.6557	0.623	0.623
Augmented	0.6356	**0.692**	0.668	0.56

Table 8 The accuracy comparison of the overall classification model and OpenComet software [15]

Data/architecture	CNN	CNN-SVM	Transfer learning 1 (VGG16-MLP)	Transfer learning 2 (VGG19-MLP)	OpenComet
No augmentation	0.635	0.623	**0.705**	0.656	0.115
Augmented	0.519	0.568	0.68	0.692	–

Several potential research topics in Indonesia

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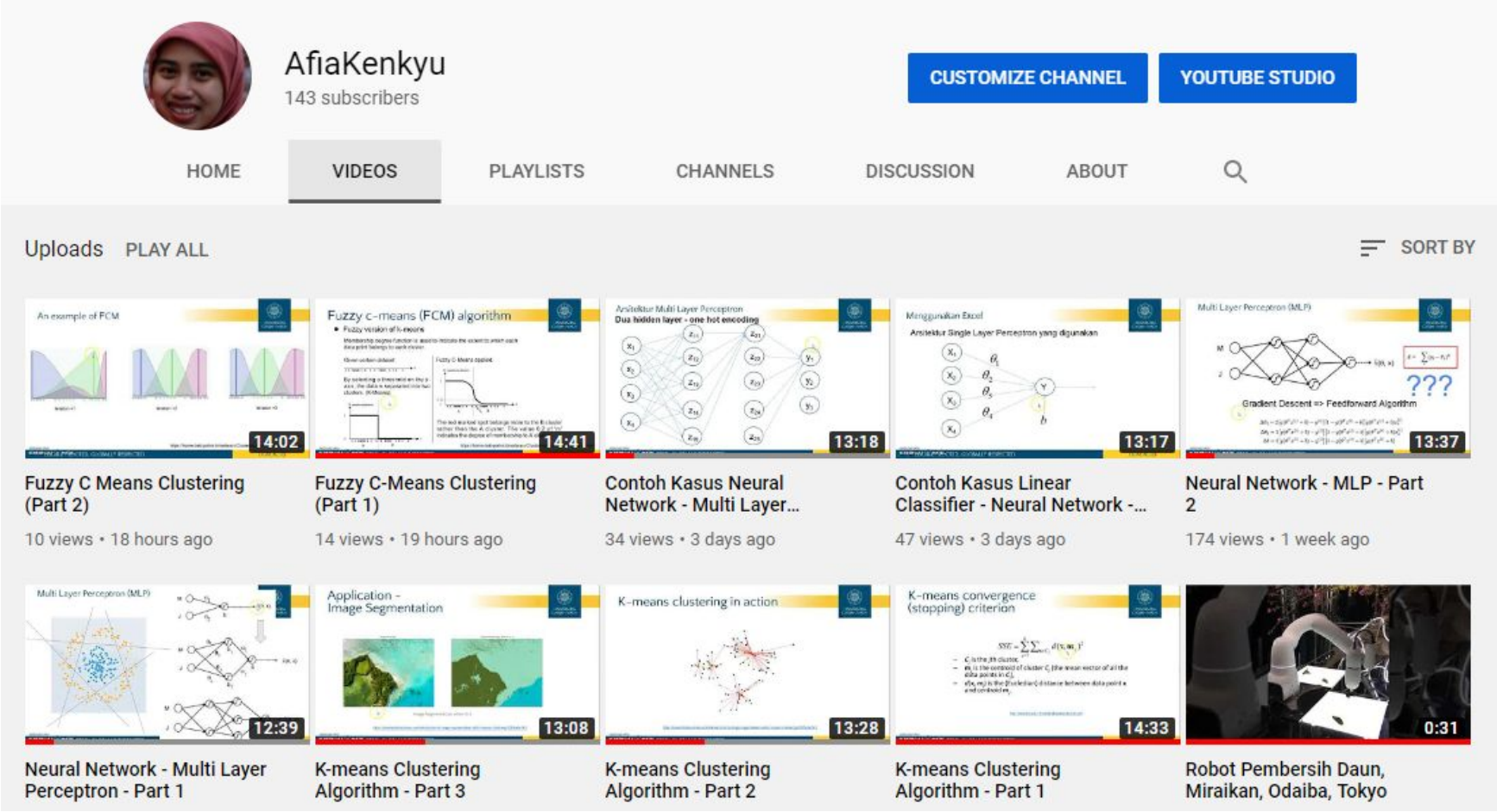
- Bioinformatics basic tasks
- Indonesia's Cancer analysis
- Indonesia's NGS analysis
- COVID19 Genome Analysis
- Machine learning in bioinformatics : Protein Secondary Structure Prediction, ...

Youtube Channel : **AfiaKenkyu**
Please subscribe! :)



Thank you for your attention!
Maturnuwun!

Assembly with de Bruijn graph

Original sequence

ATGCGAGGCGTGG

ATGCG
GCGAG
AGGCG
CGTGG

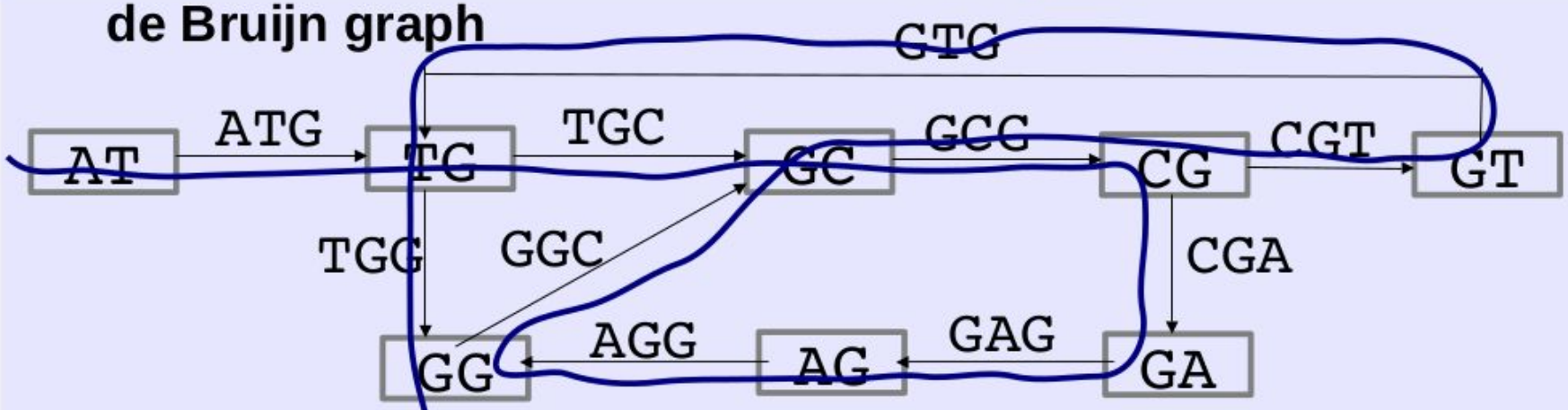
reads

***k*-mers (*k*=3)**

ATG TGC GCG CGA
GAG AGG GGC CGT
GTG TGG

ATG → AT , TG
***k*-mer** **(*k*-1)-mer x 2**

de Bruijn graph



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