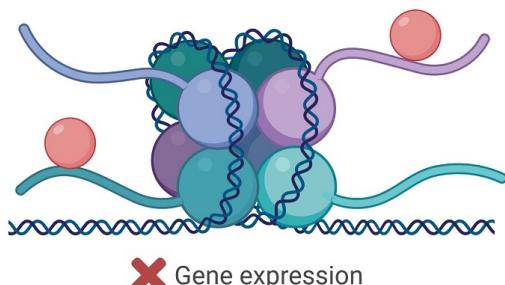
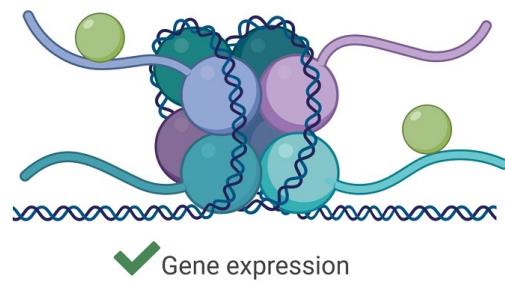


Epigenetics, nanopore sequencing & deep learning

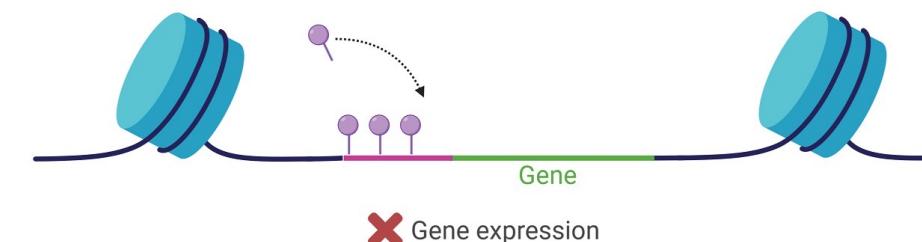
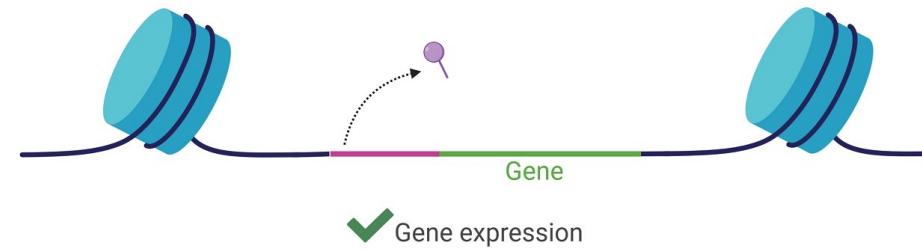
Marc Pagès-Gallego

Epigenetics

Chemistry that allows cells to do different things while having the same genetic material



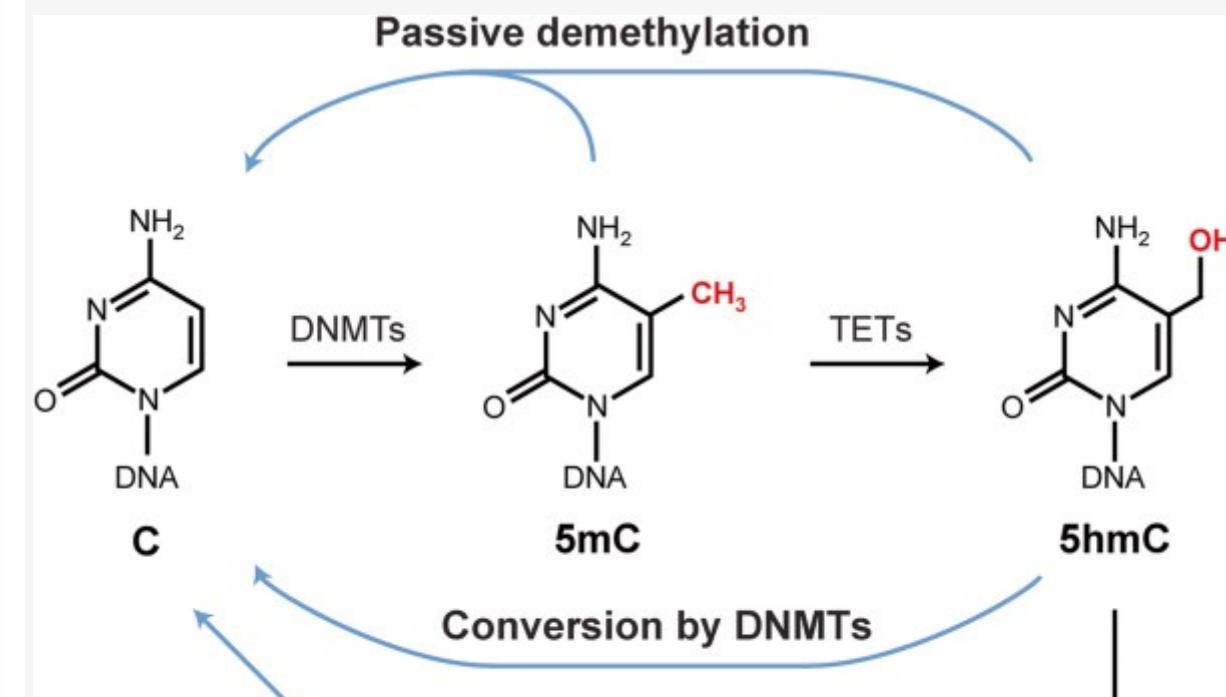
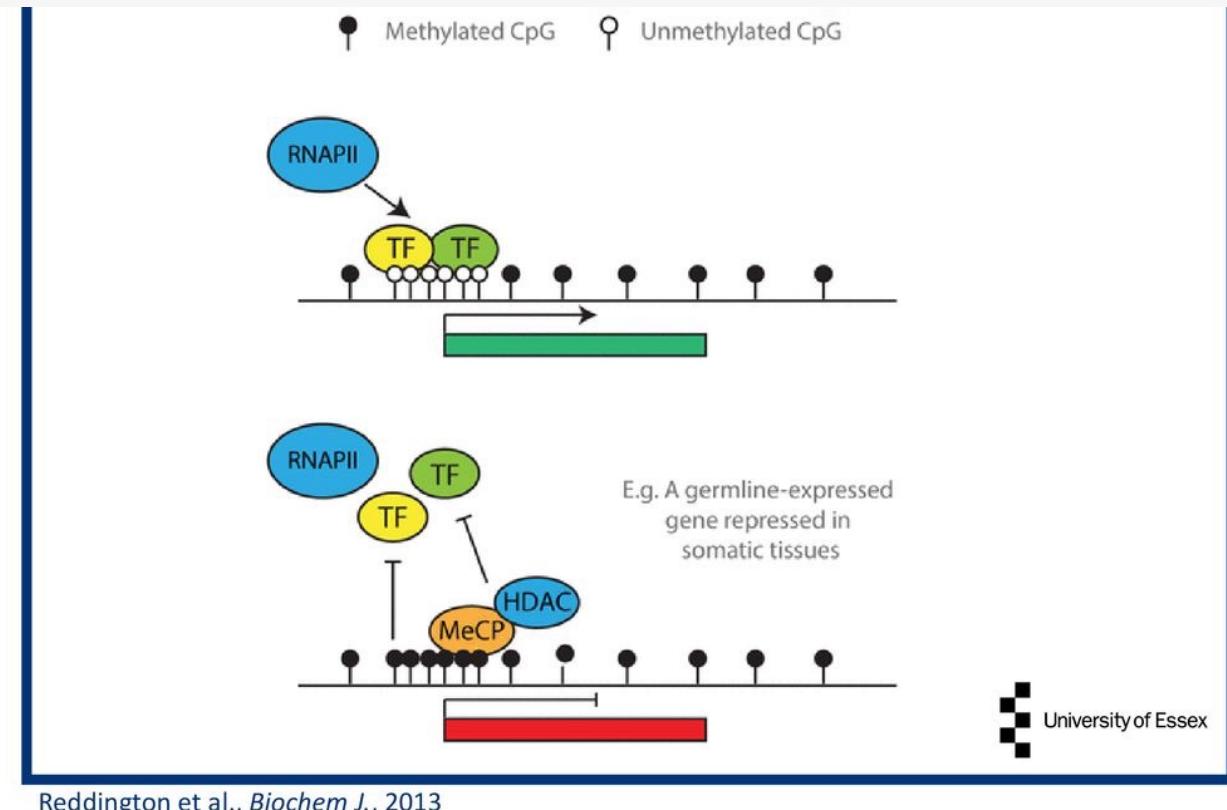
Histone epigenetics



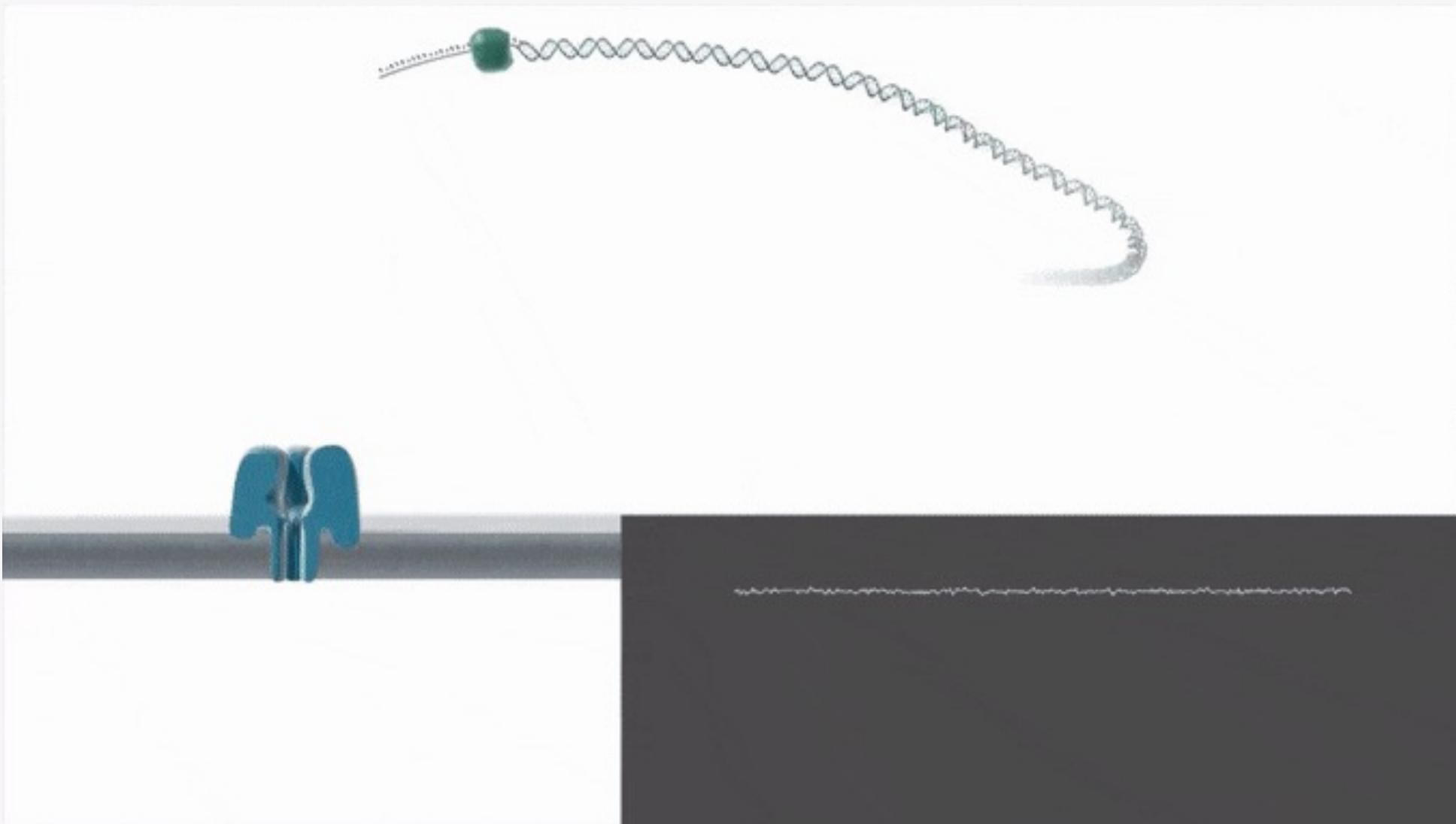
DNA epigenetics

DNA Epigenetics

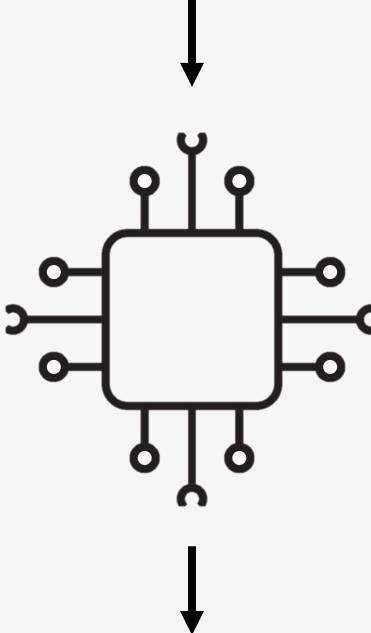
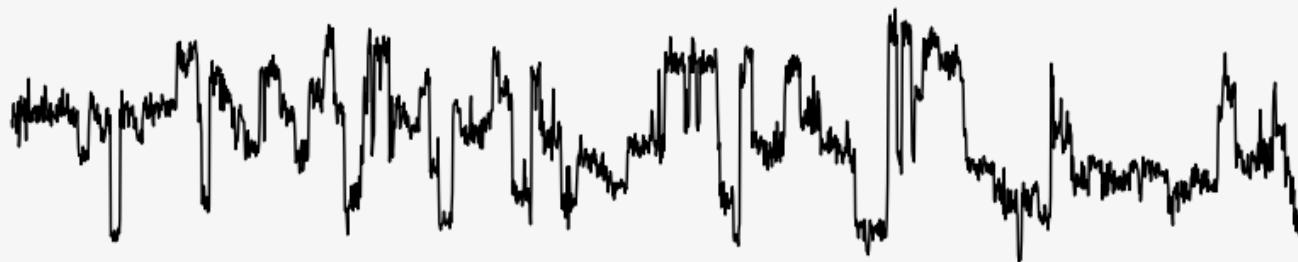
Chemistry that allows cells to do different things while having the same genetic material



Nanopore sequencing



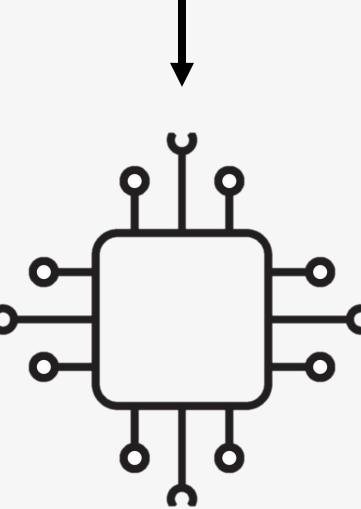
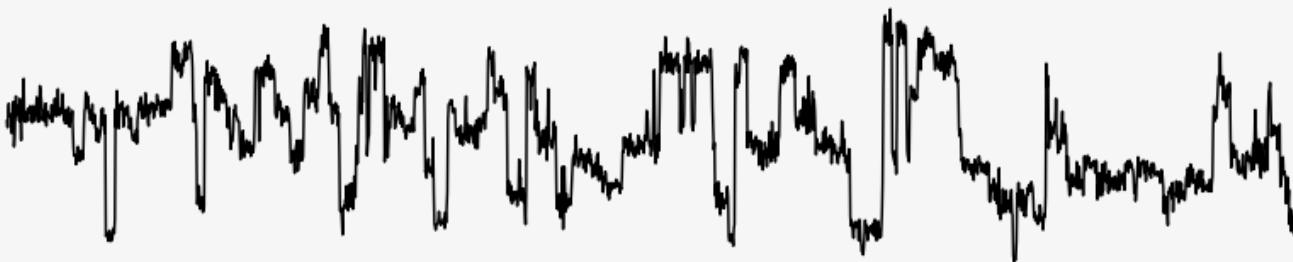
Nanopore sequencing



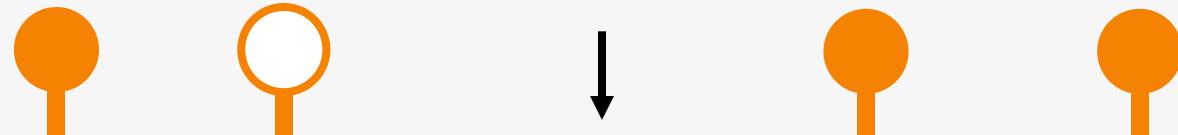
Machine learning
Deep learning

ACGATACAGATTACAGATAACAGATTCA

Nanopore sequencing



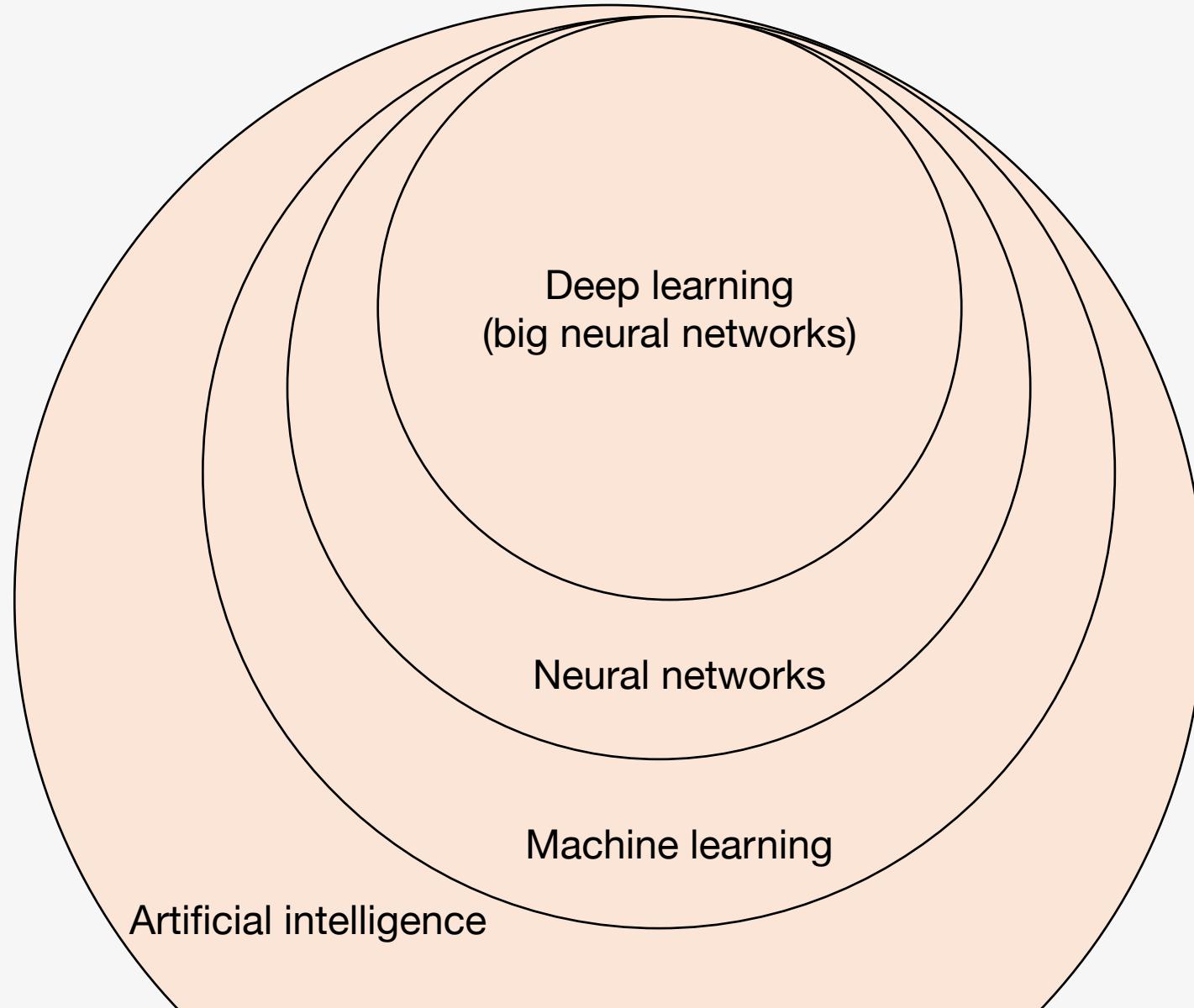
Machine learning
Deep learning



ACGATACAGATTACAGATAACAGATTCA

DNA methylation

Deep learning



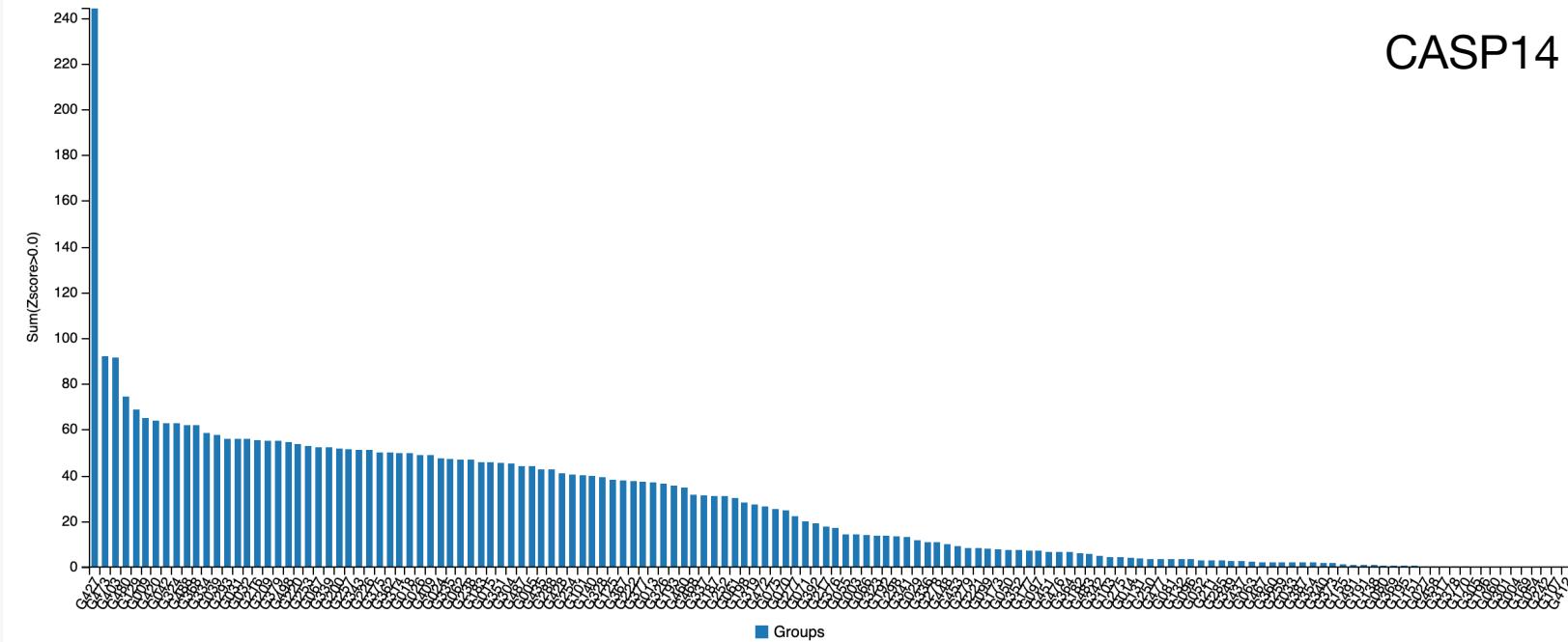
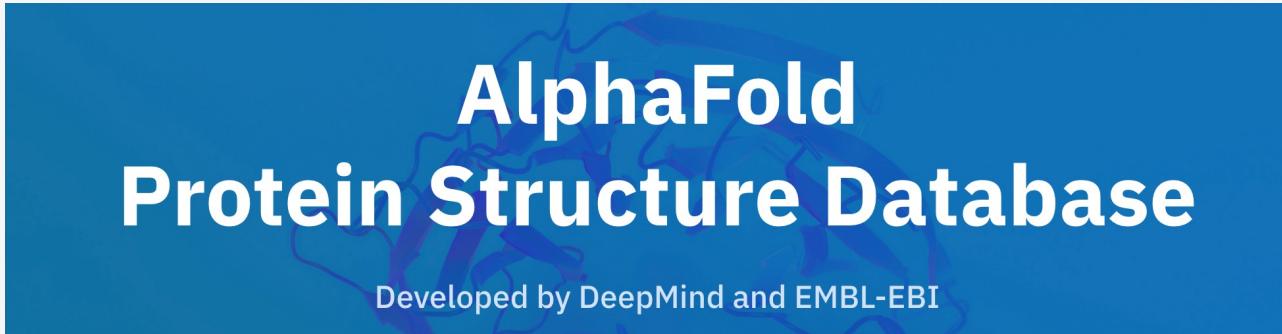
Deep learning



Deep learning

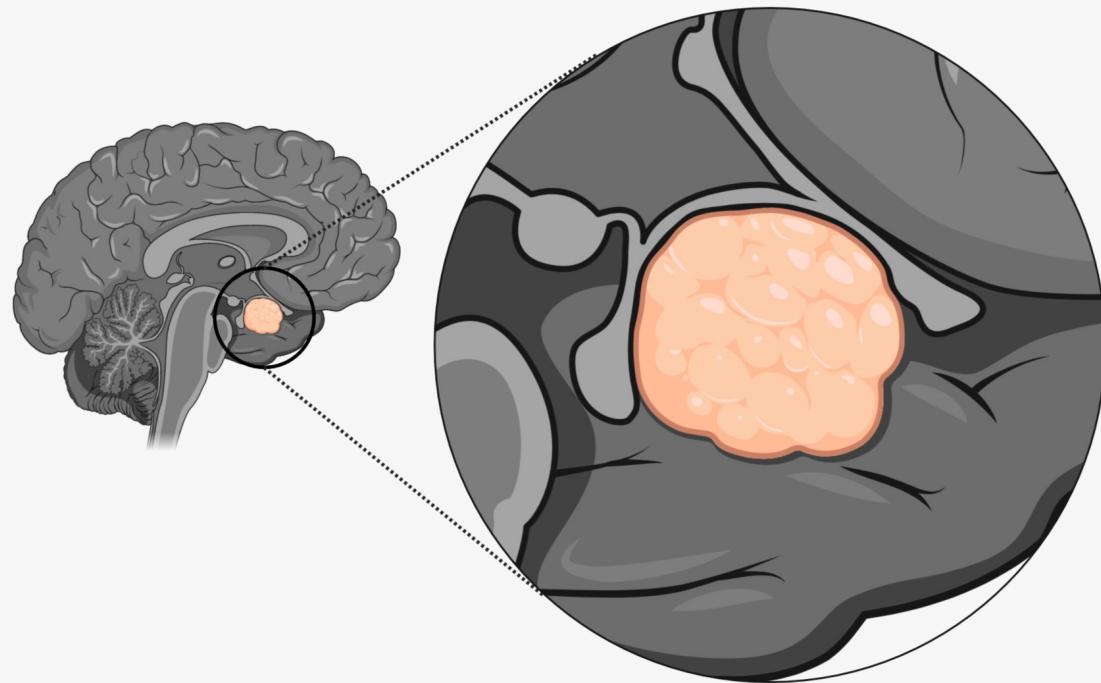


Deep learning



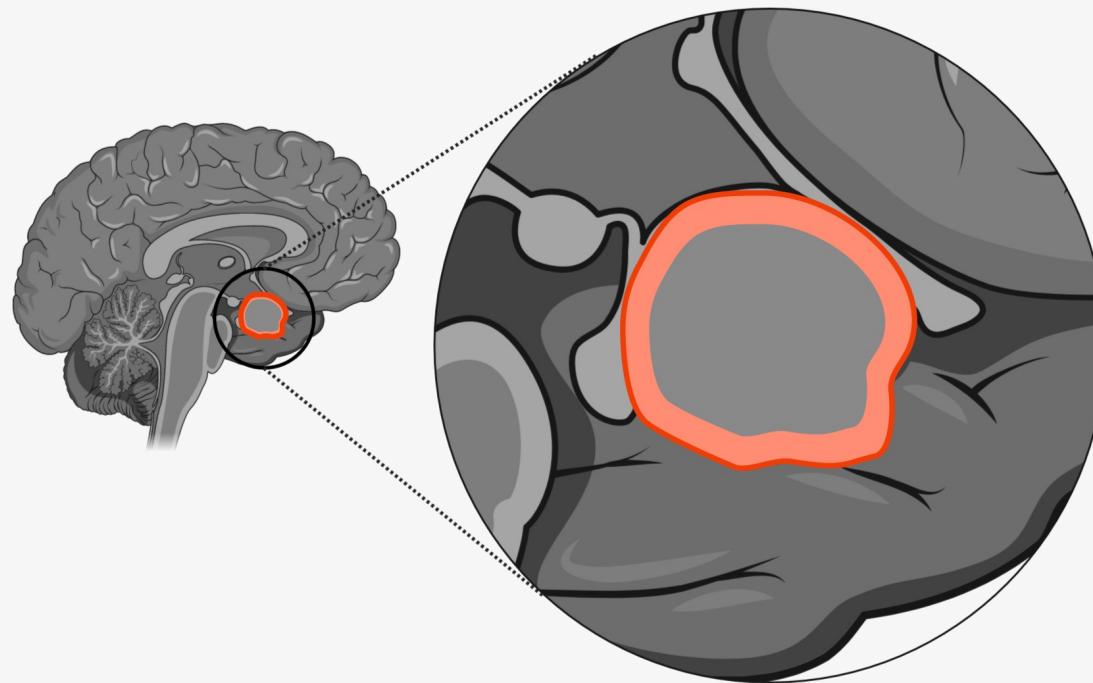
Central nervous system tumor classification during surgery

Surgical resection



First line of treatment
surgical resection

Surgical resection

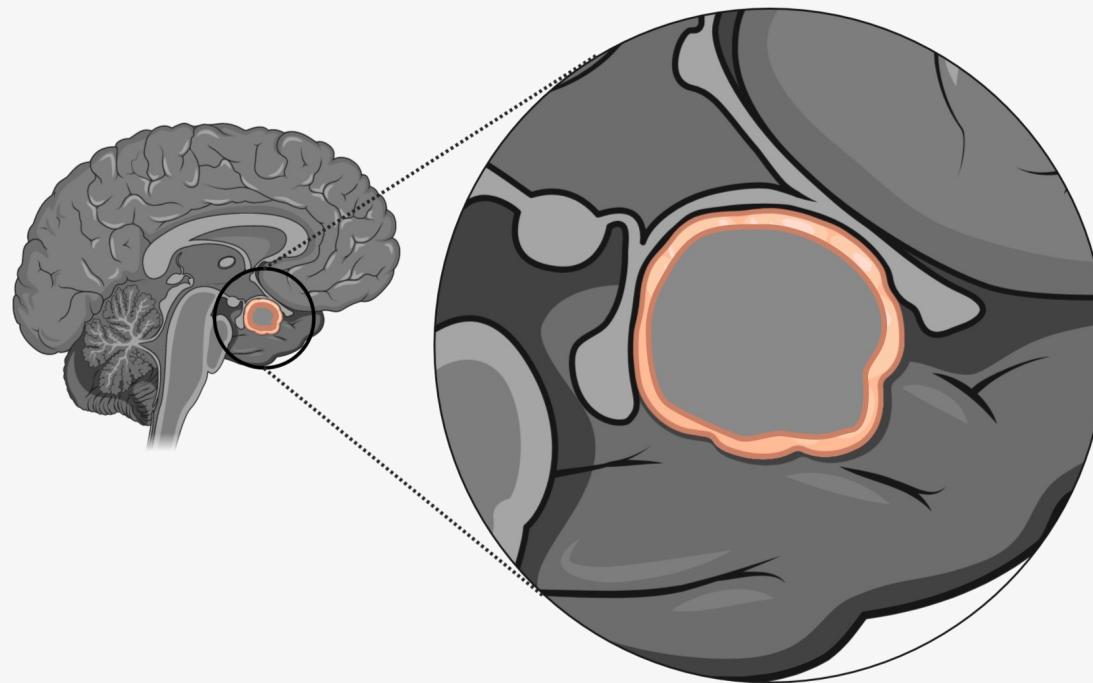


**How much resection
should be done?**

Aggressive

Maximal resection
(Severe loss in quality of life)

Surgical resection

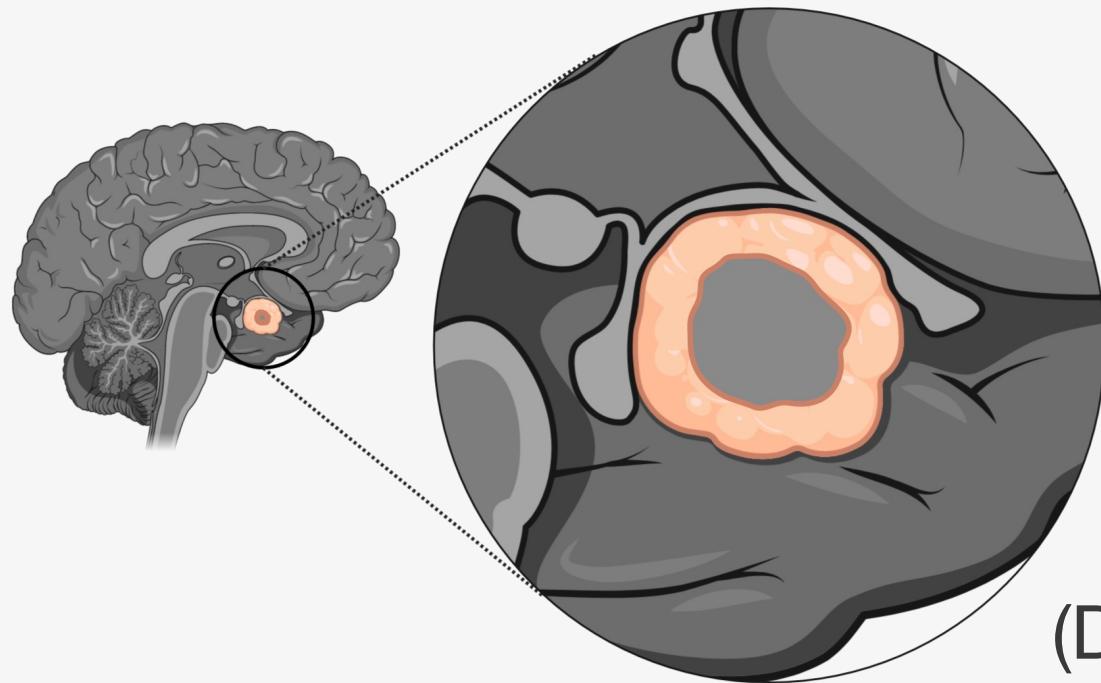


**How much resection
should be done?**

Benign

Conservative resection

Surgical resection

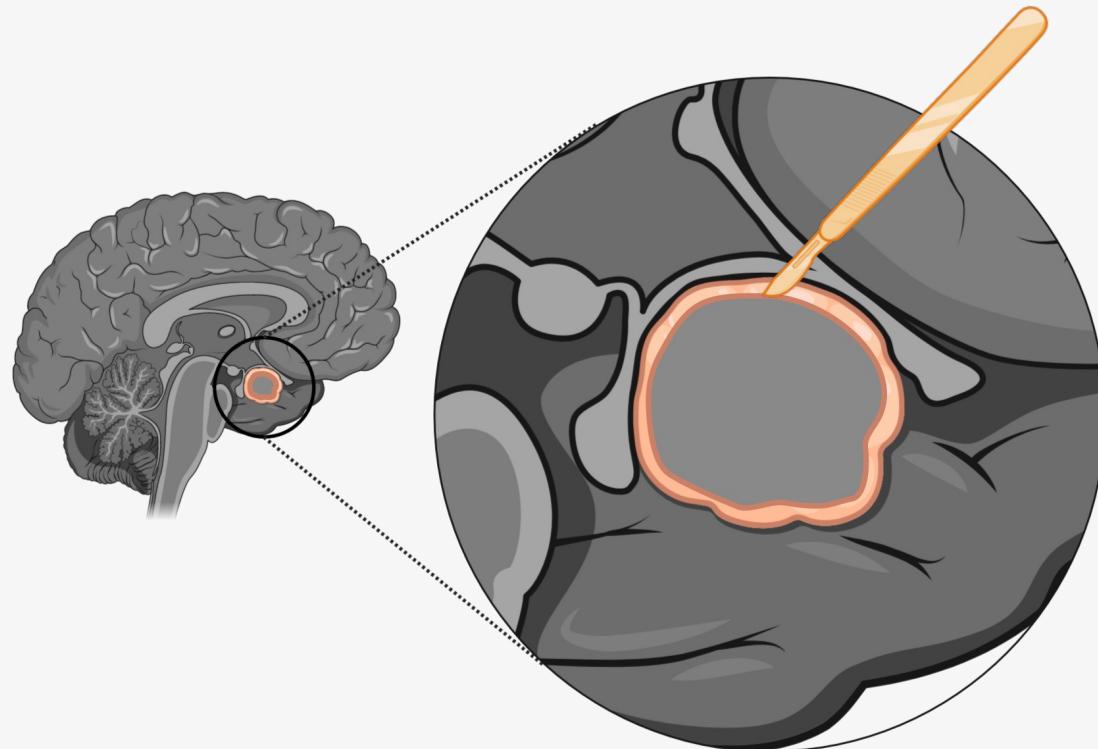


**How much resection
should be done?**

Benign Aggressive

Conservative resection
(Disease progression, second surgery)

Surgical resection

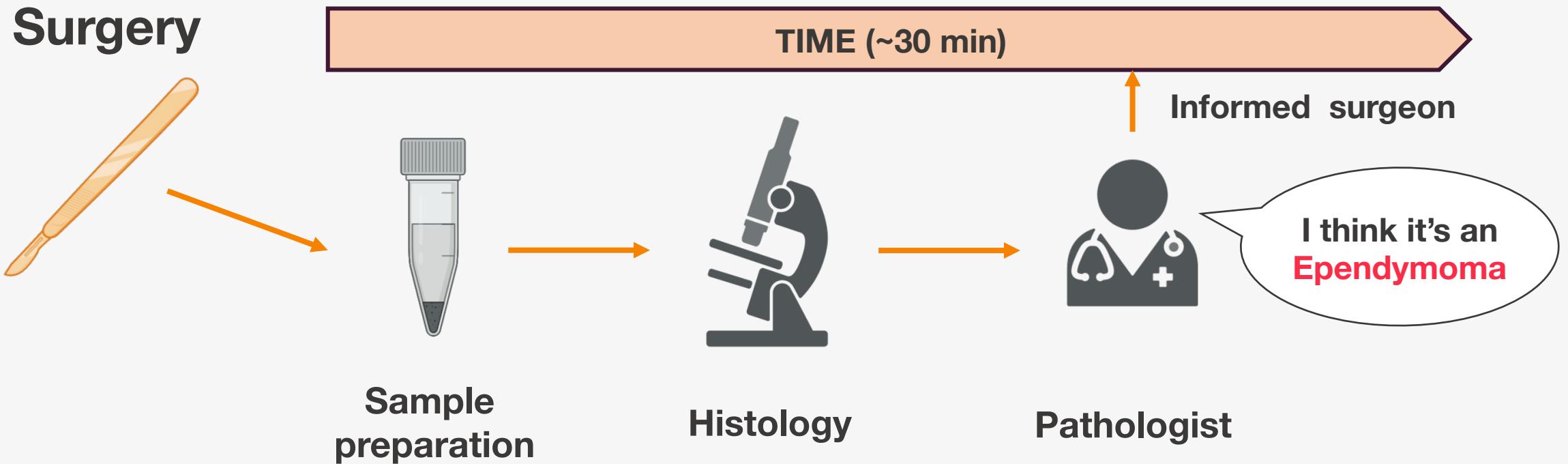


**How much resection
should be done?**

Medulloblastoma
Conservative resection

Ependymoma
Maximal resection

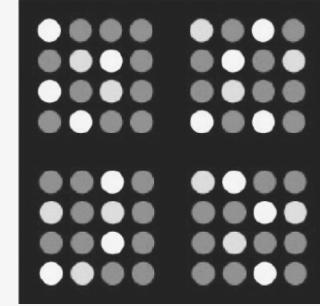
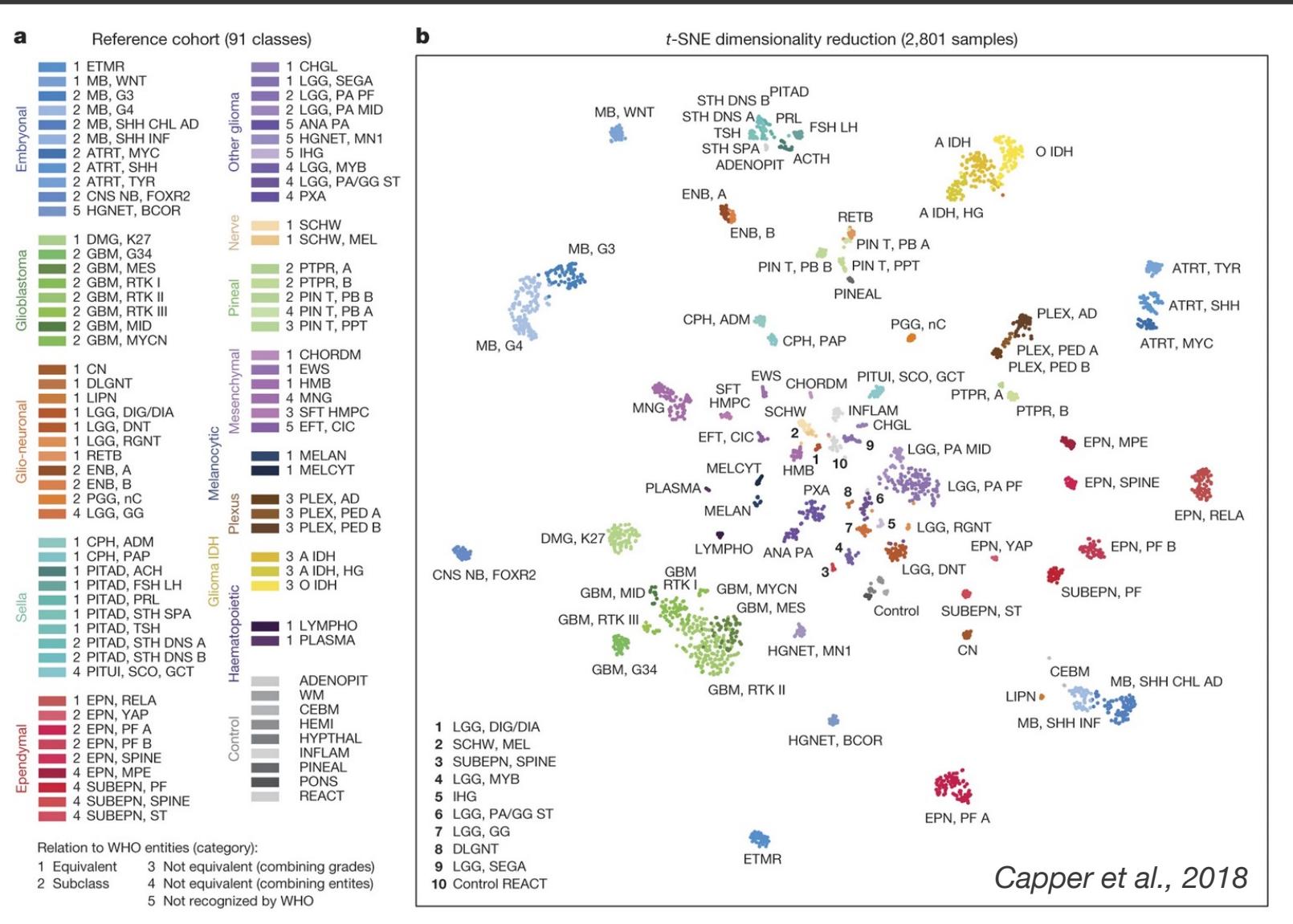
Intra-operative classification



Post-operative classification



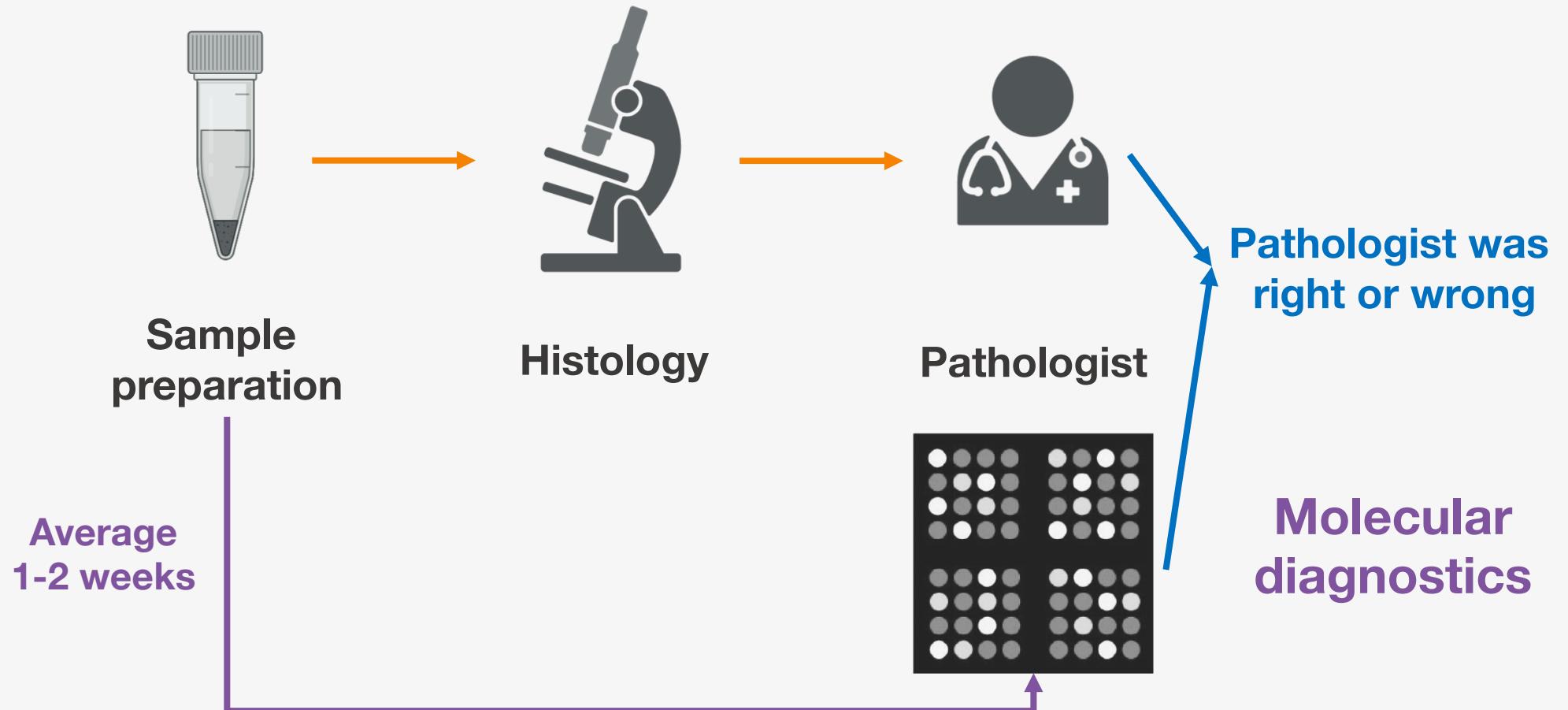
Methylation is a CNS type biomarker



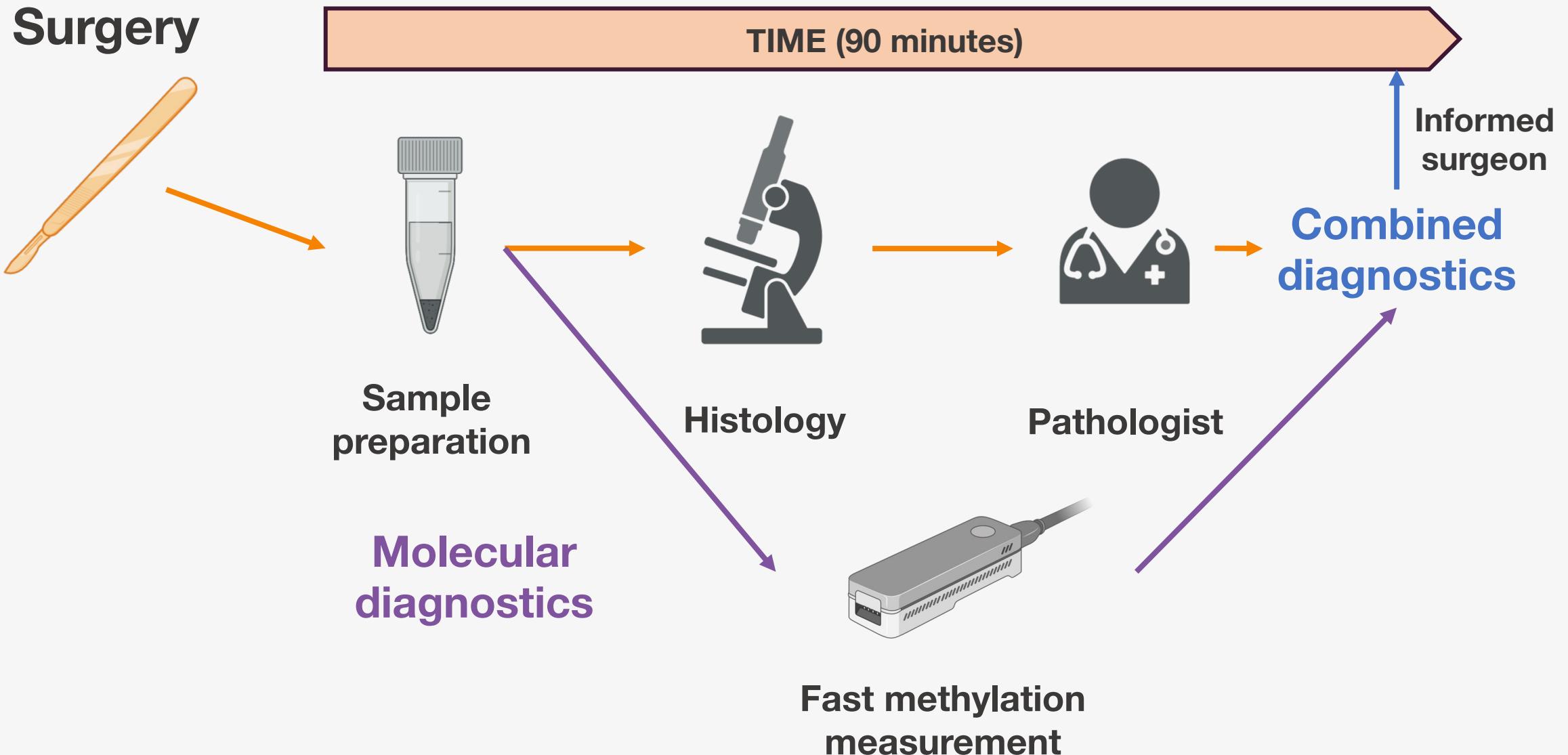
Methylation microarrays

82 tumor subtypes

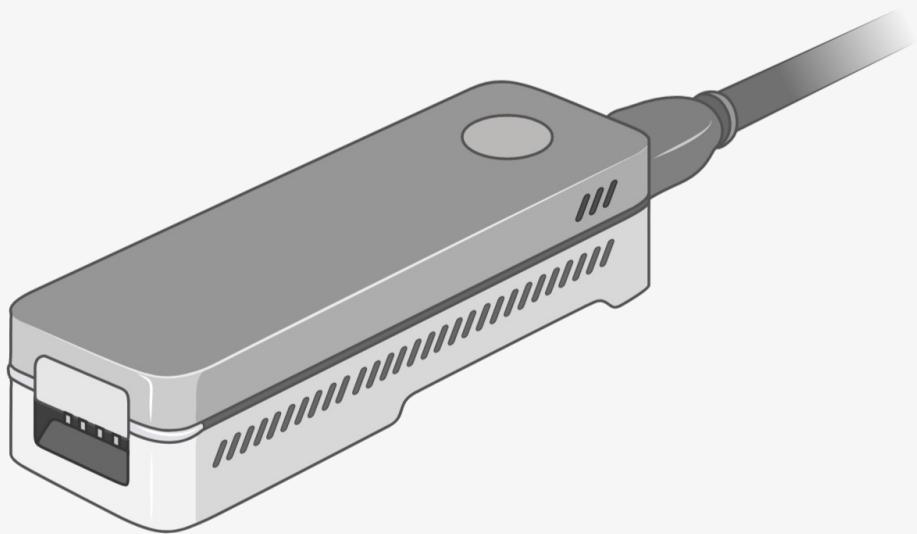
Post-operative classification



Intra-operative classification



Nanopore sequencing

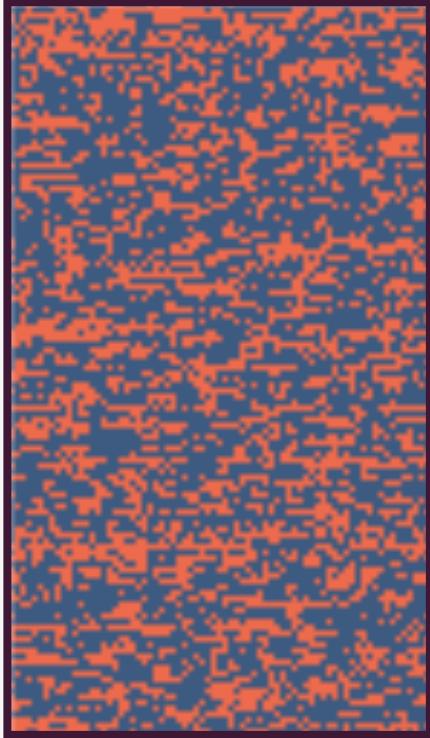


Native DNA sequencing

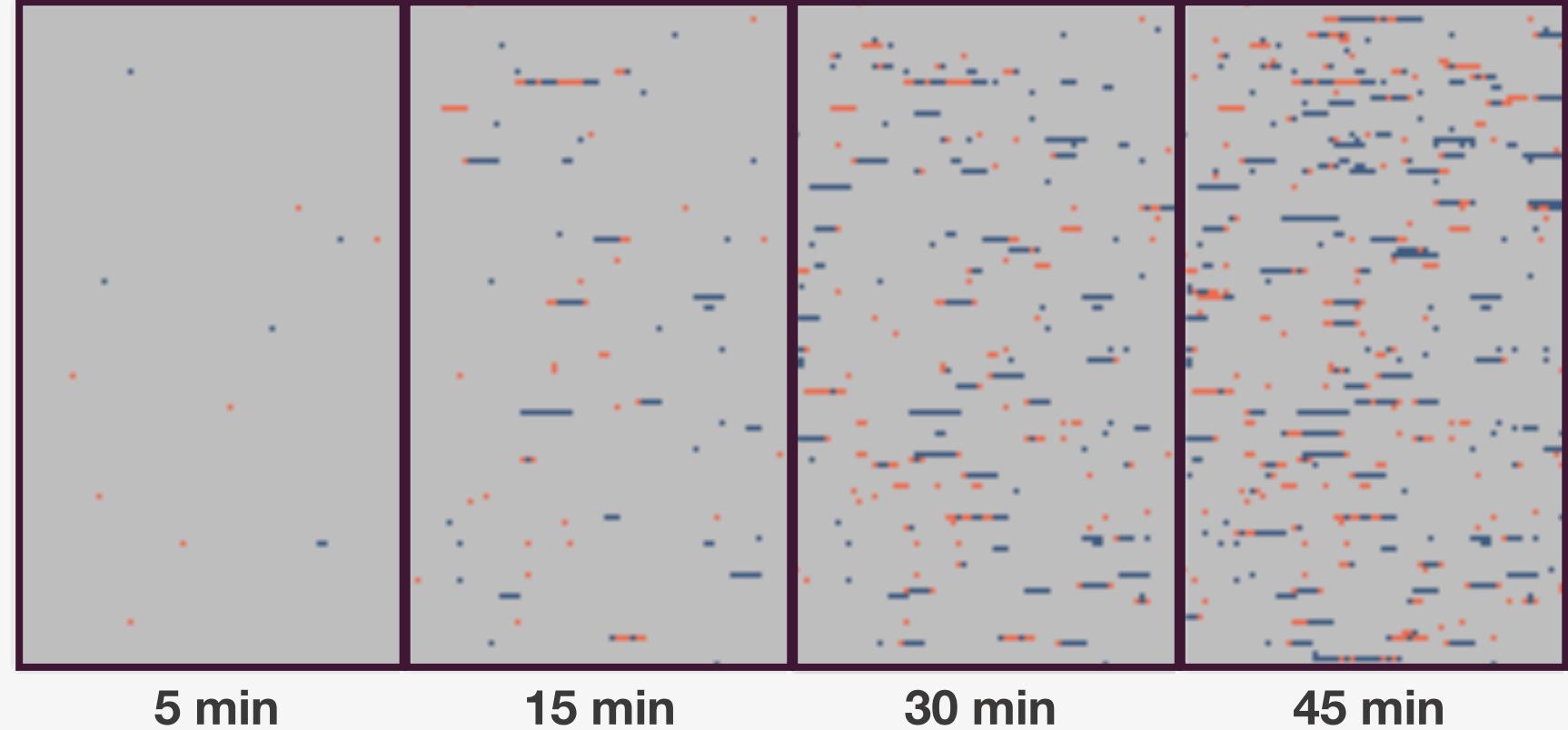
15 minutes sample preparation

Real time data output

Main problem: random sparsity



Methylation
microarray

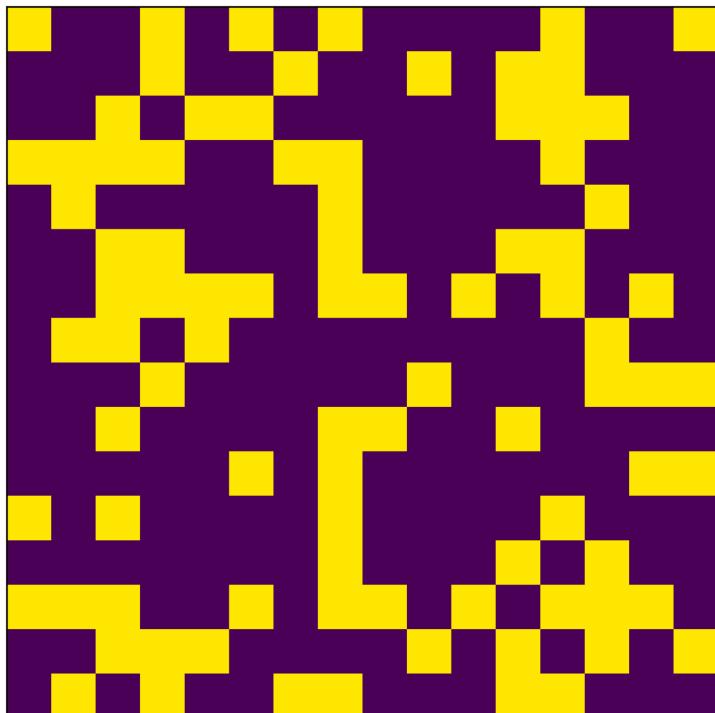


Nanopore sequencing

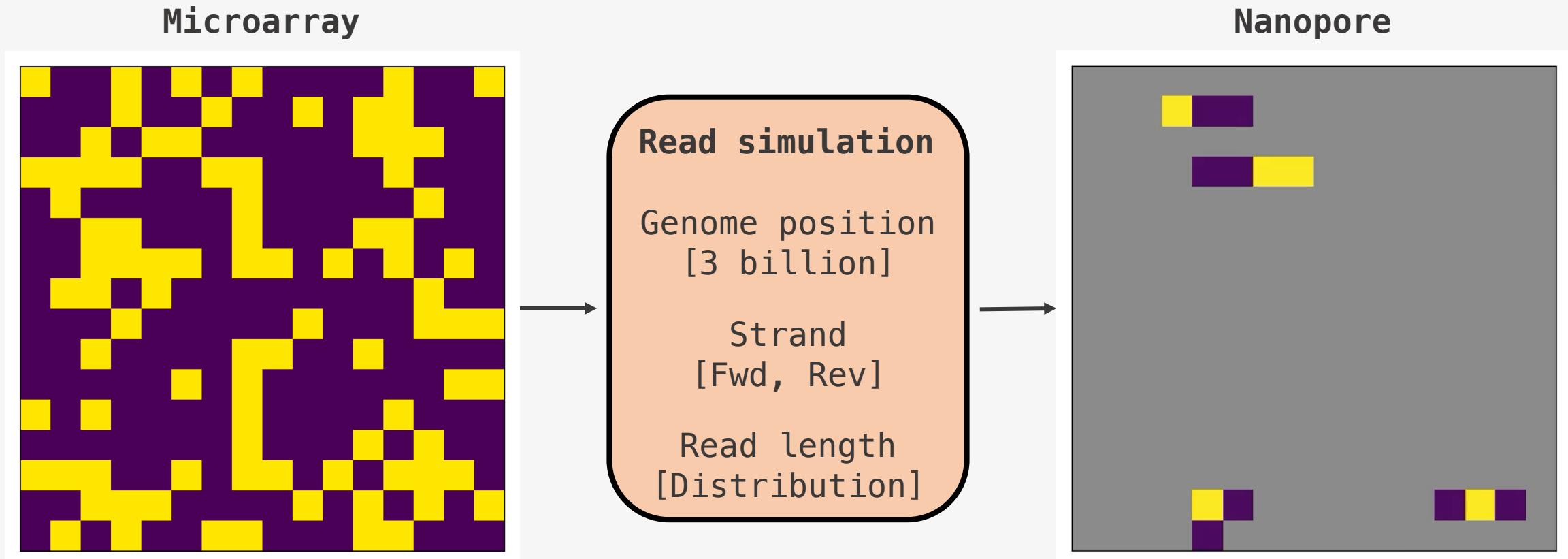
Can we develop a model that can handle an arbitrary number of random missing values?

Data simulation

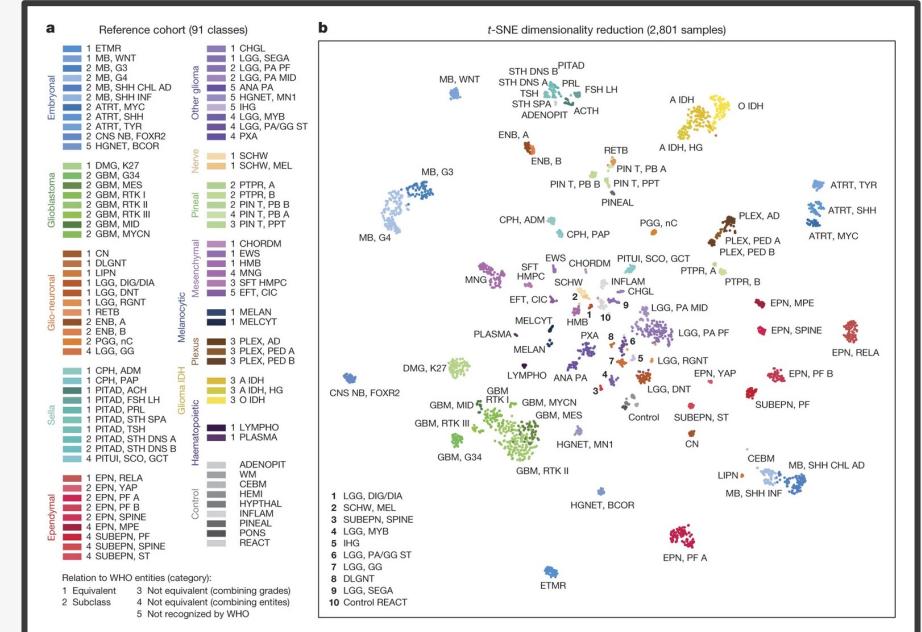
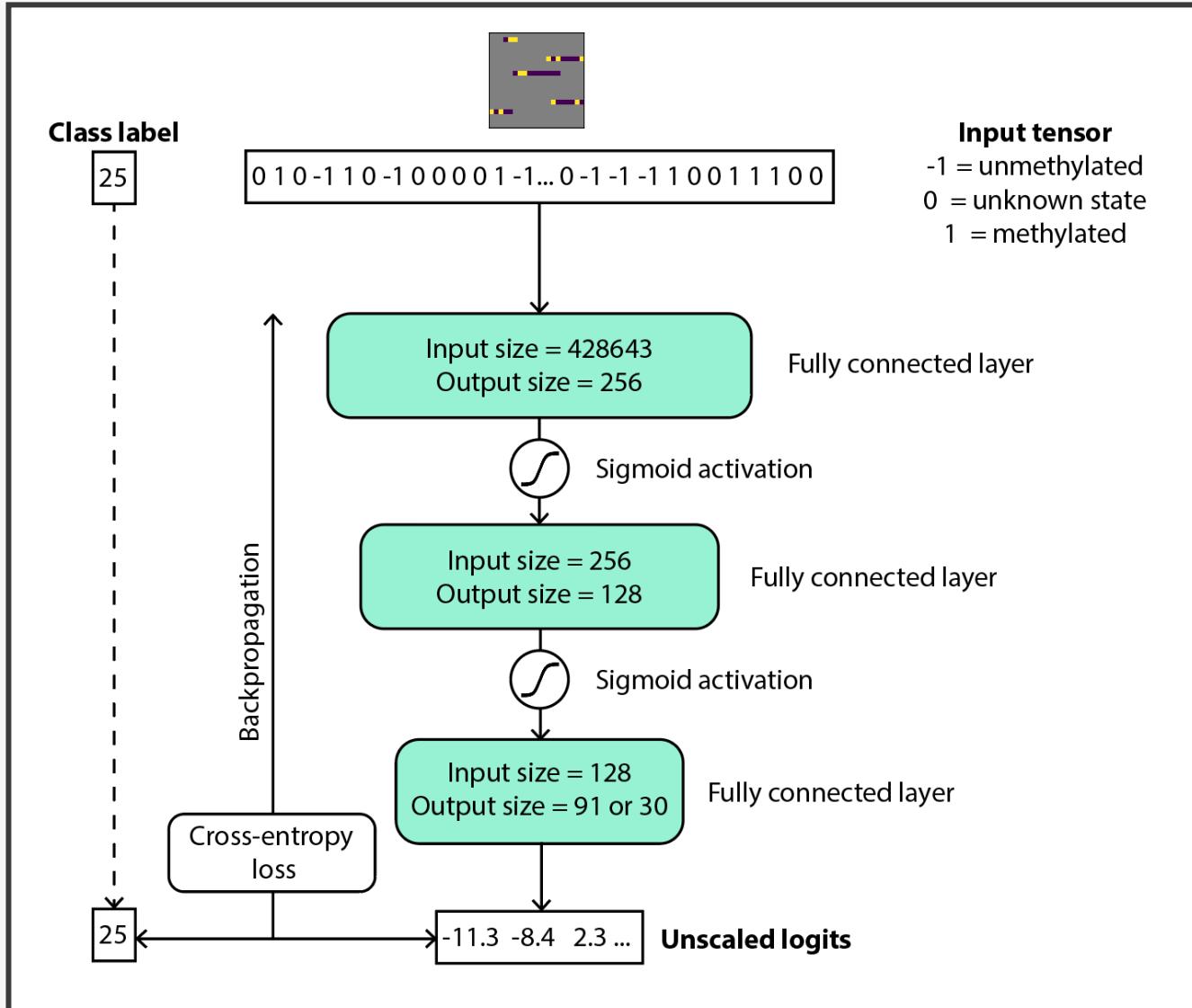
Microarray



Data simulation



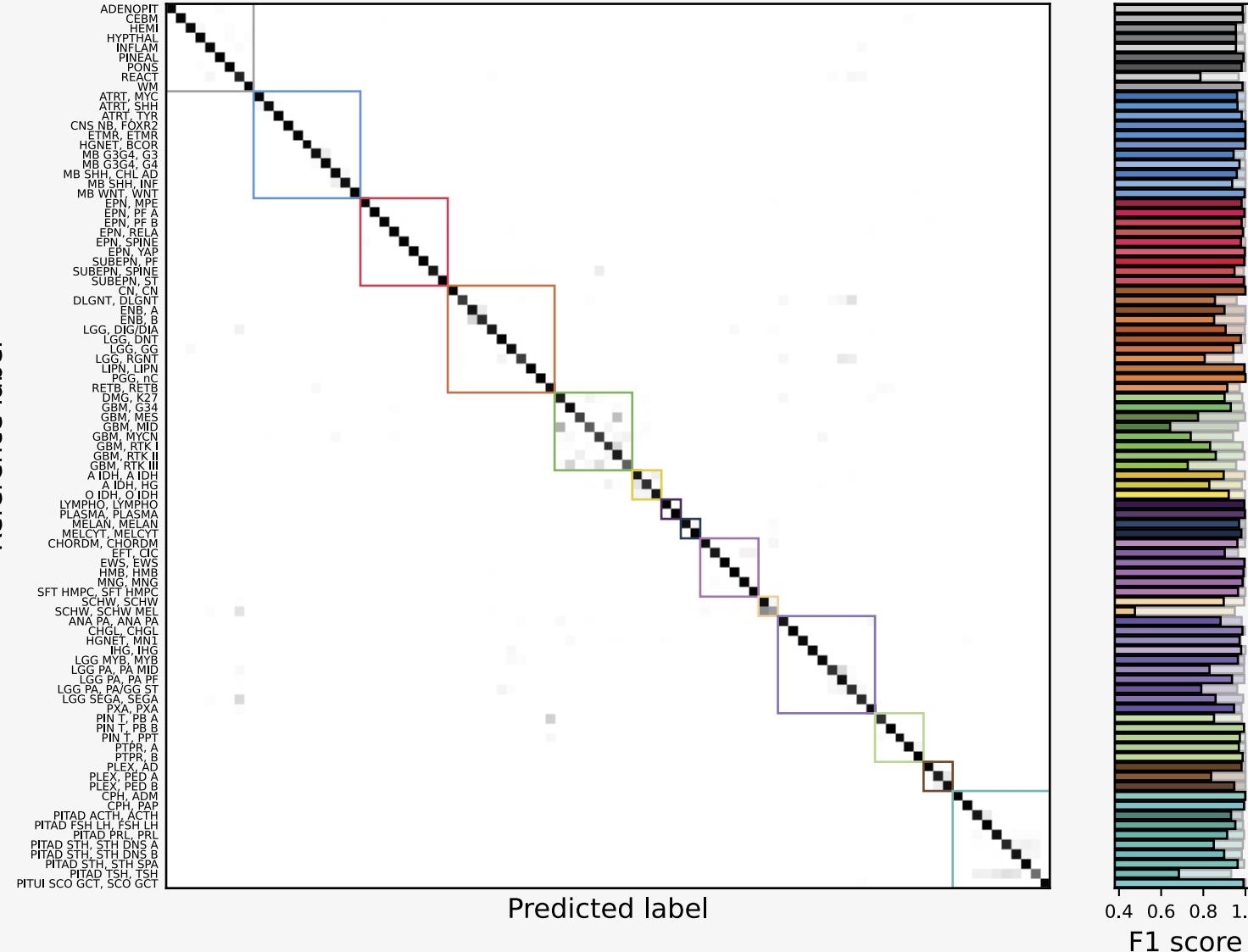
Neural network model



2801 microarray samples

36.8 million nanopore simulated samples

Cross-validation on simulations

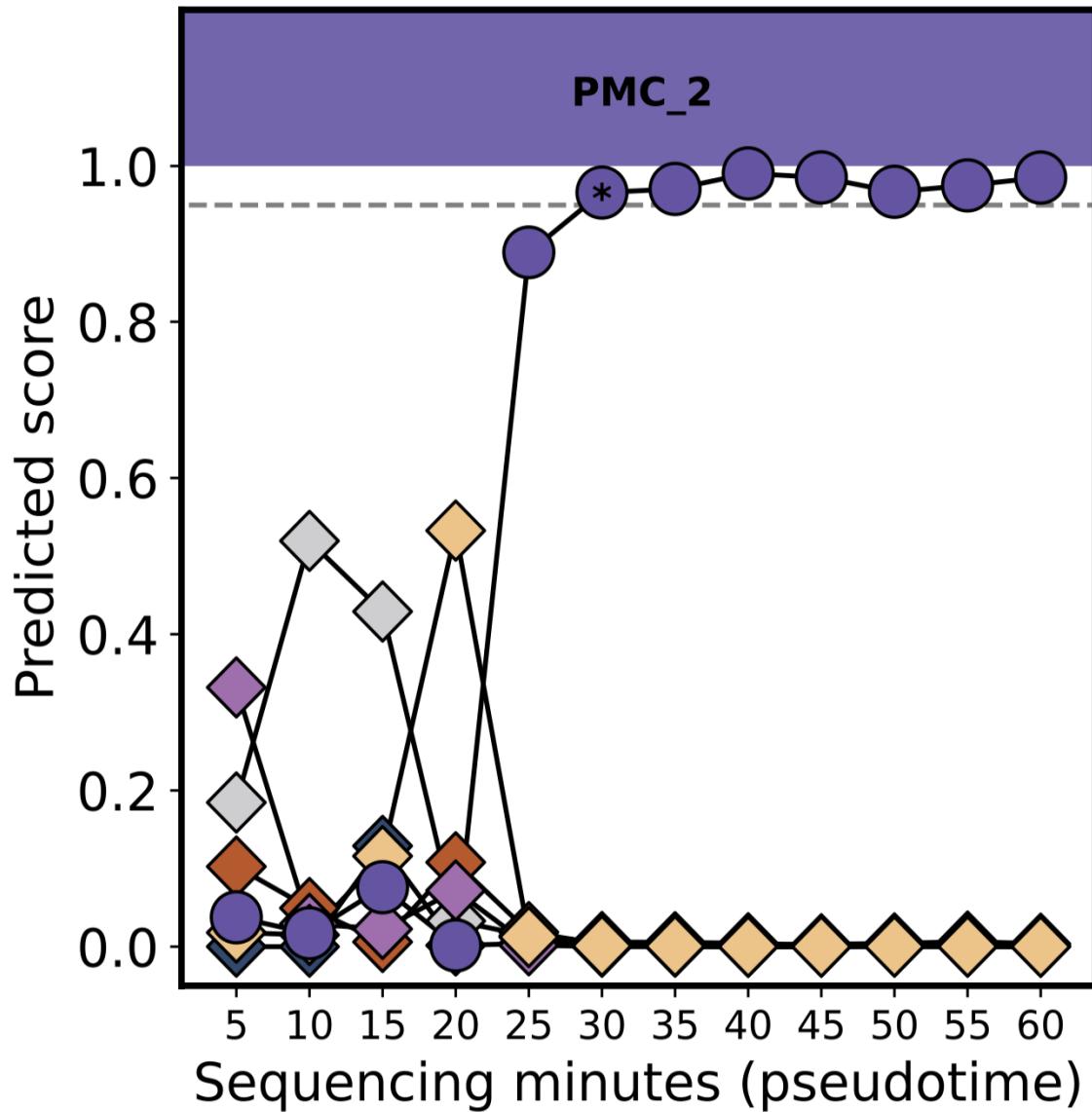


Performance at **40 minutes**
simulations

F1-Score
Top1: 0.926
Top3: 0.990

**Our model has been trained on simulated data,
will it work on real nanopore data?**

Nanopore retrospective sequencing

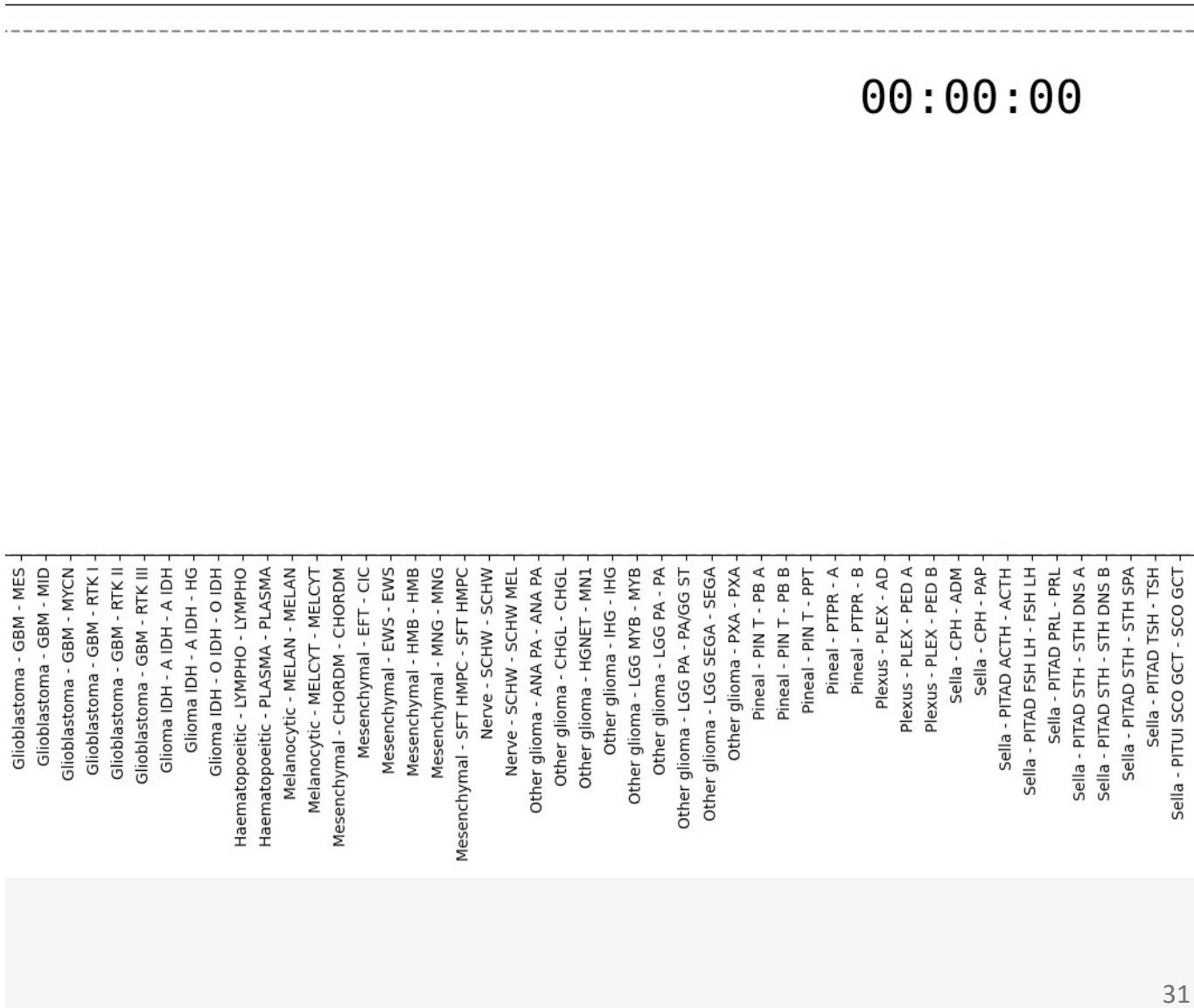
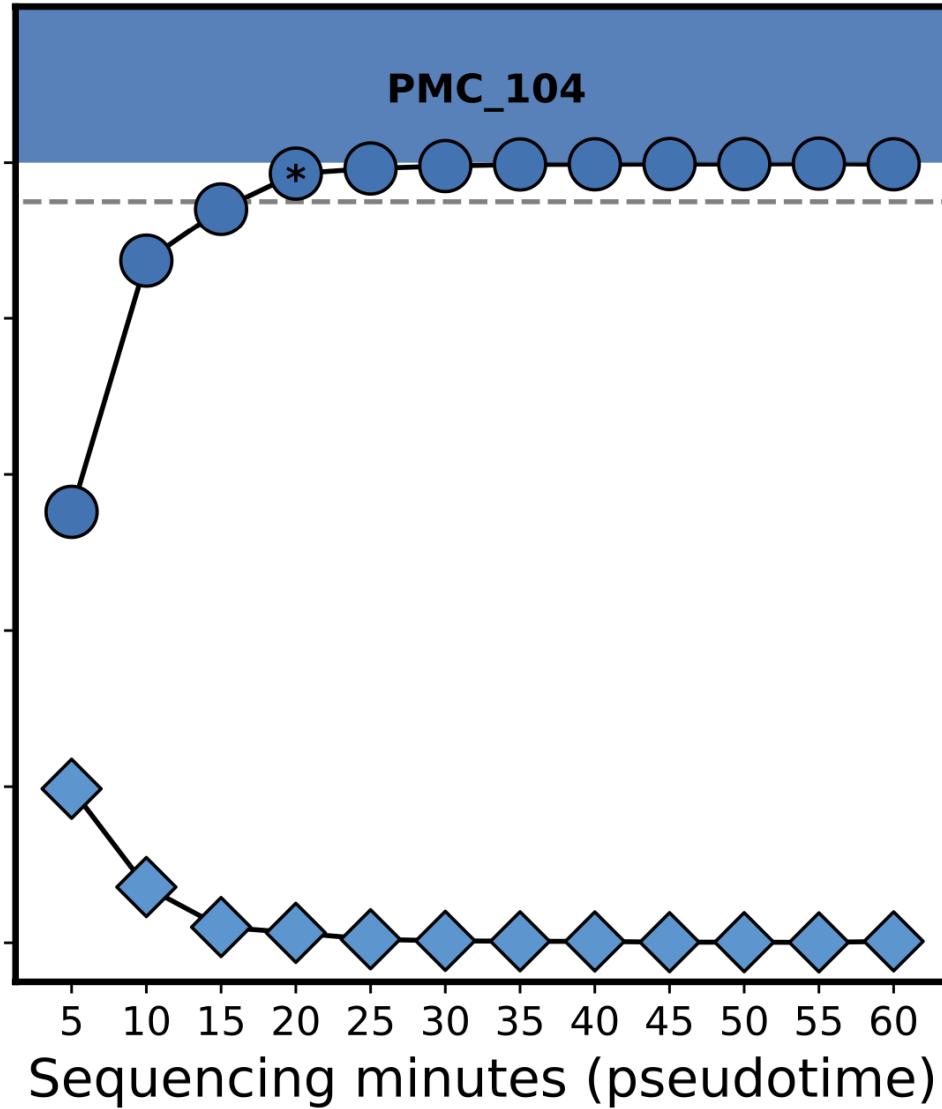


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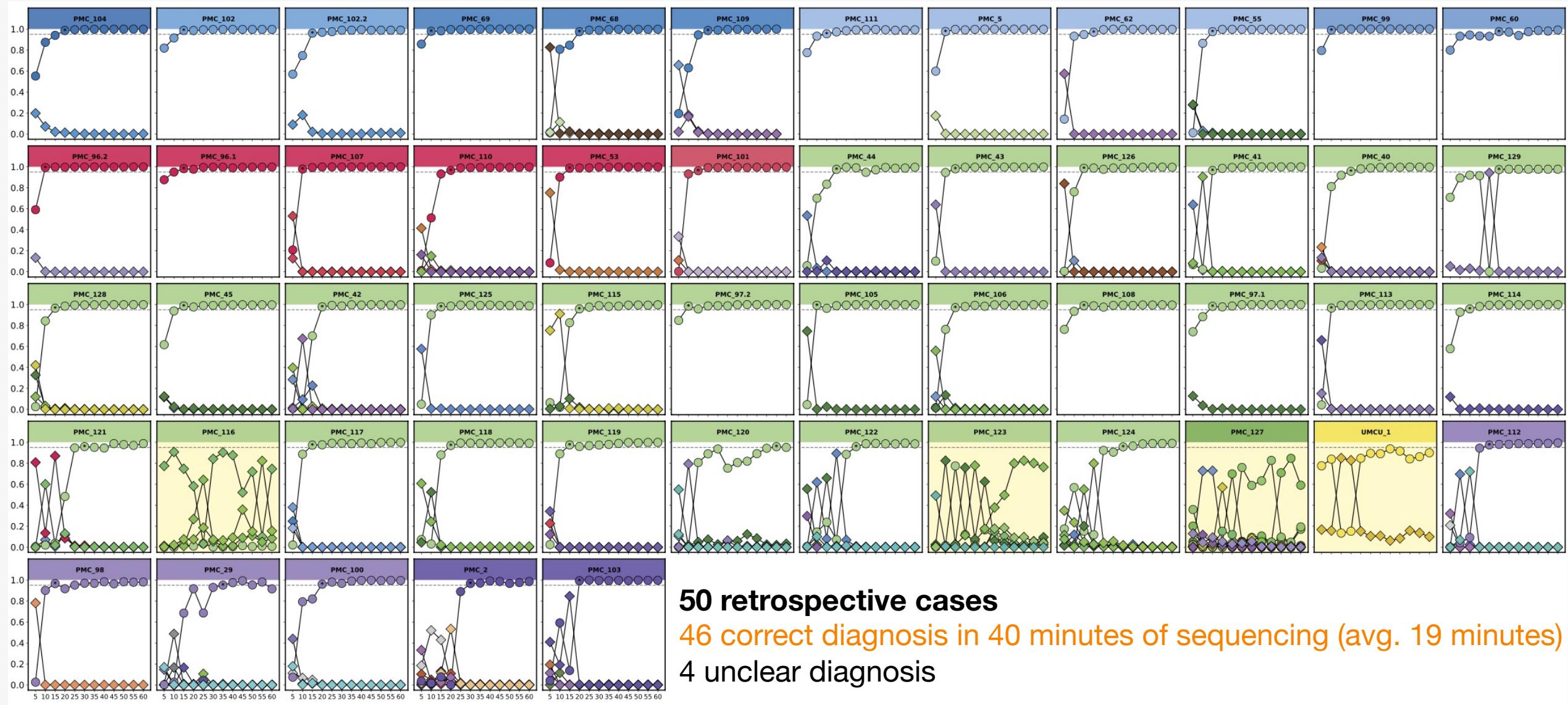
Glioblastoma - GBM - G34
Glioblastoma - GBM - MES
Glioblastoma - GBM - MID
Glioblastoma - GBM - MYCN
Glioblastoma - GBM - RTK I
Glioblastoma - GBM - RTK II
Glioblastoma - GBM - RTK III
Glioma IDH - A IDH - A IDH
Glioma IDH - A IDH - HG
Glioma IDH - O IDH - O IDH
Haematopoietic - LYMPHO - LYMPHO
Haematopoietic - PLASMA - PLASMA
Melanocytic - MELAN - MELAN
Melanocytic - MELCYT - MELCYT
Mesenchymal - CHORDM - CHORDM
Mesenchymal - EFT - CIC
Mesenchymal - EWS - EWS
Mesenchymal - HMB - HMB
Mesenchymal - MNG - MNG
Mesenchymal - SFT HMPC - SFT HMPC
Nerve - SCHW - SCHW
Nerve - SCHW - SCHW MEL
Other glioma - ANA PA - ANA PA
Other glioma - CHGL - CHGL
Other glioma - HGNET - MN1
Other glioma - IHG - IHG
Other glioma - LGG MYB - MYB
Other glioma - LGG PA - PA
Other glioma - LGG PA - PA/GG ST
Other glioma - LGG SEGA - SEGA
Other glioma - PXA - PXA
Pineal - PIN T - PB A
Pineal - PIN T - PB B
Pineal - PIN T - PPT
Pineal - PTPR - A
Sella - CPH - ADM
Plexus - PLEX - AD
Plexus - PLEX - PED A
Plexus - PLEX - PED B
Sella - CPH - PAP
Sella - PITAD ACTH - ACTH
Sella - PITAD FSH LH - FSH LH
Sella - PITAD PRL - PRL
Sella - PITAD STH - STH DNS A
Sella - PITAD STH - STH DNS B
Sella - PITAD STH - STH SPA
Sella - PITAD TSH - TSH
Sella - PITUI SCO GCT - SCO GCT

Nanopore retrospective sequencing

Predicted score

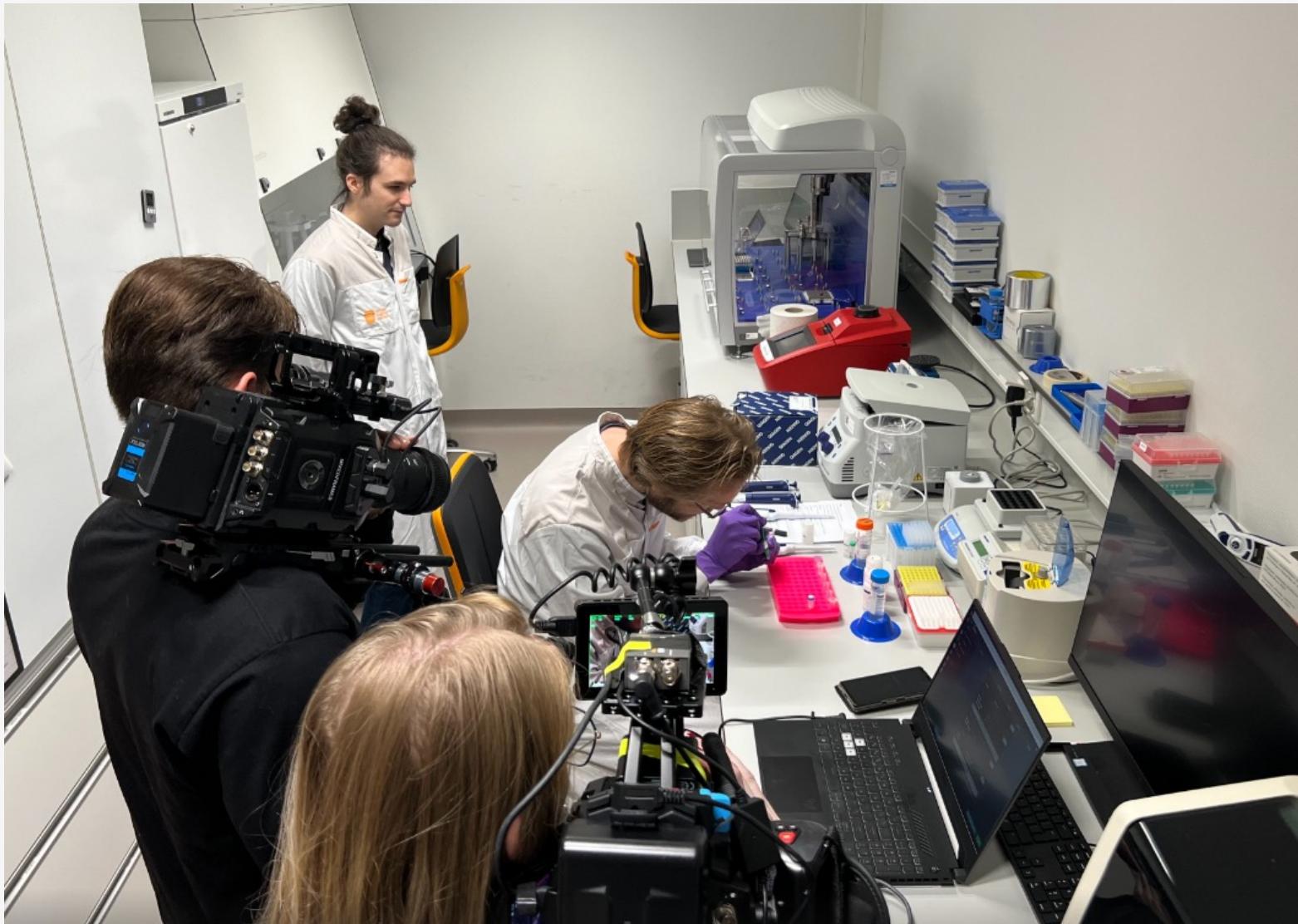


Nanopore retrospective sequencing



**Our model also works real nanopore data,
can we be fast enough to do it during surgery?**

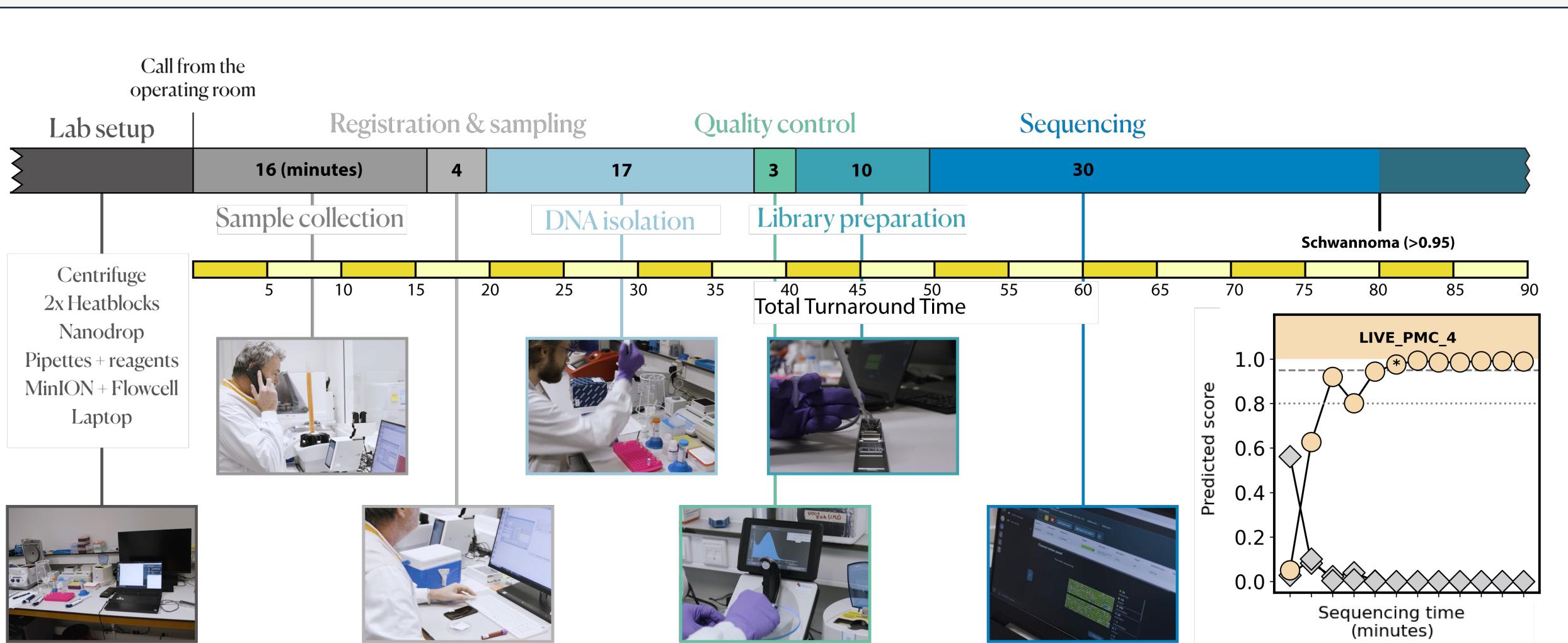
Intraoperative sequencing



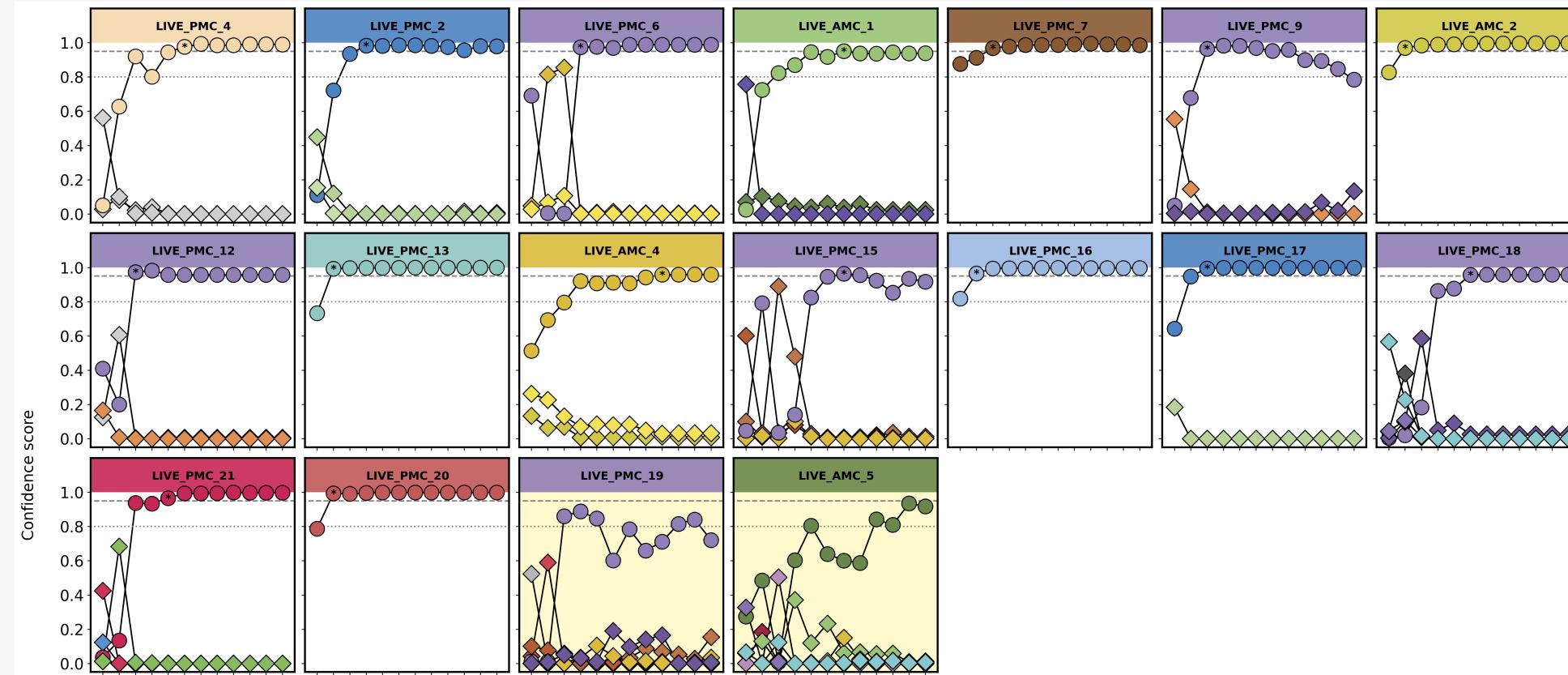
Intraoperative sequencing



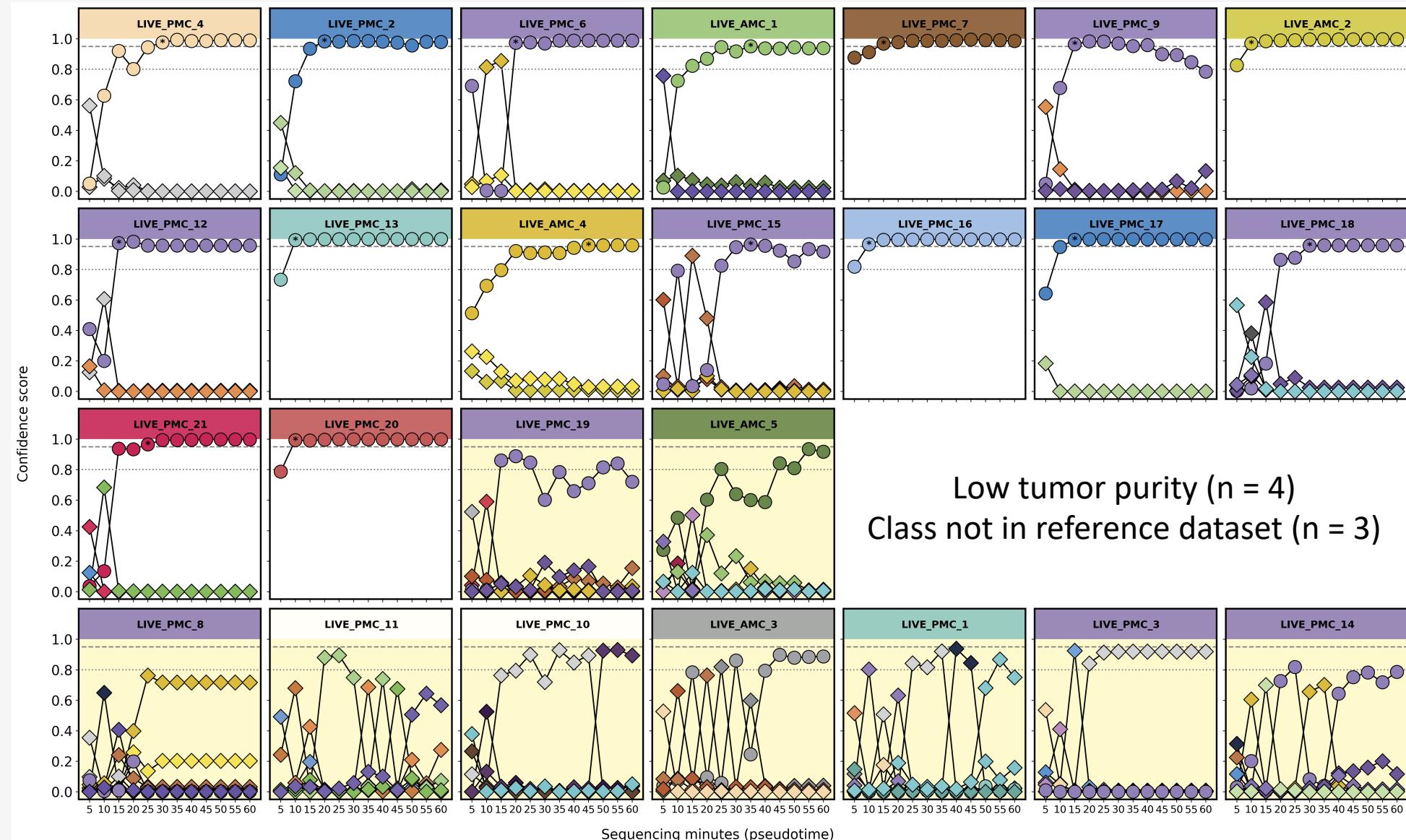
Intraoperative sequencing



Intraoperative sequencing (shadow-testing)



Intraoperative sequencing (shadow-testing)



Sturgeon as a diagnostic tool at the **PMC**

23 pediatric cases

Sturgeon as a diagnostic tool at the PMC

23 pediatric cases

1 incorrect

Posterior fossa ependymoma subtype A (misclassified as subtype B)

Sturgeon as a diagnostic tool at the PMC

23 pediatric cases

1 incorrect

Posterior fossa ependymoma subtype A (misclassified as subtype B)

4 inconclusive results

Low purity (3) and class not in reference set (1)

Sturgeon as a diagnostic tool at the PMC

23 pediatric cases

1 incorrect

Posterior fossa ependymoma subtype A (misclassified as subtype B)

4 inconclusive results

Low purity (3) and class not in reference set (1)

18 correct classifications

Pathologist was unsure (3) and was incorrect (1)

We have developed Sturgeon, a model that can classify CNS tumours given a random amount of data

The complete protocol is fast enough to aid in surgical decision-making

Sturgeon is currently being used at the PMC, and has been successfully used in other centres

Acknowledgements

de Ridder group

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Ultra-fast deep-learned CNS tumour classification during surgery

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Ultra-fast deep-learned pediatric CNS tumor classification during surgery

Marc Pagès-Gallego