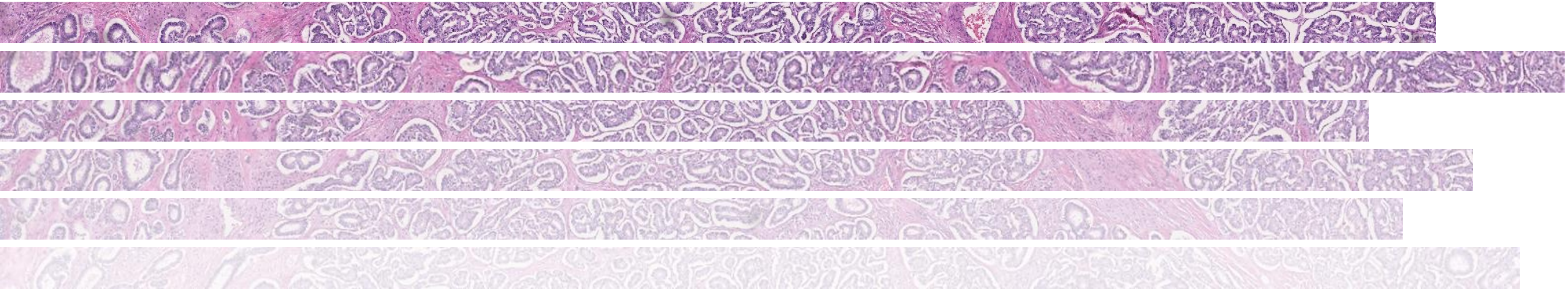
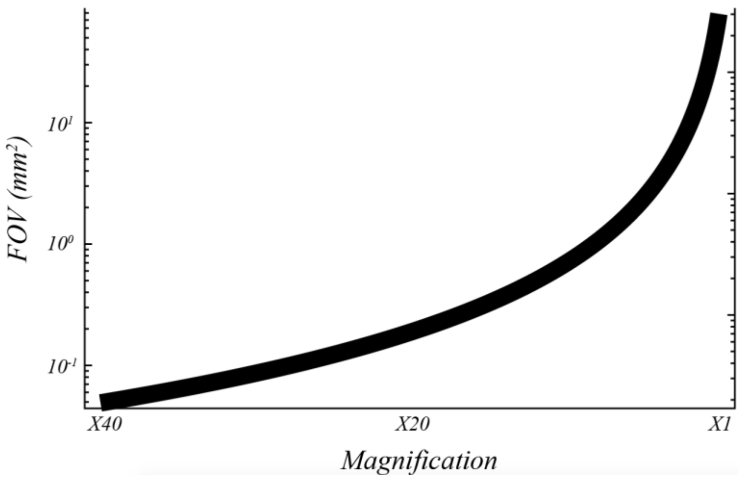


A cognitive model of whole-slide image viewing and interpretation

Mark D. Zarella, Ph.D.
Department of Pathology & Laboratory Medicine
Drexel University College of Medicine

DREXEL UNIVERSITY
Advanced Pathology Imaging Laboratory
College of Medicine



WHOLE-SLIDE IMAGE VIEWING

A natural relationship between **Magnification** and **Field of View** forces pathologists to balance this tradeoff according to the requirements of the task.

For many diagnostic tasks, high power regions are sequentially sampled from the low power image.

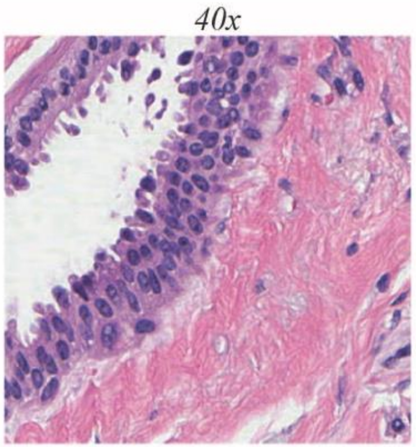
WHOLE-SLIDE IMAGE VIEWING BY EXPERIENCED PATHOLOGISTS

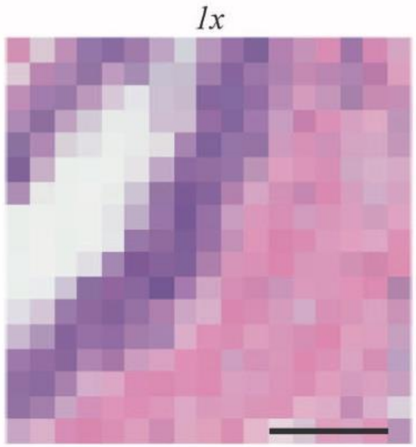
Experienced pathologists spend less time at high magnifications than trainees.

> **Eye-movement study and human performance using telepathology virtual slides. Implications for medical education and differences with experience.**
> *Krupinski, E., Tillack, A., Richter, L., et al. Hum Pathol (2006)*

Possible explanations include:

- Utilize high resolution information more quickly than trainees
- Require less evidence, so fewer areas of the slide are sampled at high resolution
- Better at identifying regions of interest from the low power image





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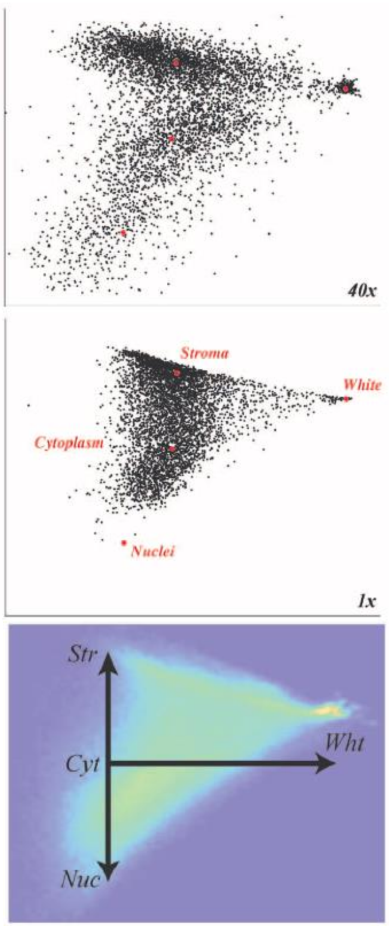

Estimation of fine-scale histologic features at low magnification.
Zarella, M., Quaschnick, M., Breen, D., Garcia, F. Arch Pathol Lab Med (2018)

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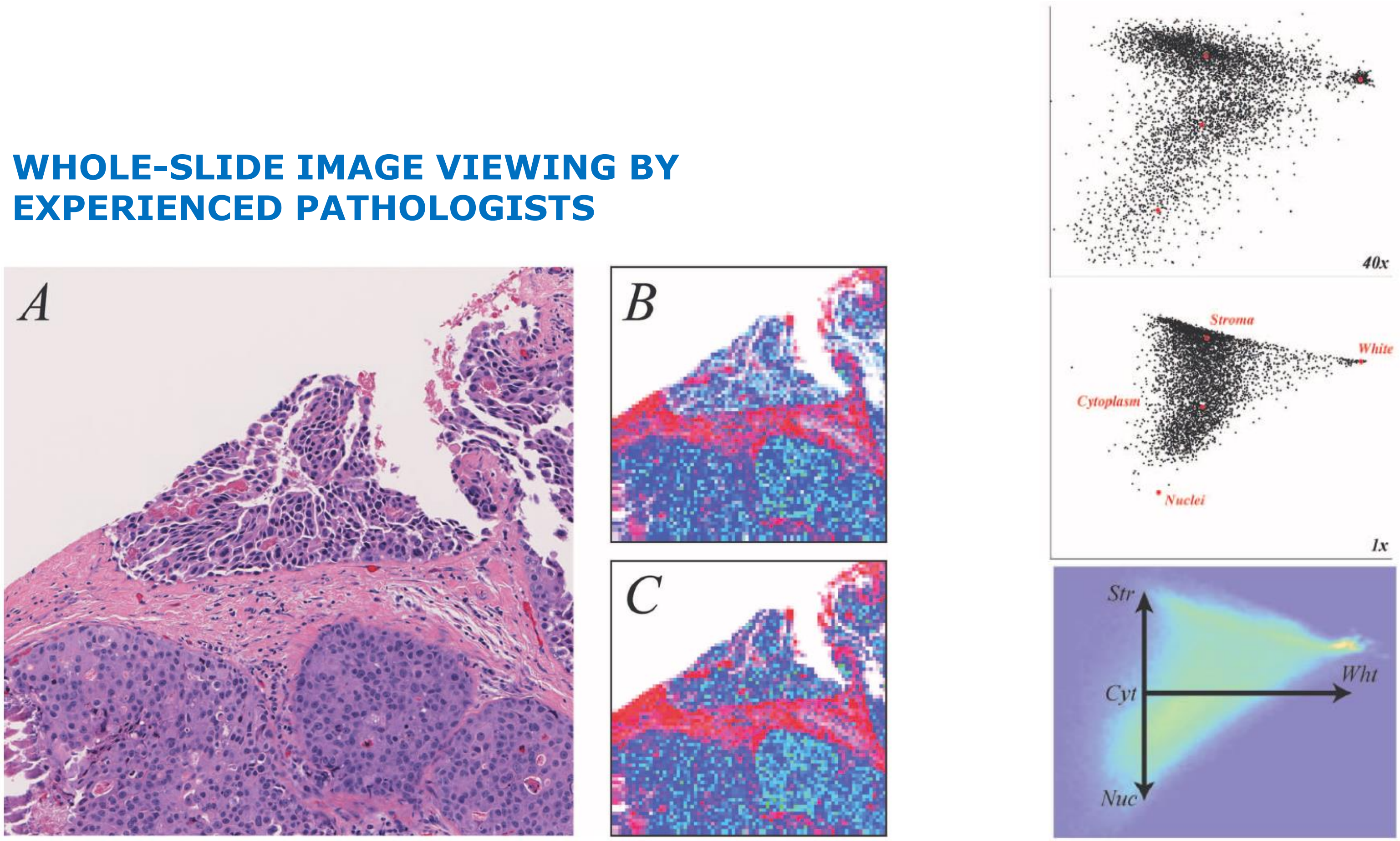

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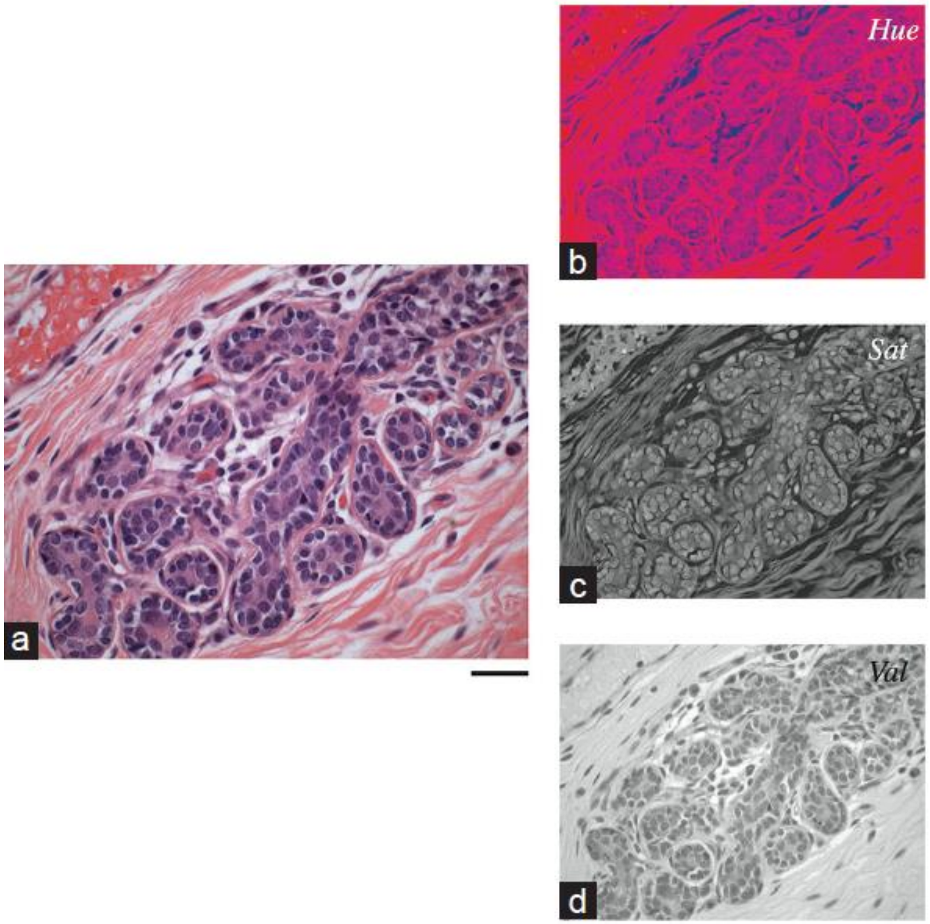


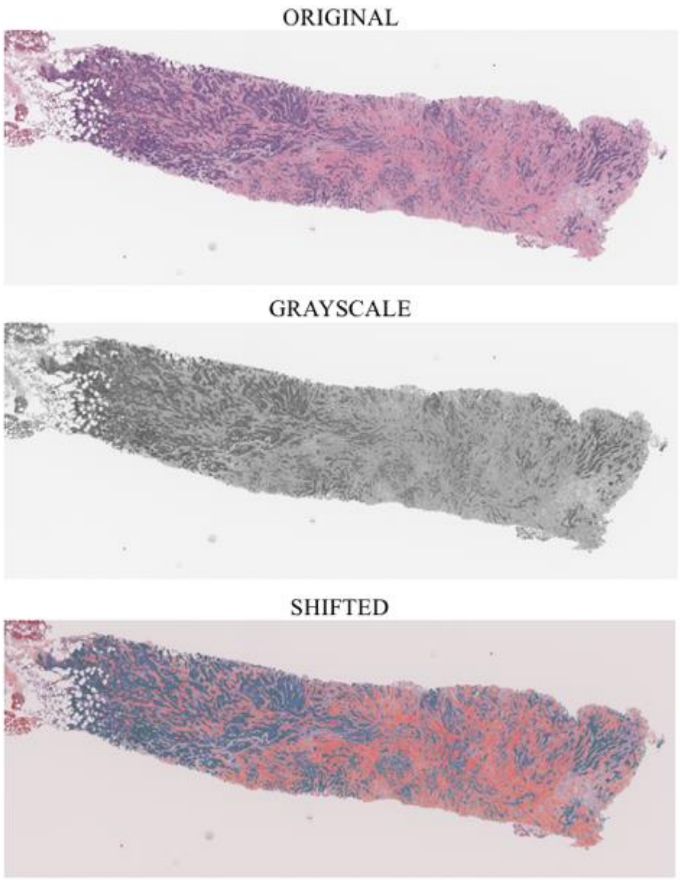
ACHROMATIC FACTORS CONTRIBUTE STRONGLY TO HISTOLOGIC IDENTITY

Direct relationship between luminance and hematoxylin.

An optimized color transformation for the analysis of digital images of hematoxylin & eosin stained slides.
Zarella, M., Breen, D., Plagov, A., Garcia, F. J Pathol Inform (2015)

CONTRIBUTION OF COLOR TO REGION SELECTION

Subjects were asked to identify three regions of interest to examine at high power at a later experimental session.

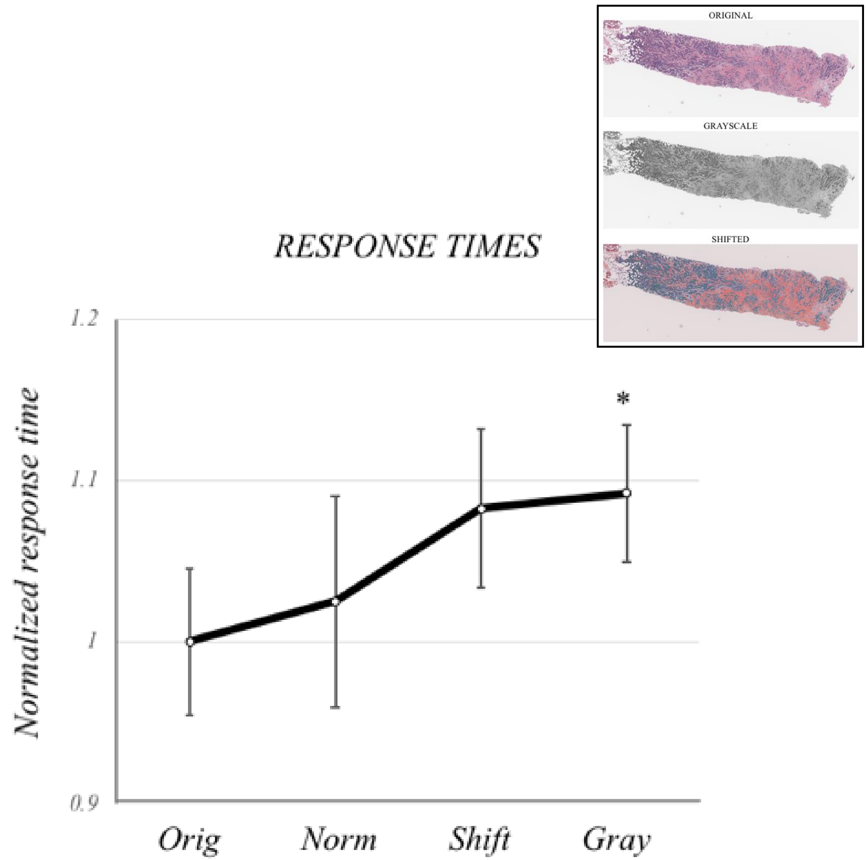


CONTRIBUTION OF COLOR TO REGION SELECTION

Subjects were asked to identify three regions of interest to examine at high power at a later experimental session.

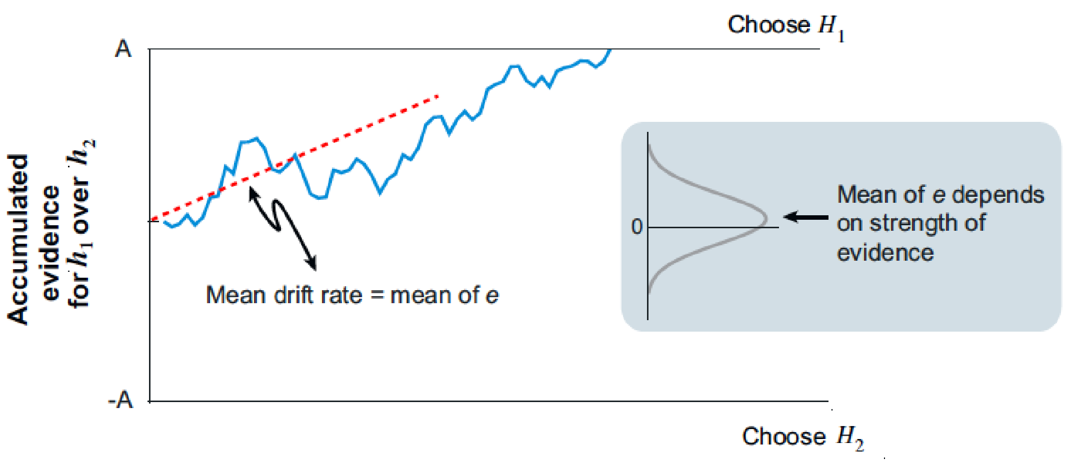
Longer response times ($p<0.01$) are consistent with greater task difficulty.

Possibly longer response times in color-shifted condition may indicate a learned effect specific to H&E staining.



Applications of cognitive science to pathology

- Evaluation of human performance
- Training and assessment
- Validation of new systems/technologies
- AI guidance
- Development of efficient DL algorithms

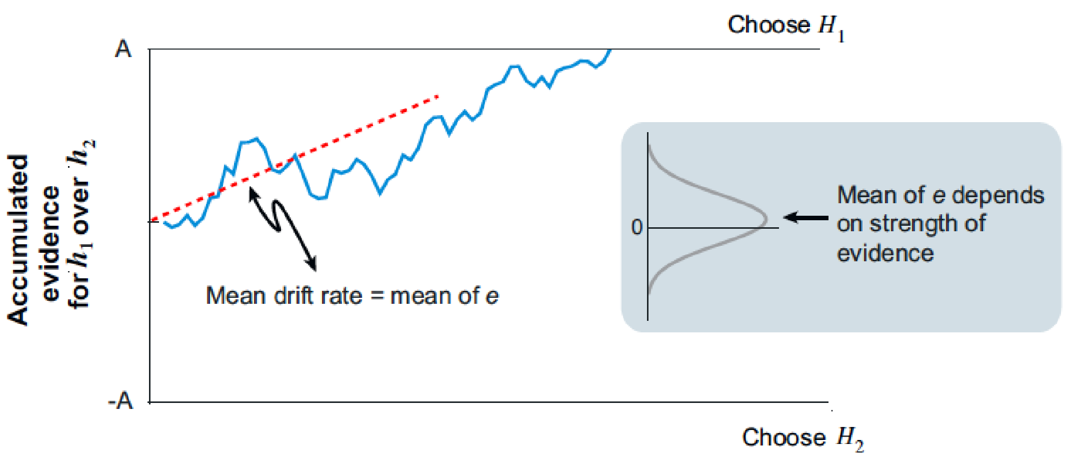


DIFFUSION DECISION MODEL

Notion of serial evidence accumulation

DDM has been described for **discrete** and **continuous** sampling

Can easily be extended beyond 2AFC decisions (e.g. race model)



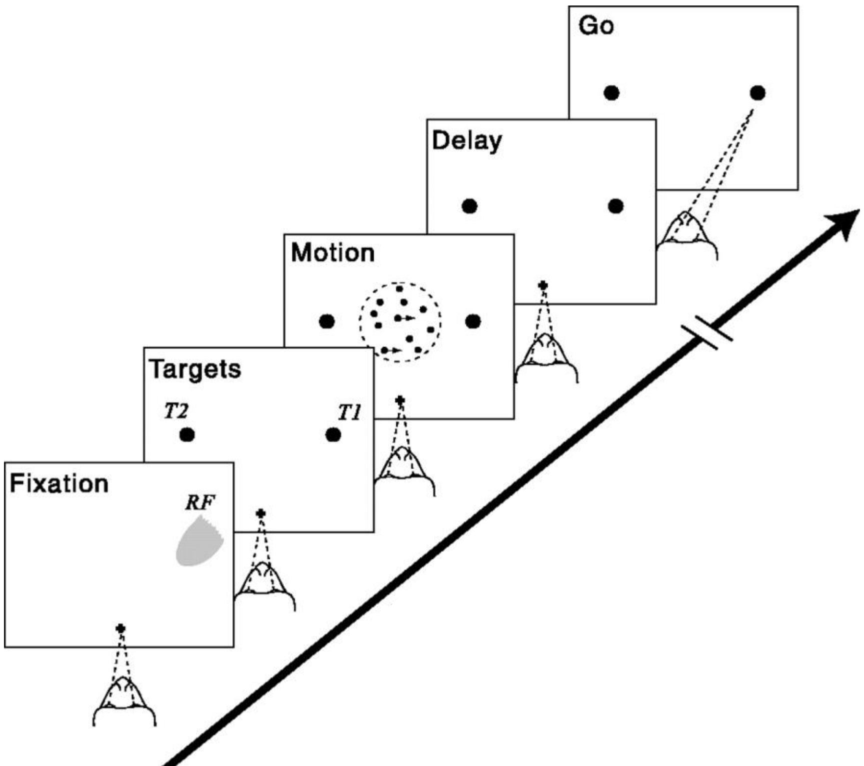
DIFFUSION DECISION MODEL

Four main parameters:

- Decision threshold (A)
- Bias (e_0)
- Delay
- Drift rate (e)

NEURAL CORRELATE OF THE DIFFUSION DECISION MODEL

Monkeys judged the direction of motion of random dot displays

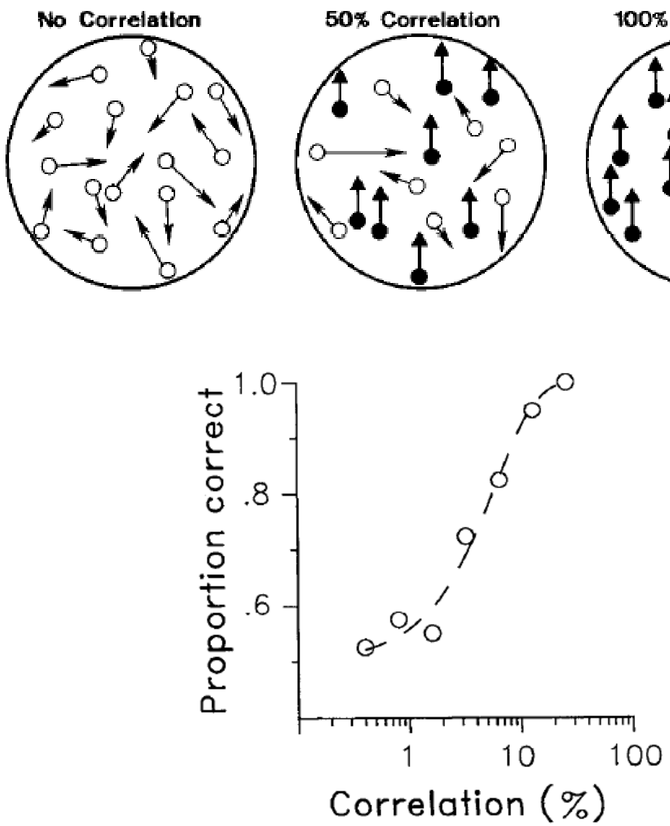


Neural basis of a perceptual decision in the parietal cortex (area LIP) of the rhesus monkey.
Shadlen, M. and Newsome, W. J Neurophysiol (2001)

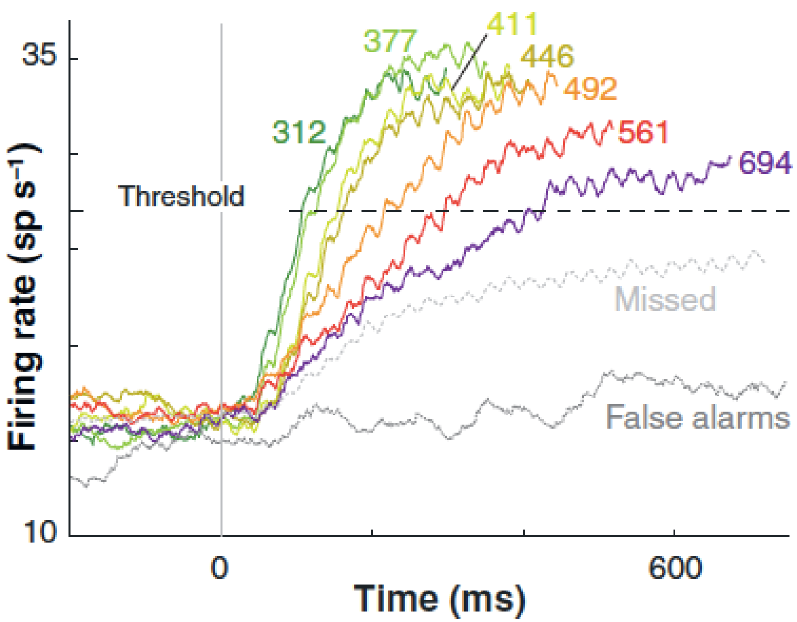
NEURAL CORRELATE OF THE DIFFUSION DECISION MODEL

Monkeys judged the direction of motion of random dot displays

Task difficulty was dictated by the coherence of dot motion



The analysis of visual motion: A comparison of neuronal and psychophysical performance.
Britten, K., Shadlen, M., Newsome, W., Movshon, J. J Neurosci (1992)



NEURAL CORRELATE OF THE DIFFUSION DECISION MODEL

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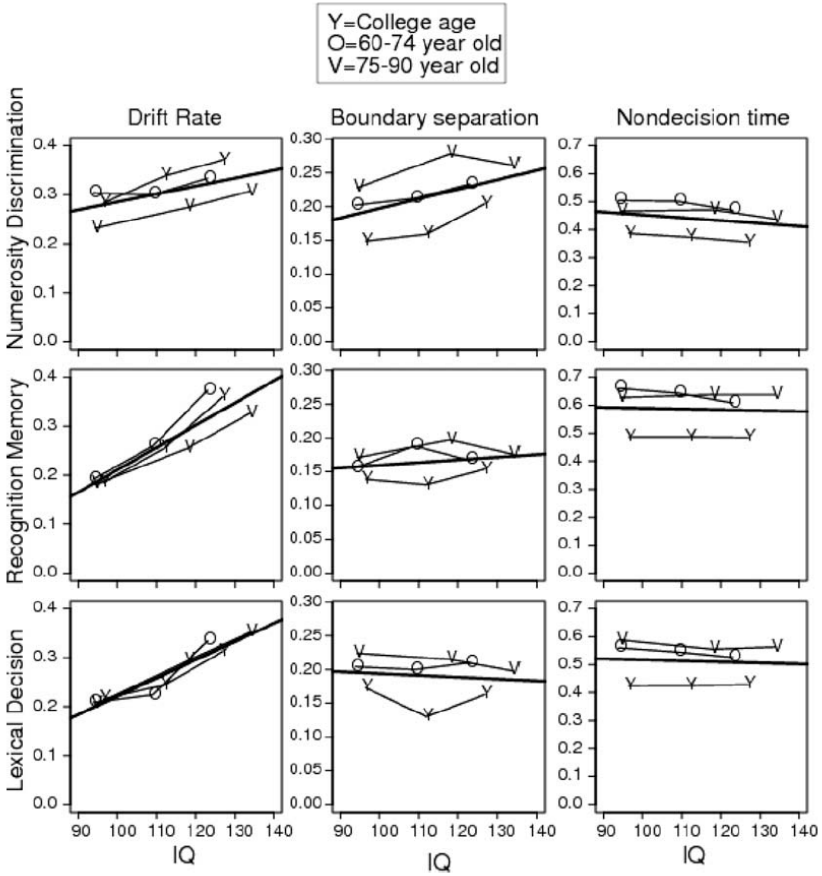
Area MT neuron firing rates exhibit the properties of a decision variable as predicted by the DDM

The neural basis of decision making.
Gold, J. and Shadlen, M. Annu Rev Neurosci (2007)



DIFFUSION DECISION MODEL IN COGNITIVE SCIENCE

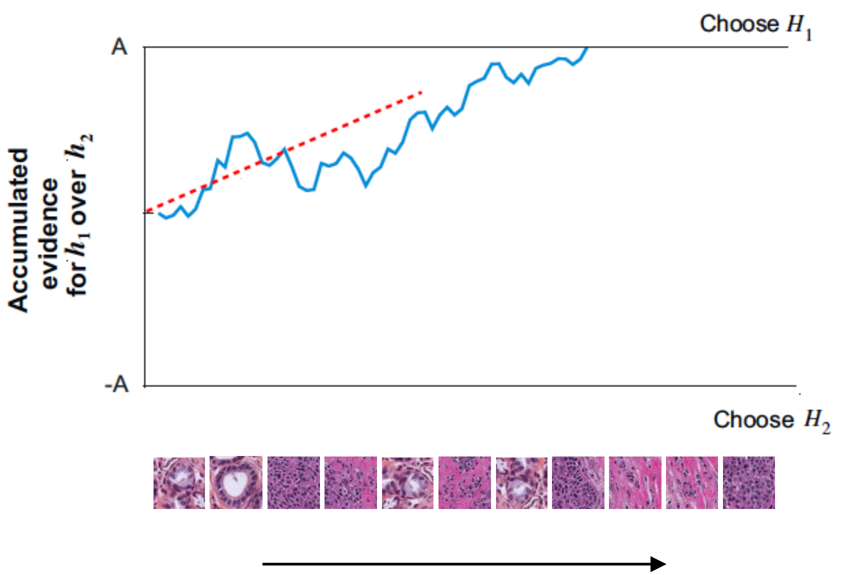
Three tasks designed to span different requirements of perceptual or memory load were applied to subjects of varying age and IQ.

Aging accounts for a change in boundary separation and delay but does not significantly impact drift rate.

Conversely, boundary separation and delay do not vary with IQ, but drift rate exhibits a linear dependence on IQ.

Individual differences, aging, and IQ in two-choice tasks.
Ratcliff, R., Thapar, A., McKoon, G. Cognitive Psychology (2010)

DIFFUSION DECISION MODEL AND PATHOLOGIST DECISION

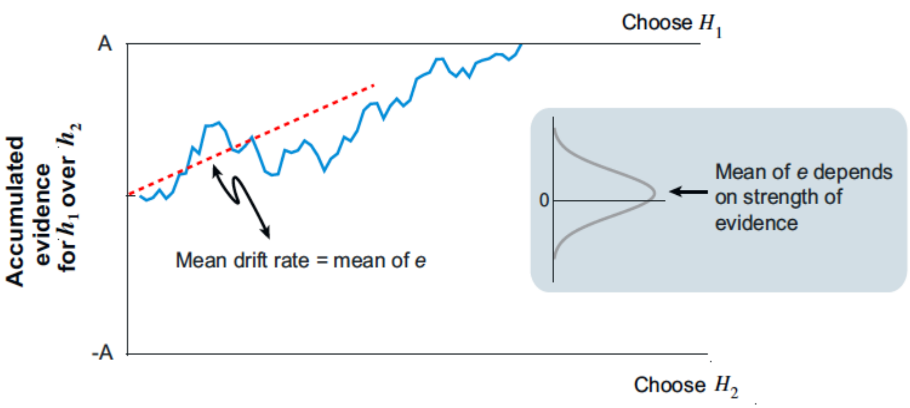


DDM suits <u>sequential sampling</u> paradigms

Sequential Sampling Models in Cognitive Neuroscience: Advantages, Applications, and Extensions.
Forstmann, B., Ratcliff, R., Wagenmakers, E.
Annu Rev Psychol (2016)

We applied <u>ideal observer analysis</u> to measure the expected impact on performance by task demands and level of training

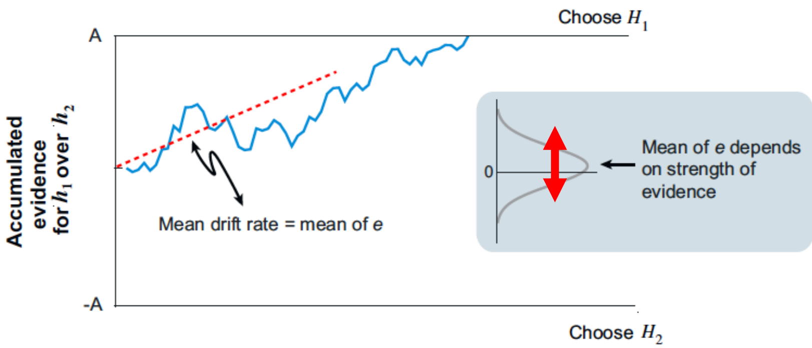
Contributions of ideal observer theory to vision research.
Geisler, W. Vision Research (2011)

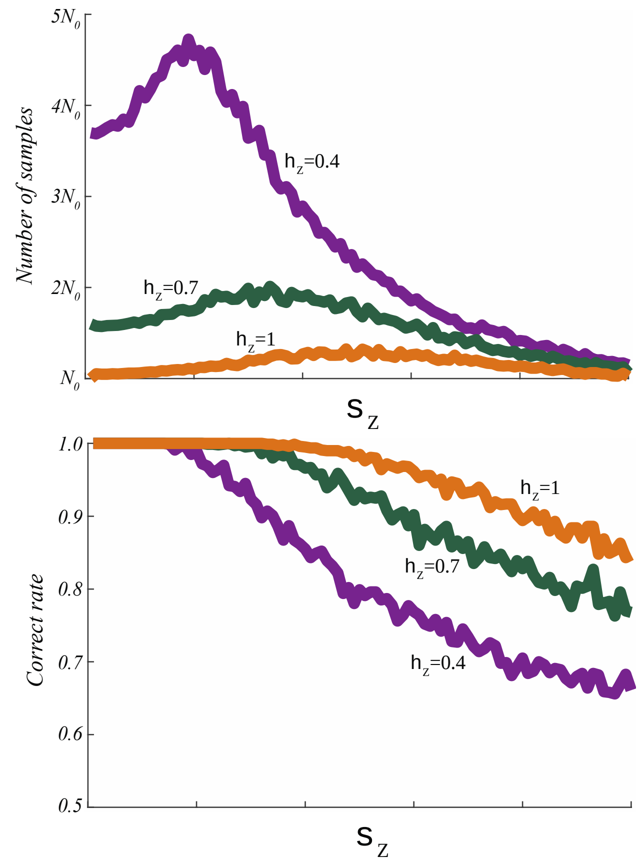


SEQUENTIAL SAMPLING AND DRIFT RATE

In most diagnostic tasks, drift rate is impacted by:

- interpretation inaccuracy: uncertainty in the information presented (σ_Z)
- visual cue capture: the ability to extract useful information from a viewed region (η_Z)
- sampling efficiency: the selection of high power regions with informative potential from the low power image (σ_S)

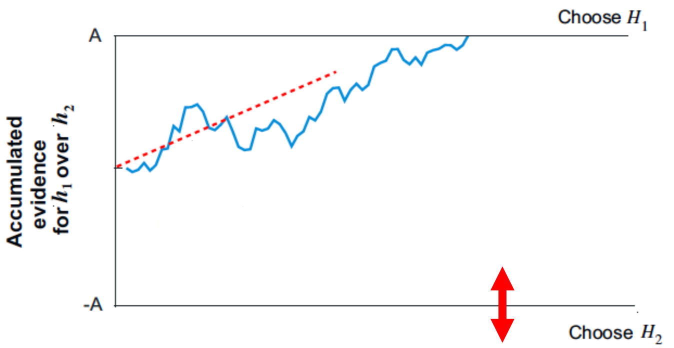


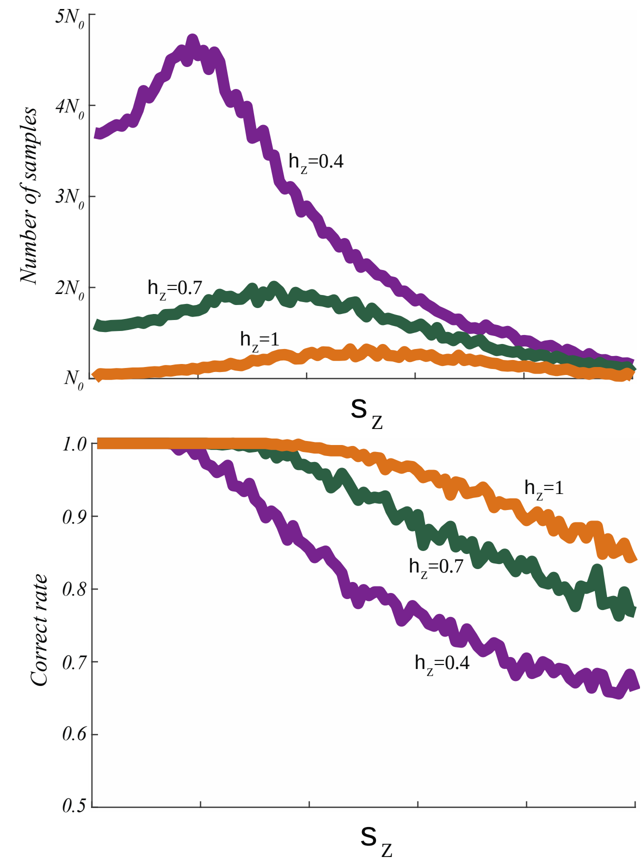


MODULATION OF INTERPRETATION ACCURACY INCREASES NUMBER OF SAMPLES

Greater inaccuracy leads to a higher number of samples required <u>before</u> it negatively impacts correct rate.

Decreasing the amount of information extracted from a given high power sample increases the sensitivity to σ_Z.





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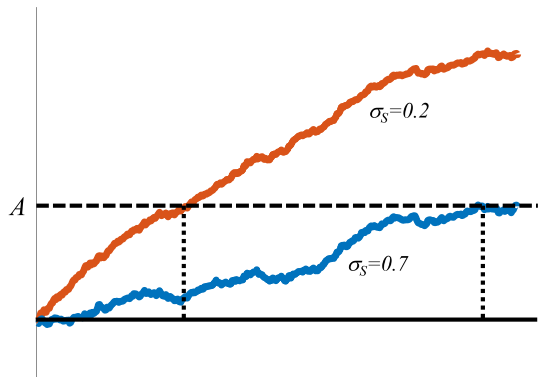
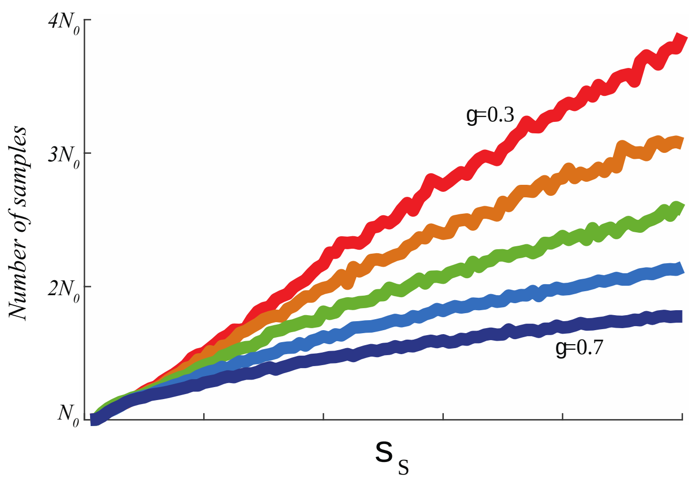
Modulating the decision threshold has the same impact on sensitivity to σ_Z.

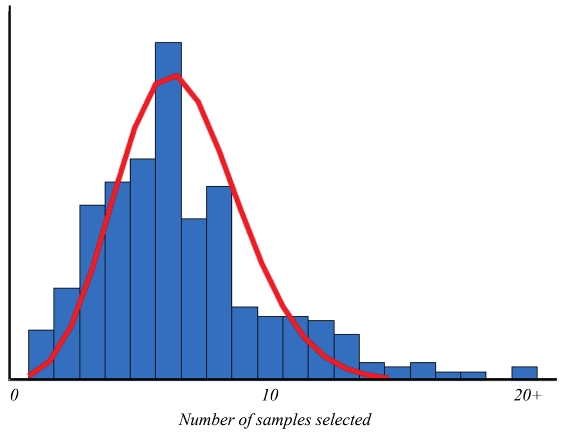


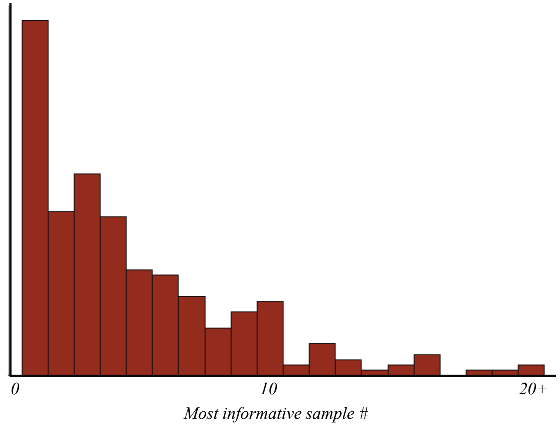


EFFICIENT SAMPLING

By identifying and sampling the most informative regions early, the drift rate rises at a faster rate.

Simulations reveal that efficient rank ordering reduces the amount of information needed, leading to faster response times.





SEQUENTIAL SAMPLING AND DRIFT RATE

Trainees were asked to report tubule formation and nuclear grade at two allowed spatial scales.

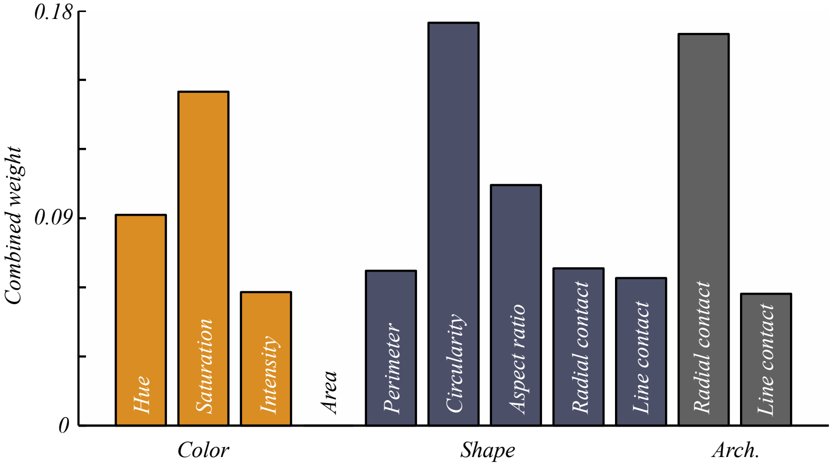
The most representative sample was typically sampled toward the beginning of the sequence (p<0.01).

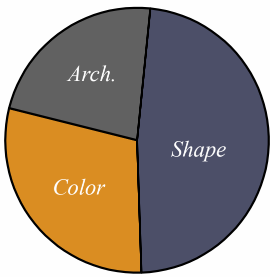
Estimation of σ_S from preferred selection suggests a value of approximately 0.6.

PREDICTION OF LYMPH NODE METASTASIS FROM H&E FEATURES

Our previously trained classifier used architectural, morphologic, and staining variables to predict metastasis to the lymph nodes

Lymph node metastasis status in breast carcinoma can be predicted via image analysis of tumor histology.
Zarella, M., Breen, D., Reza, A., Milutinovic, A., Garcia, F.
Anal Quant Cytol Histol (2015)





EYE TRACKING ENABLES RECONSTRUCTION OF VISUAL INPUT

We used a Gazepoint GP3 to monitor the eye position of subjects during the grading task.

Eye position was captured.

EYE TRACKING ENABLES RECONSTRUCTION OF VISUAL INPUT

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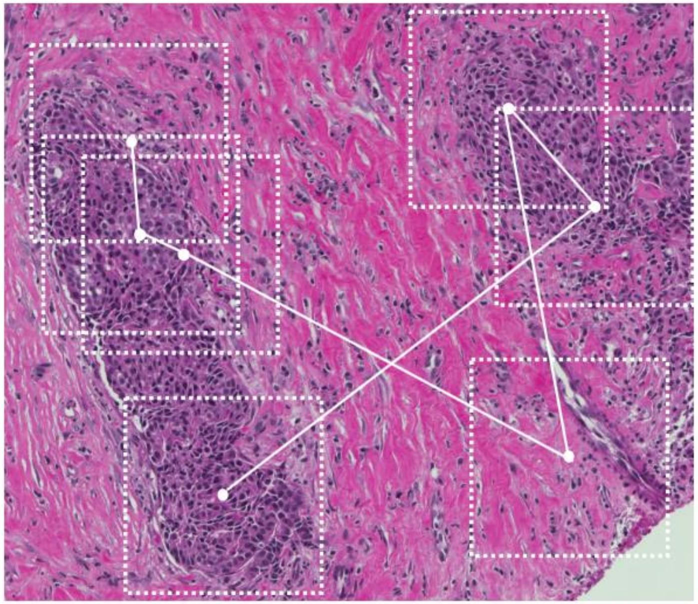
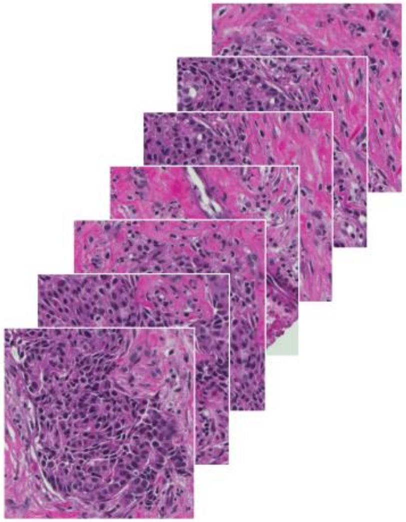
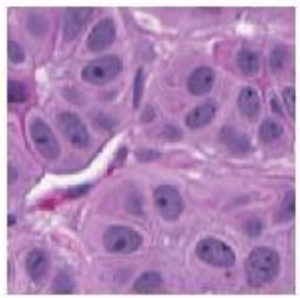
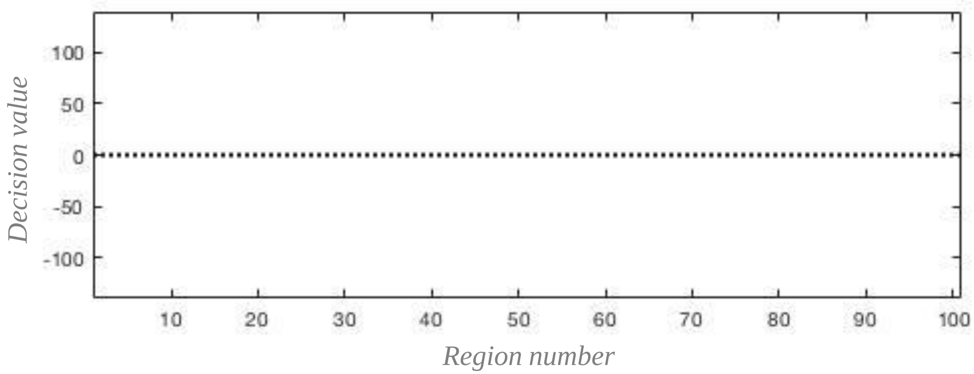
Eye position was captured.

We selected image patches centered on regions fixated for longer than 100 ms.





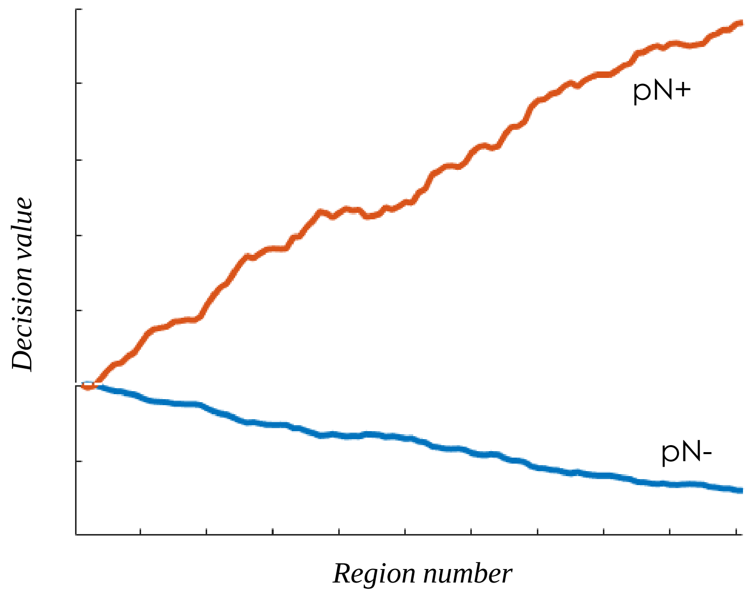




PREDICTION OF LYMPH NODE METASTASIS FROM H&E FEATURES

A decision value for each patch was derived from a measure of prediction certainty (based on the distance to the SVM hyperplane).

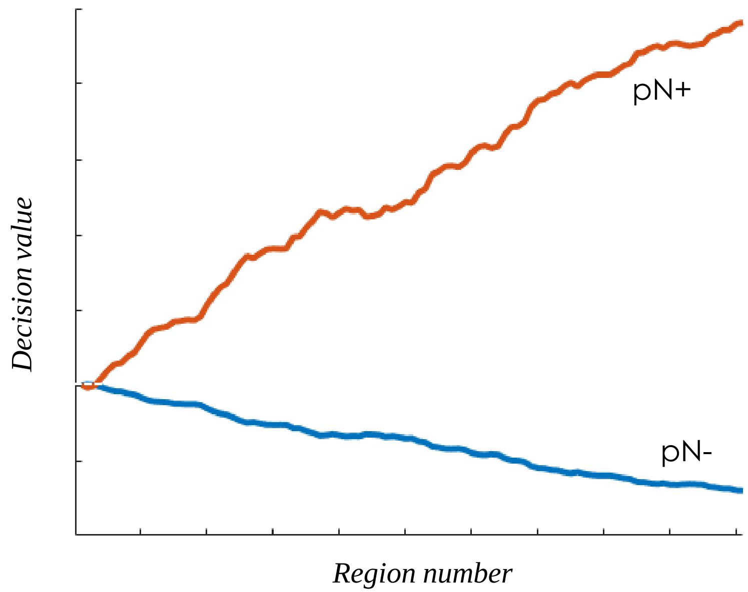
pN0 and *pN*(+) cases defined the ground truth.



PREDICTION OF LYMPH NODE METASTASIS FROM H&E FEATURES

Average curves were derived from 58 cases.

Prediction accuracy = 0.62 (vs. 0.65 for all features).



FUTURE (CURRENT) DIRECTION

Asymmetry can be accounted for by <u>bias</u> in the DDM

Does an improvement in sampling efficiency improve ML accuracy and efficiency?

Contributors

Fernando U. Garcia, M.D.

Medical Director of Pathology
Department of Pathology & Laboratory Medicine
Cancer Treatment Centers of America

David E. Breen, Ph.D.

Associate Professor
Department of Computer Science
Drexel University

Additional thanks to:

Sebastian Jofre, M.D.

Andrei Plagov, M.D.

Callan Powell

Jessica Hoban

DREXEL UNIVERSITY
Clinical & Translational
Research Institute

DREXEL UNIVERSITY
Center for Biological Discovery from Big Data
School of Biomedical Engineering, Science and Health Systems