Building and Evaluating Computational Pathology Foundation Models for Breast Cancer

Fredrik K. Gustafsson
Karolinska Institutet
Department of Medical Epidemiology and Biostatistics, Rantalainen Group
www.fregu856.com

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About the Presentation

I'm a postdoc in the group of Mattias Rantalainen at Karolinska Institutet (Department of Medical Epidemiology and Biostatistics), since December 2023.

Will give a snapshot of some ongoing work in the group, focusing on how we train and evaluate *computational pathology foundation models* on in-house breast cancer data.

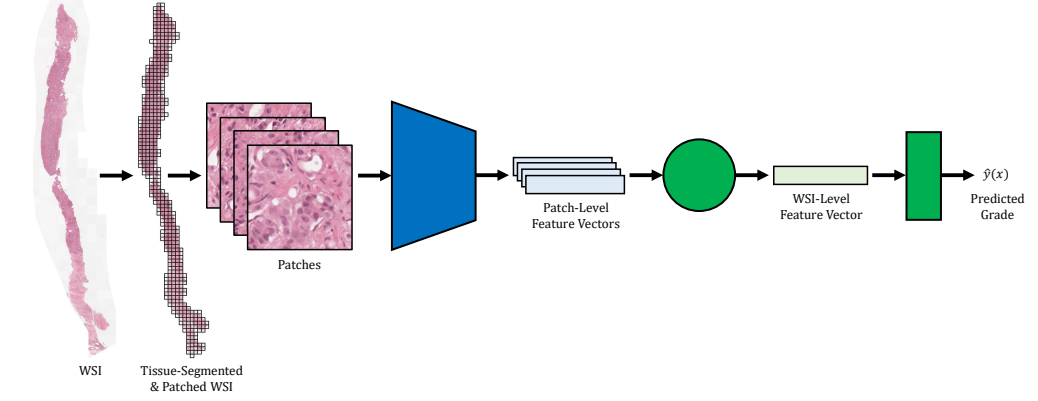
Rantalainen Group:

Mattias Rantalainen.

Constance Boissin, Kajsa Ledesma Eriksson, Bojing Liu, Francisco J. Peña, Abhinav Sharma, Erik Thiringer, Duong Tran, Yujie Xiang, Anne-May Österholm.

Computational pathology uses machine learning and computer vision to automatically extract useful information from histopathology whole-slide images (WSIs).

Given datasets of (WSI, label) pairs, models can be trained for applications such as *histological grading*, patient outcome prediction, and prediction of various biomarkers.



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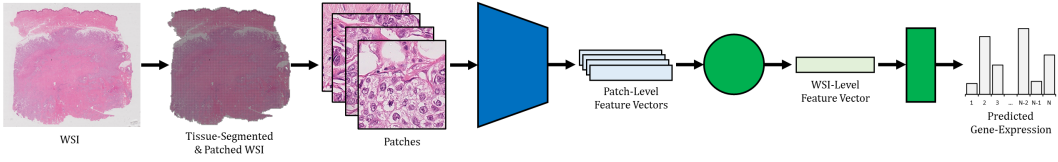

Foundation Models

Foundation models are large models trained on *large amounts of unlabeled data* using *self-supervised learning*. They are intended to be general-purpose feature extractors.

Self-supervised learning enables models to be trained on "raw" unlabeled data. Large collections of unlabeled WSIs – *WSIs without known clinical info, patient outcomes or any other type of annotations* – can thus be directly utilized in model training.

Has recently become a popular research direction within computational pathology:

UNI: **Towards a General-Purpose Foundation Model for Computational Pathology**
Nature Medicine, 2024

Prov-GigaPath: **A Whole-Slide Foundation Model for Digital Pathology from Real-World Data**
Nature, 2024

Virchow: **A Foundation Model for Clinical-Grade Computational Pathology and Rare Cancers Detection**
Nature Medicine, 2024

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Details for two recent computational pathology (CPATH) foundation models:

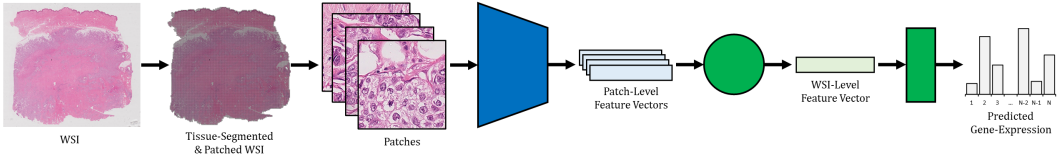
UNI:

- Pretrained using self-supervised learning (DINOv2) on a *pan-cancer dataset* (20 major tissue types) of *100 million tissue patches* from more than *100,000 WSIs*.
- Most WSIs are collected from the Massachusetts General Hospital and Brigham and Women's Hospital in Boston, USA.
- Vision transformer ViT-Large model, 303 million parameters.

Virchow:

- Pretrained using self-supervised learning (DINOv2) on a *pan-cancer dataset* (17 major tissue types) of *2 billion patches* from more than *1.4 million WSIs*.
- WSIs are collected from the Memorial Sloan Kettering Cancer Center (New York, USA), from more than *119,000 patients*.
- ViT-Huge model, 632 million parameters.

Using CPATH Foundation Models



Typical workflow:

- Tissue-segment each WSI and divide it into image patches (e.g. 224×224 pixels).
- Use a *frozen* foundation model to extract feature vectors for all images patches in each WSI (*typical range: 5,000 - 25,000 image patches per WSI*).
- Train a small model that, for each WSI, takes the extracted patch-level feature vectors as input and outputs a WSI-level prediction (standard supervised training).

Observation:
In various downstream breast cancer-related tasks, CPATH foundation models trained on pan-cancer histopathology image data (e.g. UNI & Virchow) significantly outperform regular foundation models trained on natural images.

Hypothesis:
In various downstream breast cancer-related tasks, *tissue-specific* foundation models trained on *breast-specific* histopathology image data will outperform pan-cancer CPATH foundation models (e.g. UNI & Virchow).

Approach:
Train ViT model using DINOv2 on an *in-house dataset of more than 60,000 WSIs from Swedish breast cancer patients*, compare with UNI and other pan-cancer models.

Training CPATH Foundation Models for Breast Cancer - Details

Dataset details:

- More than *60,000 WSIs*, *100 TB* of data in total.
- More than *1.1 billion* 224×224 image patches after preprocessing.
- Data from six different sites, 80% of WSIs are from Kalmar, Örebro or Jönköping.
- Only H&E-stained WSIs (future work: Utilize the IHC-stained WSIs as well).
- All WSIs have been digitized/scanned in-house.

First approach: Randomly sample 1,000 tissue patches per WSI to create the final training dataset, resulting in more than *60 million* image patches (800 GB of data).

Initial experiments are ongoing, training ViT-Large and ViT-Base models.

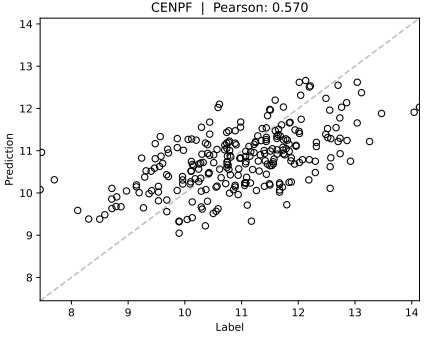
Evaluating CPATH Foundation Models for Breast Cancer (1/3)

Two examples of tasks we are benchmarking public CPATH foundation models on:

Benchmarking task 1: **Gene-expression prediction**.

Using the public TCGA-BRCA dataset, containing WSIs and corresponding gene-expression labels of *20,000 genes* for more than *1,000 patients*. Train model to predict all 20,000 genes, evaluate on subset of *50 breast cancer-related genes (PAM50)*.

Rank	Model name	PAM50 mean Pearson (↑)
1	H-optimus-1	0.595±0.016
2	H0-mini	0.591±0.014
3	H-optimus-0	0.587±0.012
4	UNI2-h	0.583±0.016
5	Virchow2	0.582±0.019
6	CONCHv1.5	0.576±0.021
7	CONCH	0.574±0.019
8	Prov-GigaPath	0.571±0.009
9	Virchow	0.563±0.020
10	UNI	0.562±0.026
11	CTransPath	0.517±0.029
12	RetCCL	0.449±0.034
13	Resnet-IN	0.379±0.034

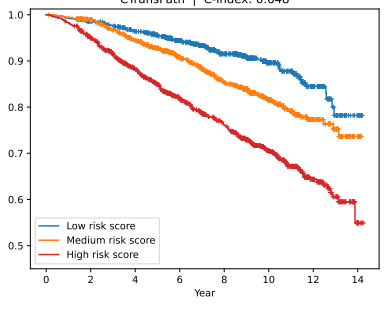


Benchmarking task 2: **Survival prediction**.

Using in-house datasets with WSIs and corresponding patient outcomes (overall survival + recurrence events) for Swedish breast cancer patients from 3 different sites.

- Training: *2,300 patients*, mean follow-up time of *7.5 years*, 350 events.
- Evaluation: *3,100 patients*, mean follow-up time of *7.6 years*, 510 events.

Rank	Model name	C-index (↑)
1	H0-mini	0.689±0.012
2	H-optimus-1	0.687±0.012
3	Virchow2	0.682±0.012
4	H-optimus-0	0.677±0.012
4	UNI2-h	0.677±0.012
6	CONCH	0.675±0.012
7	Prov-GigaPath	0.674±0.012
8	CONCHv1.5	0.672±0.012
9	Virchow	0.671±0.013
10	UNI	0.666±0.012
11	RetCCL	0.659±0.012
12	CTransPath	0.648±0.013
13	Resnet-IN	0.633±0.013



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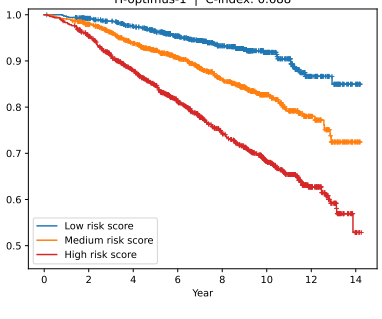
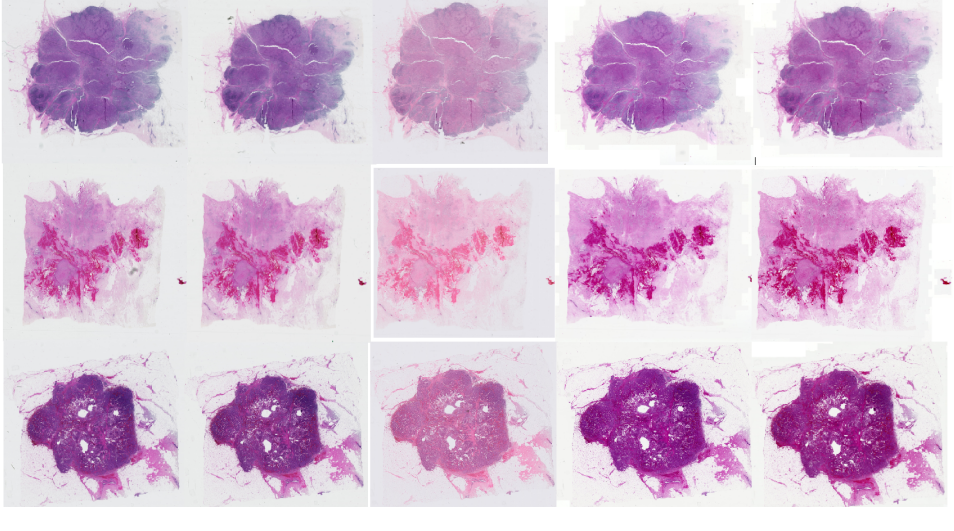


Evaluating CPATH Foundation Models for Breast Cancer (3/3)

We are also evaluating **scanner-variability robustness** of CPATH foundation models, using an in-house dataset of WSIs digitized/scanned with five different scanners.



Main Takeaways

(1/4) We are training foundation models specifically for breast cancer using an *in-house dataset of more than 60,000 WSIs from Swedish breast cancer patients*.

(2/4) Our hypothesis is that such *tissue-specific* foundation models will outperform current pan-cancer models in important breast cancer-related CPATH applications.

(3/4) Being able to train in-house foundation models also enables the group to explore strategies for improved model robustness (different scanners, labs & hospitals), train models for IHC-stained WSIs, develop new self-supervised learning methods tailored for pathology data, study how performance scales with the model and dataset size, etc.

(4/4) Our in-house foundation models will serve as the backbone for various *breast cancer precision diagnostics* solutions developed by the group moving forward.

Contact & Acknowledgements

Fredrik K. Gustafsson
fredrik.gustafsson@ki.se
www.fregu856.com

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