
Computer Vision
and
Pattern Discovery
Laboratory

Development of AI research for:

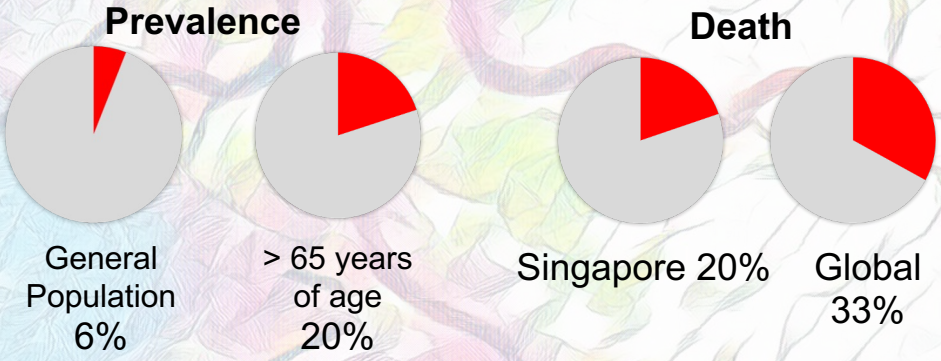
- Digital Pathology and oncology
- Cardiovascular diseases
- Skin diseases
- Hematology
- Protein structures and drug discovery
- Agriculture technology

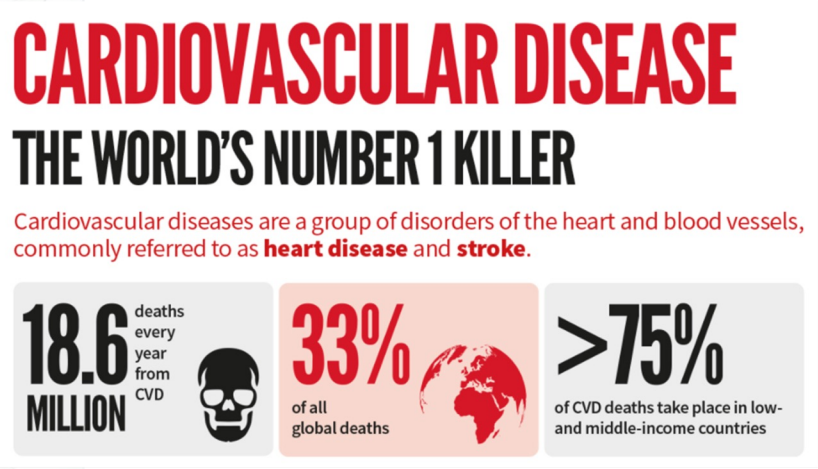
Institute of Materials Research and Engineering IMRE
Institute of High Performance Computing HPC
Institute for Infocomm Research I²R
Institute of Bioengineering and Bioimaging IBB
Institute of Molecular and Cell Biology IMCB
Genome Institute of Singapore GIS
Experimental Drug Development Centre EDDC
Nanyang Technological University Singapore
Duke-NUS Medical School
NUS National University of Singapore
National Skin Centre National Healthcare Group
National Heart Centre Singapore SingHealth
NUHS National University Health System
Tan Tock Seng Hospital National Healthcare Group
NUH National University Hospital
Singapore General Hospital SingHealth
National Cancer Centre Singapore SingHealth

AI driven national Platform for CT cOronary angiography for clinicaL and industriaL applicatiOns (APOLLO)

Computed Tomography Coronary Angiography (CTCA) is the first line investigation, but traditional analyses:

- Take a long time (2 - 4 hours for a specialized report)
- Lack efficient toolkits to analyze calcium score, epicardial fat, severity of stenosis, and plaque characteristics





Source: World Heart Federation (2021)

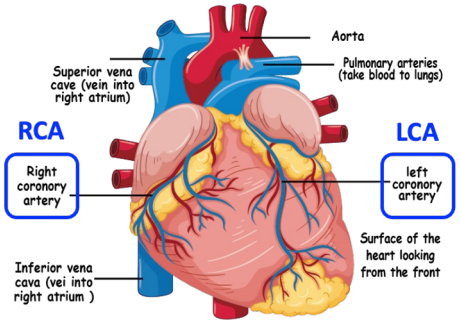
National Heart Centre Singapore SingHealth · NUH National University Hospital A member of the NUHS · Tan Tock Seng Hospital National Healthcare Group · Institute for Infocomm Research I²R · Bioinformatics Institute BII · Institute of High Performance Computing IHPC · Duke-NUS Medical School · Nanyang Technological University Singapore

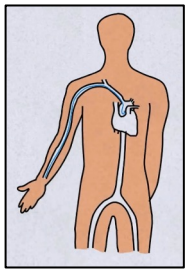
Special thanks to Jiahui Dong for making the video

Catheter x-ray guided Angiography

- Coronary angiogram is the gold standard technique to visualise **coronary arteries of the heart**.
- Performed to detect blood vessel narrowing (**stenosis**), found in **coronary artery diseases** (**Atherosclerosis**, **Thrombosis**).

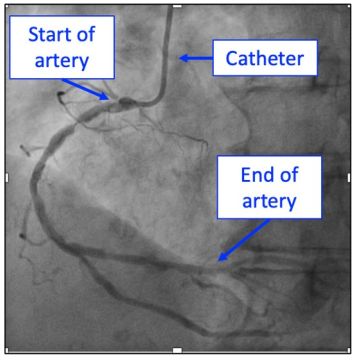
Vessels in the heart





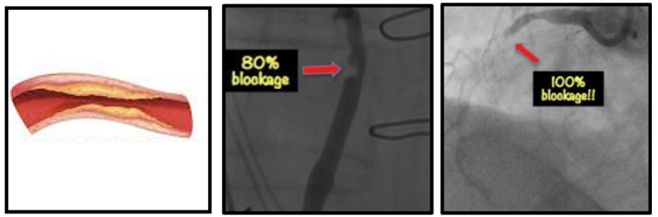
Insert catheter, Inject contrast dye

Angiography video for RCA



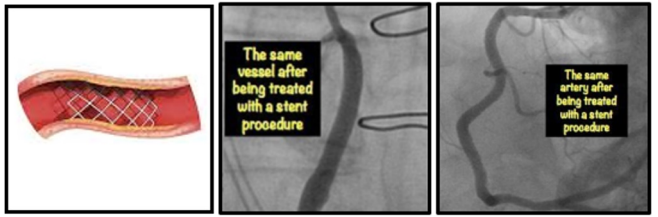
Clinical Significance:

Diagnosing coronary artery diseases



Narrowing blood vessels (Stenosis)

Monitoring intervention strategies (stenting)



After stent procedure

Limitations of current diagnosis method:

- **Inter observer variability** in grading stenosis
- Low reproducibility
- Time consuming (videos with 11 different views need to be considered)

Aims:

Use multiview **AI approaches** to develop an end-to-end pipeline for **stenosis detection** using **X-ray angiography videos.**

Bioinformatics Institute BII

Institute of Bioengineering and Bioimaging IBB

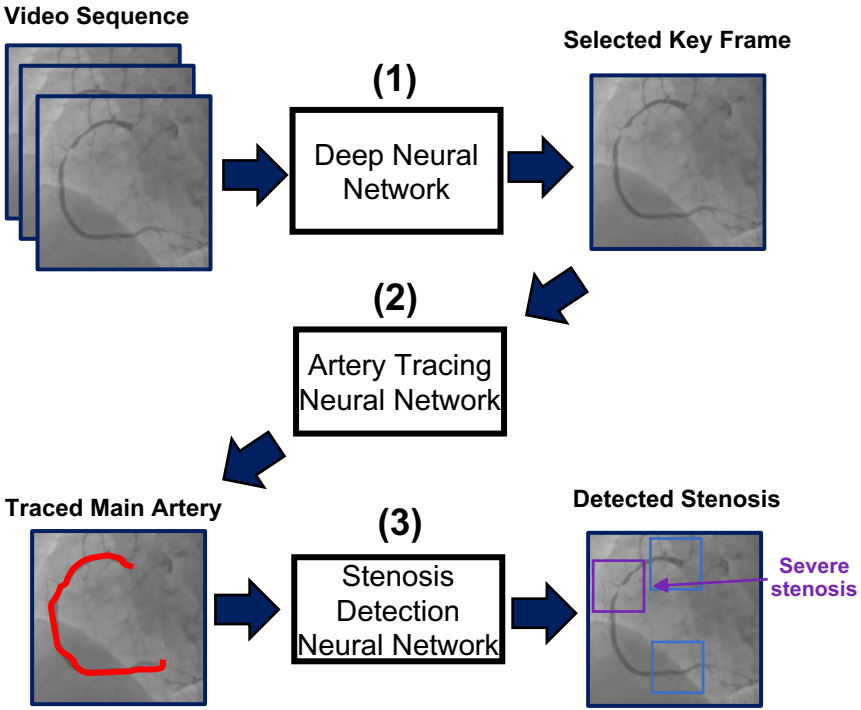
National Heart Centre Singapore SingHealth

DukeNUS Medical School

Catheter x-ray guided Angiography

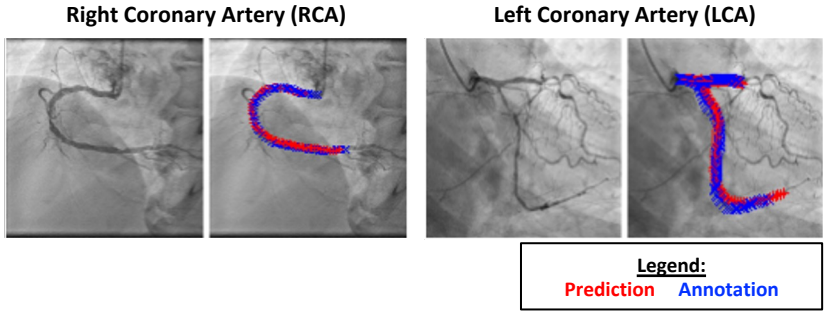
3-Stage Pipeline

(1) Key frame Selection, **(2)** Artery Tracing, and
(3) Stenosis Detection

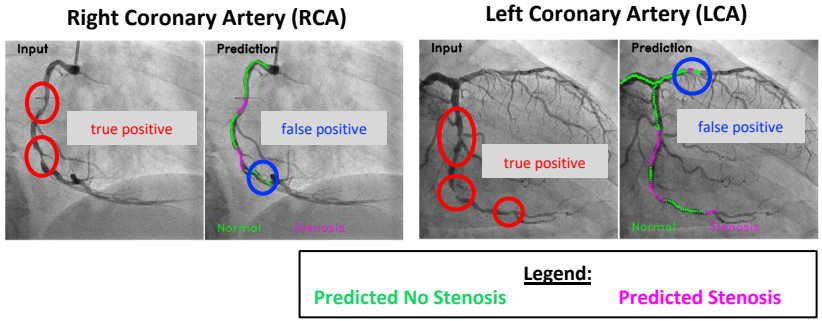


Results

(2) Artery Tracing

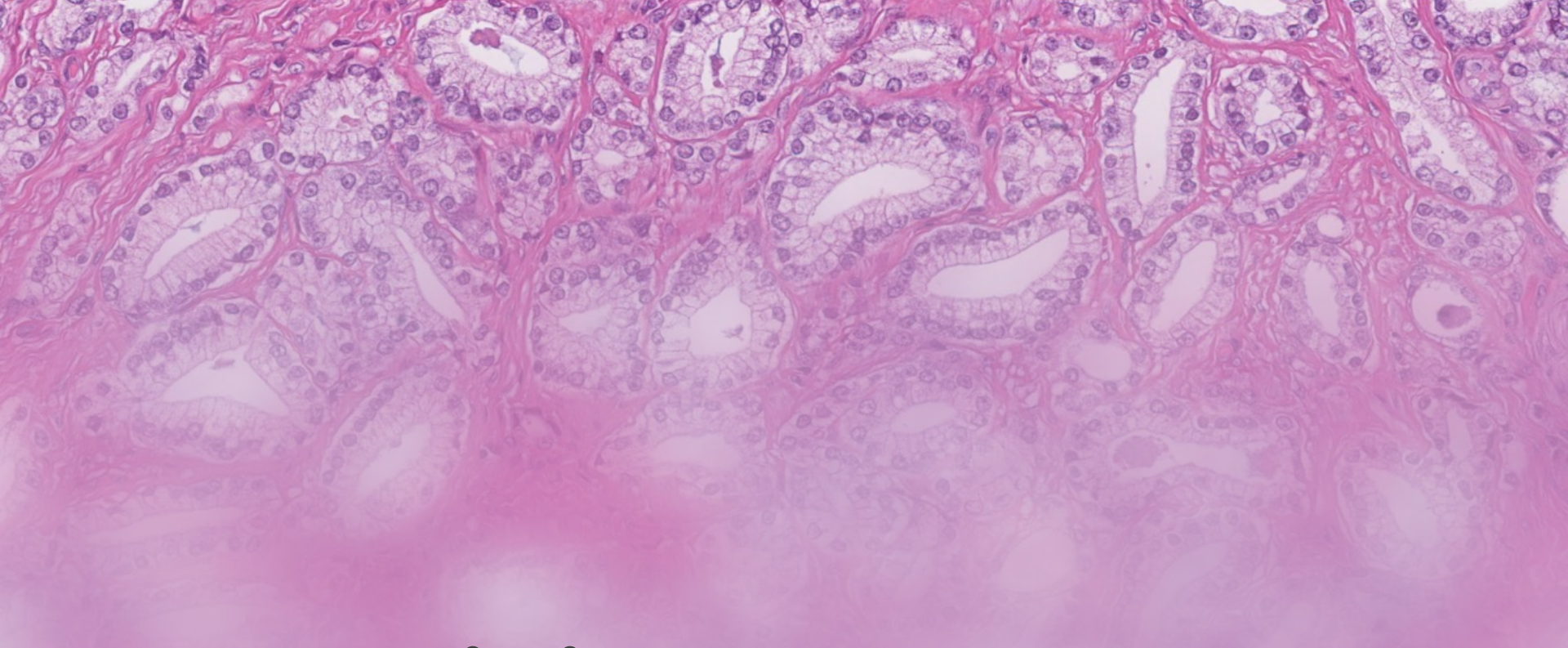


(3) Stenosis Detection



National Heart Centre Singapore SingHealth
DukeNUS Medical School
Bioinformatics Institute BII
Institute of Bioengineering and Bioimaging IBB

Done by: Liu Wei, Eddy Tan, Tiana Chen, Liang Kaicheng, Joel Ang, Nicholas Cheng, Lin Li

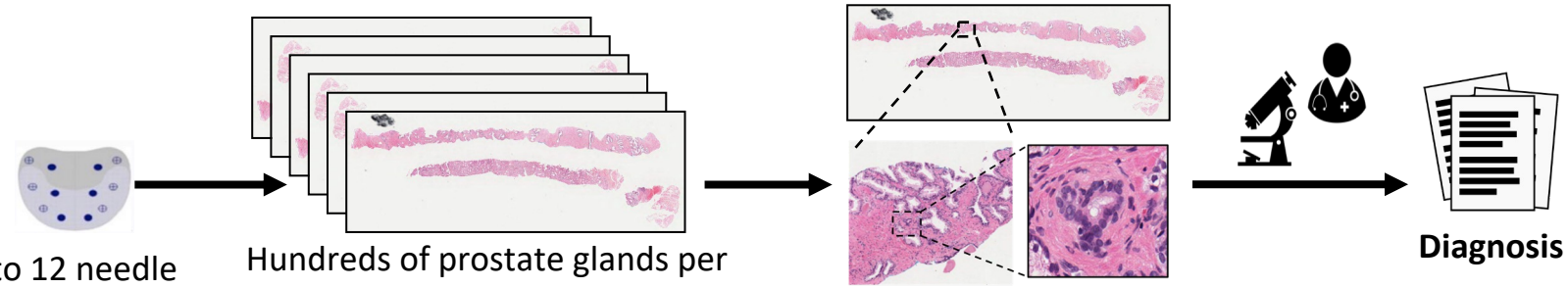


Digital Pathology

Using Deep Learning to Assist Pathologists for Prostate Cancer Biopsy

In collaboration with
Weimiao Yu

- Increased incidence rates of prostate cancer [1] -> Increased workload
- Analysis of 1000s of glands per case Tedious and time consuming
- Inter-observer and intra-observer variability
- Decreasing number of pathologists [3]



6 to 12 needle core biopsy [2]

Hundreds of prostate glands per core and the total number is about **2000 glands per case**

Pathologist evaluates histological slides

Diagnosis

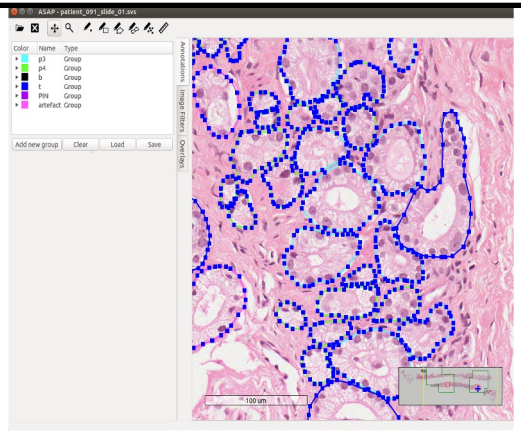
- Our pipeline is designed for use by pathologists on low-grade, low-volume cases.
- In these cases, a vast majority of the biopsy slide can consist of normal tissues with very few malignant glands
- Pathologists need to spend a long time finding any existing malignant glands and can easily miss malignant glands resulting in underdiagnosis

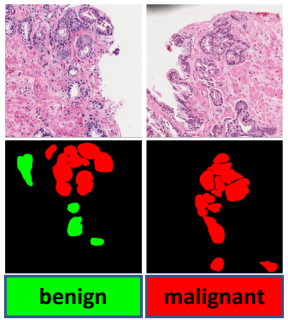
[1] Singapore Cancer Registry 50th Anniversary Monograph (1968 – 2017).
[2] Metter, D. M., Colgan, T. J., Leung, S. T., Timmons, C. F., & Park, J. Y. (2019). Trends in the US and Canadian pathologist workforces from 2007 to 2017. *JAMA network open*, *2*(5), e194337-e194337.
[3] Wang, B., Chen, C. C., Zheng, R., Hu, J., & Ou, Y. (2018). *Journal of the Chinese Medical Association, 81*(12), 1044-1051. doi:10.1016/j.jcma.2018.06.003.

Bioinformatics Institute BII
Genome Institute of Singapore GIS
NUS National University of Singapore
Tan Tock Seng HOSPITAL National Healthcare Group

Using Deep Learning to Assist Pathologists for Prostate Cancer Biopsy

In collaboration with **Weimiao Yu**

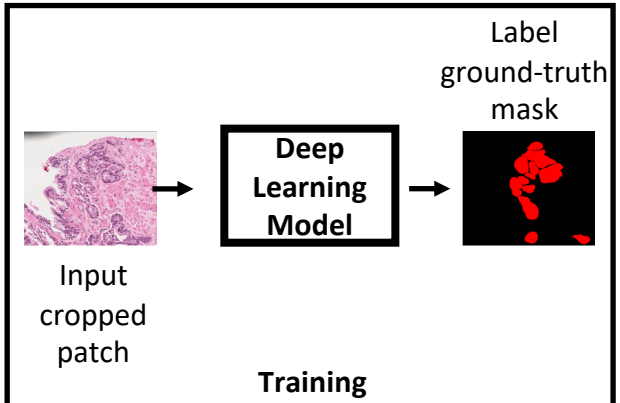




Patch Cropping

	Scanned	Annotated	Checked
# of patients	172	65	51

Manual Annotation

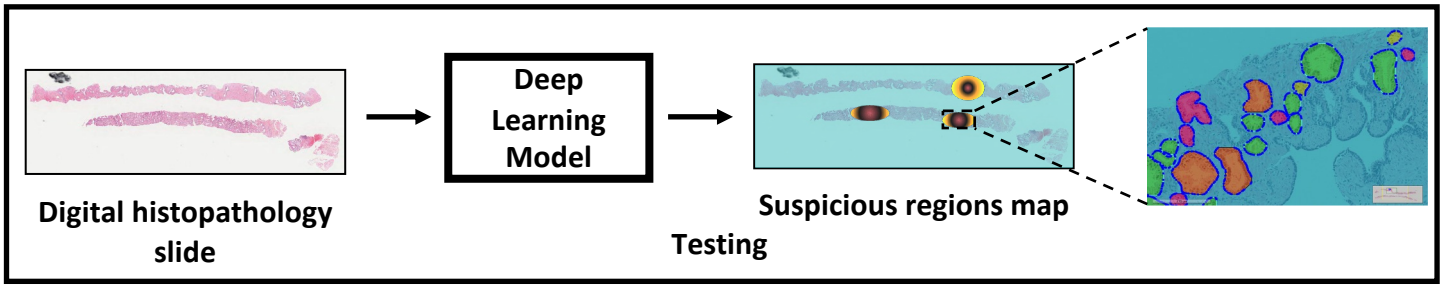


Gland Classification Performance

	Benign (Gland) Prediction	Malignant (Gland) Prediction
Benign (Gland) Label	1723	47
Malignant (Gland) Label	39	2894

Precision = 98.4%

Recall = 98.7%



Oner, Mustafa Umit et al. **An AI-assisted Tool For Efficient Prostate Cancer Diagnosis .** Submitted to Cell Patterns. 2022

Bioinformatics Institute BII

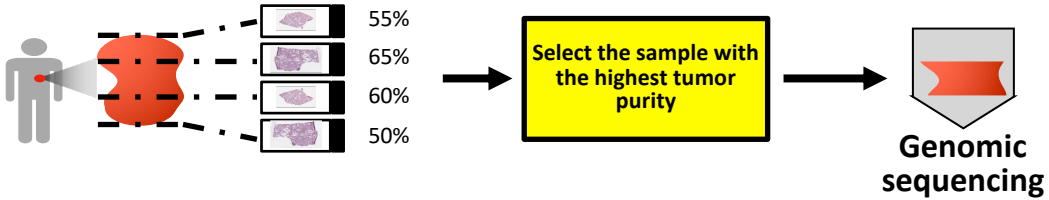
Genome Institute of Singapore GIS

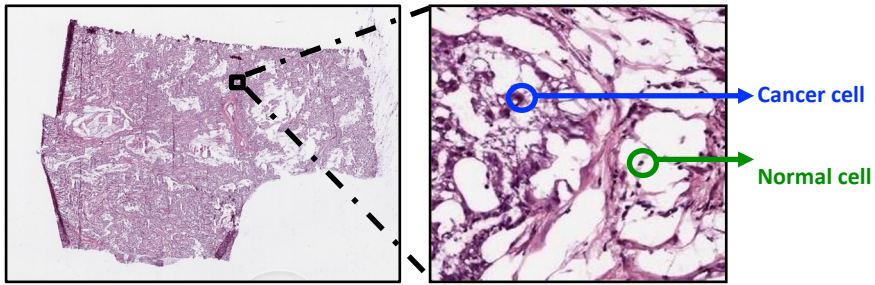
NUS National University of Singapore

Tan Tock Seng Hospital National Healthcare Group

Pan Cancer: Spatially Resolved Tumor Purity Maps

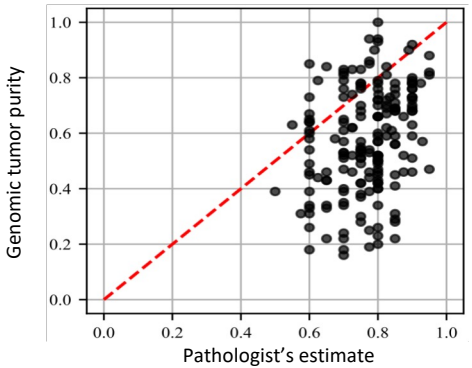
Tumor purity: percentage of cancer cells within a sample





- **Tedious and time consuming**
- **High inter-observer variability [2]**

An accurate tumor purity estimation is crucial in sample selection for genomic sequencing [1].

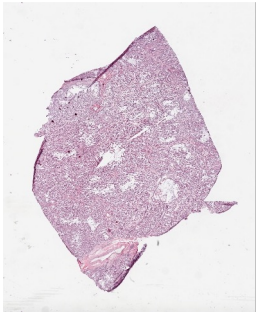


- **Pathologists's estimates are not consistent with genomic tumor purity values ("accurate")**

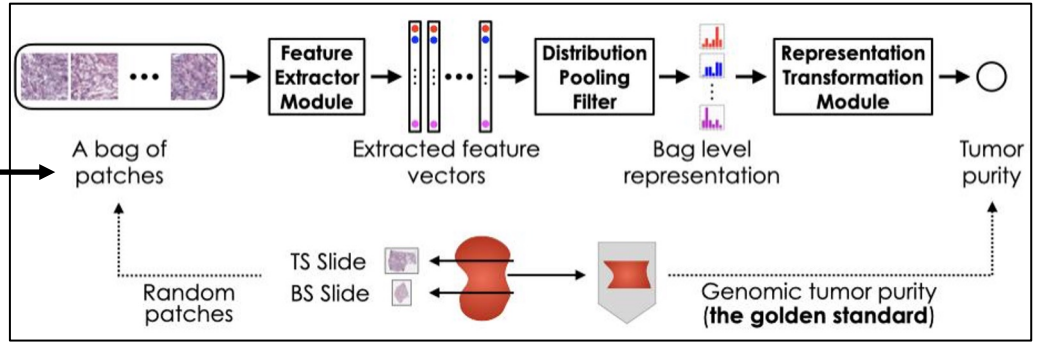
[1] *Kim et al., Journal of Pathology and Translational Medicine, 2017*
[2] *Smits et al., Modern Pathology, 2014*

NUS National University of Singapore · Genome Institute of Singapore GIS · Singapore General Hospital SingHealth · National Cancer Centre Singapore SingHealth

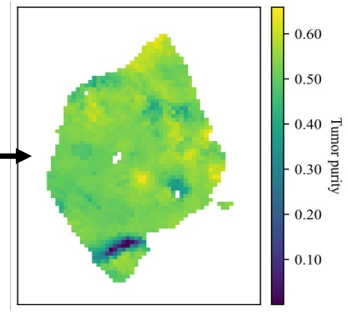
Pan Cancer: Spatially Resolved Tumor Purity Maps



Digital histopathology slide

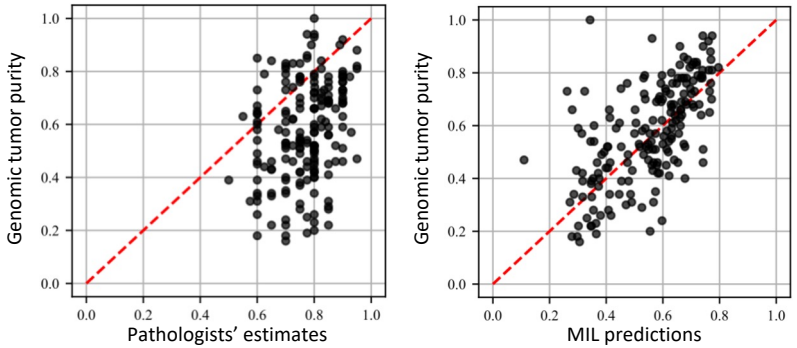


Deep Learning Model

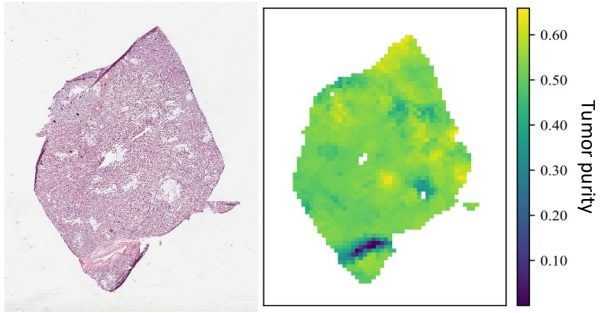


Tumor Purity Heatmap

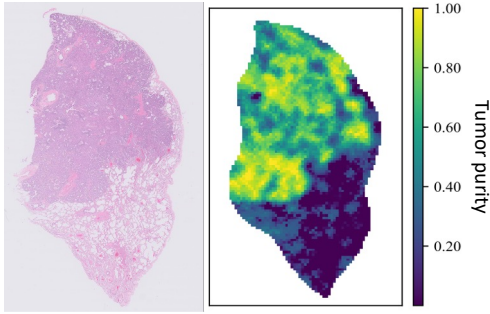
Correlation Analysis in TCGA BRCA



Example Tumor Purity Heatmaps



TCGA LUAD cohort
(fresh-frozen section)



Singapore LUAD cohort
(Formalin-fixed paraffin-embedded section)

Oner, Mustafa Umit et al. **Obtaining spatially resolved tumor purity maps using deep multiple instance learning in a pan-cancer study**. *Patterns* 3.2 (2022): 100399.

NUS National University of Singapore

Genome Institute of Singapore GIS

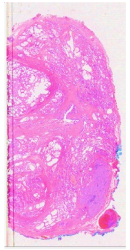
Singapore General Hospital SingHealth

National Cancer Centre Singapore SingHealth

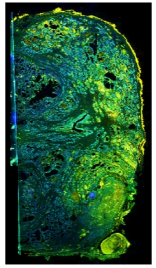
Multiplex Immunofluorescence Image Analysis

In collaboration with
Weimiao Yu

Prostate Cancer

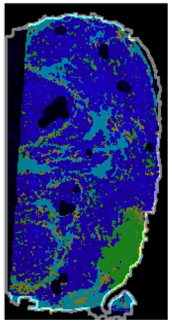


H&E Image



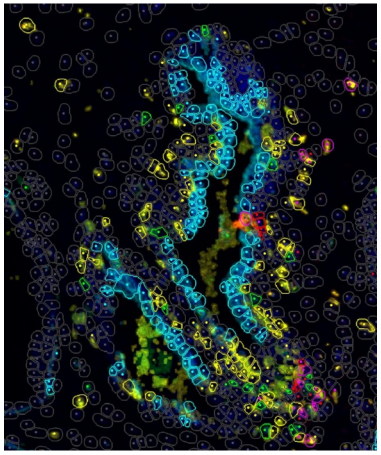
Multiplex immunofluorescence (mIF) Image

H&E Tissue Classification and Automated Immunophenotype Detection (mIF)



Automated H&E Tissue Classification

Automated Immunophenotype Detection (mIF)



- Gleason Grade 3
- Gleason Grade 4
- Gleason Grade 5
- Normal
- Stroma

Tissue classification uses Deep Learning.

Automated immunophenotype detection uses gaussian mixture models, clustering and histogram analysis.

- Non Ultivue
- CD8 positive Exclusive: Cytotoxic T Cell and NK Cell
- CD68 positive Exclusive: Macrophage and Mononcyte
- PDL1 positive Exclusive: Checkpoint Expression
- panCK/SOX10 positive Exclusive: Carcinoma(panCK) or Melanoma(SOX10)
- CD68 PDL1 positive Exclusive: Pro Tumor Macrophage
- PDL1 panCK positive Exclusive: Immune Evading Carcinoma

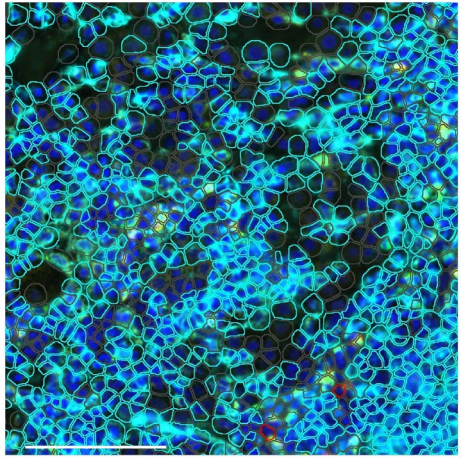
Chronic Hepatitis B

Multiplex immunofluorescence (mIF) Image

Manual Tissue Annotation and Automated Immunophenotype Detection (mIF)

Manual Tissue Annotation

Automated Immunophenotype Detection (mIF)

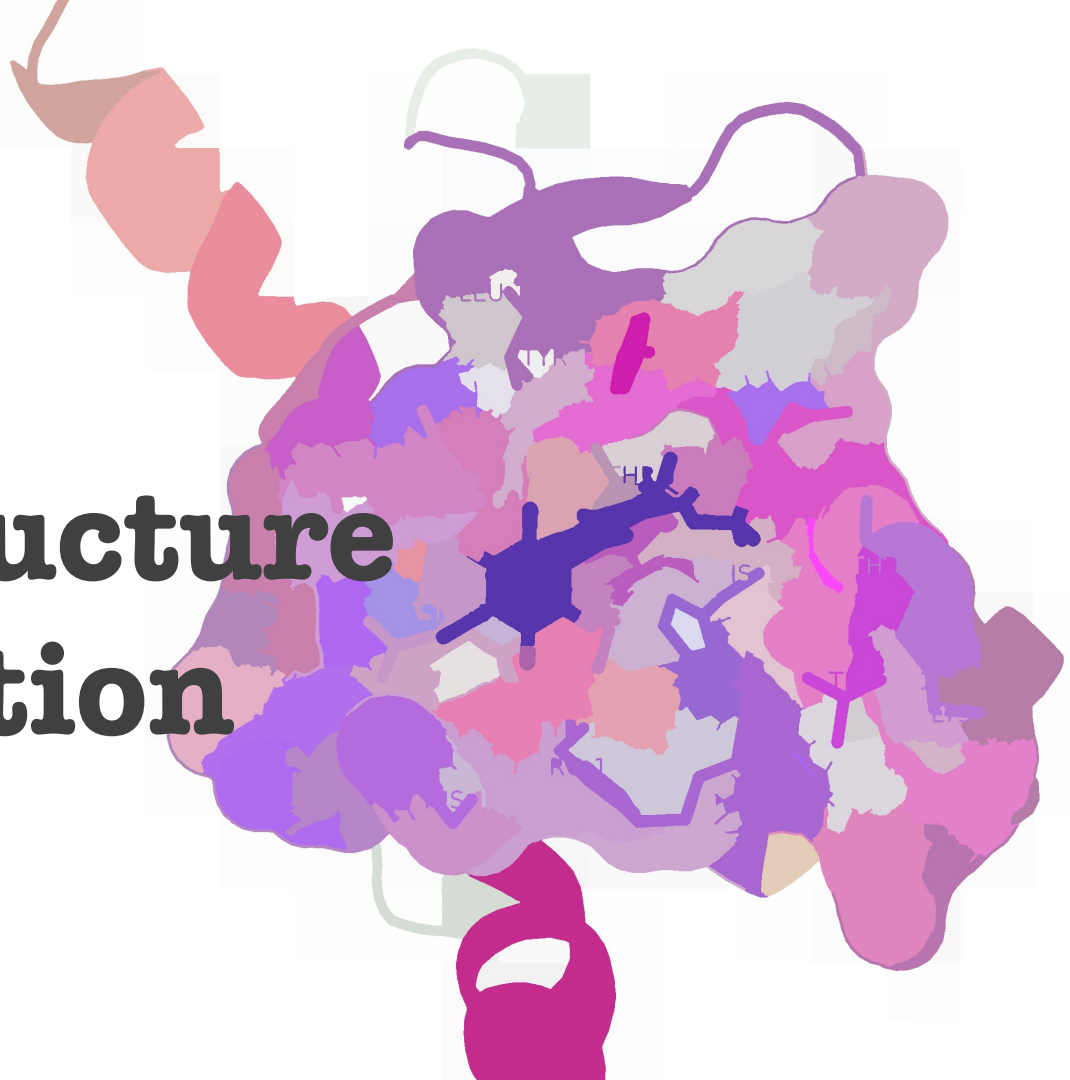


- Parenchymal Region
- APC-rich Region
- Immune Infiltrate Region

Automated immunophenotype detection uses histogram analysis

- Non Ultivue
- Ki67 positive Exclusive: Proliferating Cell
- GranzymeB positive Exclusive: Cytotoxic Cell
- CD3 positive Exclusive: T Cell
- panCK/SOX10 positive Exclusive: Carcinoma(panCK) or Melanoma(SOX10)
- Ki67 GranzymeB positive Exclusive: Proliferating Cytotoxic Cell
- Ki67 CD3 positive Exclusive: Proliferating T Cell
- Ki67 panCK positive Exclusive: Proliferative Tumor Cell
- GranzymeB CD3 positive Exclusive: Cytotoxic T Cell
- Ki67 GranzymeB CD3 positive Exclusive: Proliferating Cytotoxic T Cell

AI in Protein Structure computation



AI in structural biology research

Deep Learning of an effective Hamiltonian

$$p\left(t+\frac{\tau}{2}\right) = p(t) + \frac{\tau}{2}\dot{p}(t) = p(t) + \frac{\tau}{2}\left(-\left.\frac{dH}{dq}\right|_{t}\right)$$

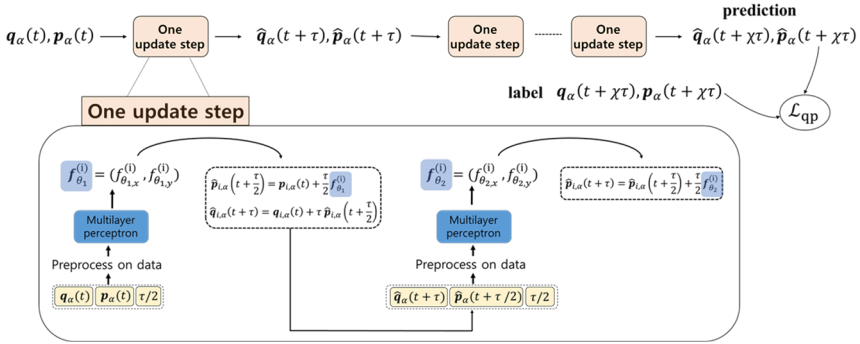
$$q(t+\tau) = q(t) + \tau\dot{q}\left(t+\frac{\tau}{2}\right) = q(t) + \tau\, p\left(t+\frac{\tau}{2}\right)$$

$$p(t+\tau) = p\left(t+\frac{\tau}{2}\right) + \frac{\tau}{2}\dot{p}(t+\tau) = p\left(t+\frac{\tau}{2}\right) + \frac{\tau}{2}\left(-\left.\frac{dH}{dq}\right|_{t+\tau}\right)$$

Force by MD simulation

large time step

Large time step molecular dynamics simulations cause fatal numerical instabilities. AI enhanced molecular dynamics can speed up simulations by > 10x – 100x



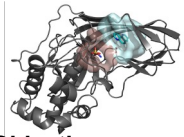
CHOSUN UNIVERSITY

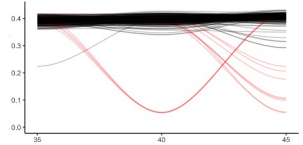
Bioinformatics Institute A*STAR

Virtual drug screening

In collaboration with **Fan Hao**

~1,500,000 protein - ligand pairs → Partition data into multiple testing configurations → Compare performance of multiple models under multiple configurations

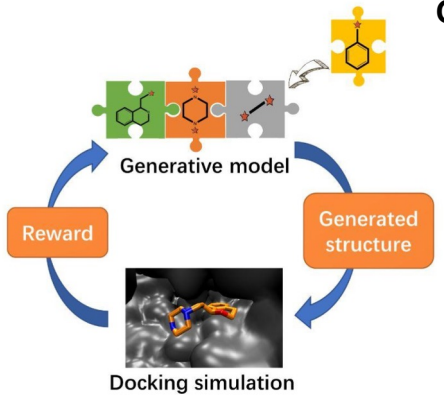




Objective:

- Compile diverse benchmarking datasets and novel evaluation methods to test machine learning-based virtual screening models.
- Diagnose test performance instabilities.
- Combine new ligand and protein featurization methods with effective regularization to create well-generalizing models.

De novo drug design using reinforcement learning



Objective:

- *In silico* fragment growing through generative model
- Employing docking simulation to evaluate the reward

In collaboration with **Yaw Sing, Chandra**

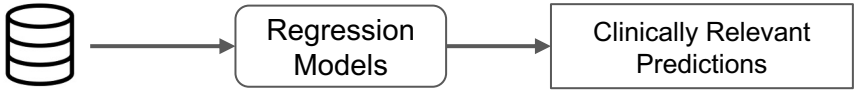
SingCLOUD

Analysis of a large multi-centre database of

Cardiac Surgery Dataset
Medication Dataset
Financial Dataset etc

In collaboration with
Wong Wing Cheong

Total **26 Datasets**



Project aims:

- Study clinicoeconomics of cardiovascular diseases for improving disease management

- Perform data integration and analysis across multiple databases to find new discoveries in clinical science and AI development

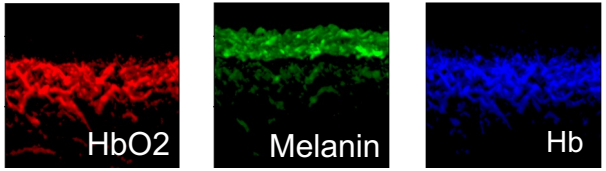
National Heart Centre Singapore
SingHealth

Photo-acoutics Image analysis for skin inflammatory disorder diagnosis

Psoriasis is **a skin disease that causes red, itchy scaly patches.** Atopic dermatitis (eczema) is also a condition that makes your skin **red and itchy**.

Objective:

- To use the information provided by photoacoustic imaging to detect different inflammatory diseases such as Psoriasis and Atopic Dermatitis
- To evaluate if there exists a strong correlation between inflammatory skin diseases and diabetes



Institute of Bioengineering and Bioimaging
IBB

NATIONAL SKIN CENTRE
National Healthcare Group

Different spatial maps provided by an photacoutics image

SCISSOR: Analysis of Spatial transcriptomics

Objective:

-Use spatial techniques to identify spatial changes in organization interaction and function for different cell types and states

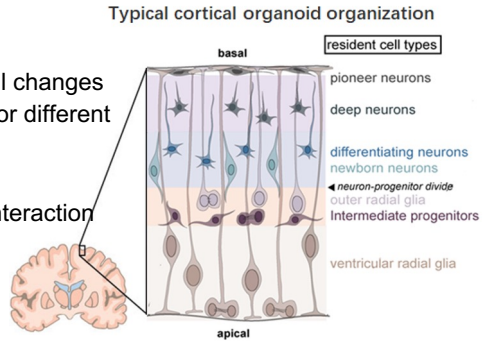
Application:

-Study spatial changes in organization interaction

-Molecular changes in cell type and tissue context

-Differential expressed gene

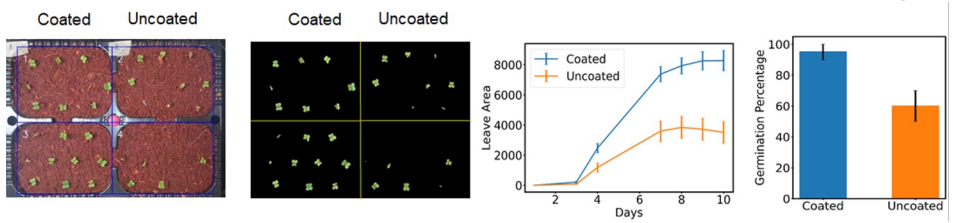
-Differential spatial signalling pathway



Genome Institute of Singapore
GIS

Nanocoating Technology for Plant Growth and Germination

Quantitative measurement software for automated plant monitoring



Objective

-Develop a quantitative measurement Software

-Monitoring plant growth over time, like germination percentage, surface area of leaves,etc.

-Single time point measurements for plant growth indices.

-Build regression model for determining the optimal nanocoating formulation

Institute of Materials Research and Engineering
IMRE

Collaborators and Acknowledgments (non-exhaustive list)

BII	ASTAR	ASTAR	Clinical centres	Clinical centres	Universities
Sebastian Maurer-Stroh	Malini Olivo	Weimin Huang	Tony Lim Kiat Hon	Yeo Khung Keong	Kong Wai Kin Adams
Lit-Hsin Loo	Kaicheng Liang	Nancy Chen	Daniel Tan	Jonathan Yap Jiunn Liang	Ken Sung Wing Kin
Bhanu Prakash	Yi Yan Yang	Anders Skanderup	Danilo Giron	Mark Chan	Ee Chien Chang
Chandra Verma	Shyam Prabhakar	Savitha Ramasamy	Chin Fong Wong	Lynette Teo	Tat Jen Cham
Yaw Sing Tan	Kok Hao Chen	Mile Sikic	Valerie Yang	Yew Min Sen	Wei Teck Ang
Fan Hao	Jackie Ying	Su Yi	Zhong Liang	Ngiam Kee Yuan	Igor Chernyavsky
Wong Wing Cheong	Mya Thway Tint	Xinyi Su	Lohendran Baskaran	Ooi Chin Chin	Kees Weijer
Weimiao Yu	Jonathan Huang	*et al*	Daniel Roger Vaughan	Celia Tan La Choo	Wooseop Kwak
Keng Hwee Chiam	Ramanuj DasGupta		Matthew Cove	Tan Soo Yong	Yutaka Okabe

Institute of Materials Research and Engineering IMRE
Institute of High Performance Computing HPC
Institute for Infocomm Research I²R
Institute of Bioengineering and Bioimaging IBB
Institute of Molecular and Cell Biology IMCB
Genome Institute of Singapore GIS
Experimental Drug Development Centre EDDC
Nanyang Technological University Singapore
Duke-NUS Medical School
NUS National University of Singapore
National Skin Centre National Healthcare Group
National Heart Centre Singapore SingHealth
NUHS National University Health System
Tan Tock Seng Hospital National Healthcare Group
NUH National University Hospital
Singapore General Hospital SingHealth
National Cancer Centre Singapore SingHealth

Laboratory members

Staff	PhD students	Interns
Mahsa Paknezhad	Davide Coppola	Tiana Chen
Eddy Tan	Isaac Cheong	Yiqing Xia
Nicholas Cheng	Brian Chen	Paul Chee
Malay Singh	Wan Tianran	Andre Villanuevs
Liu Wei		Aubrey Ng
Lin Li		Chen Rong
Robin Ramdin		Sarah Chan
Park Sojeong		Zheng Yilong
Kavita Kuar		Christopher Wyrtzen
		Patrick Wan