

Image Translation with Generative Models

Image-to-Image Translation with Conditional Adversarial Networks

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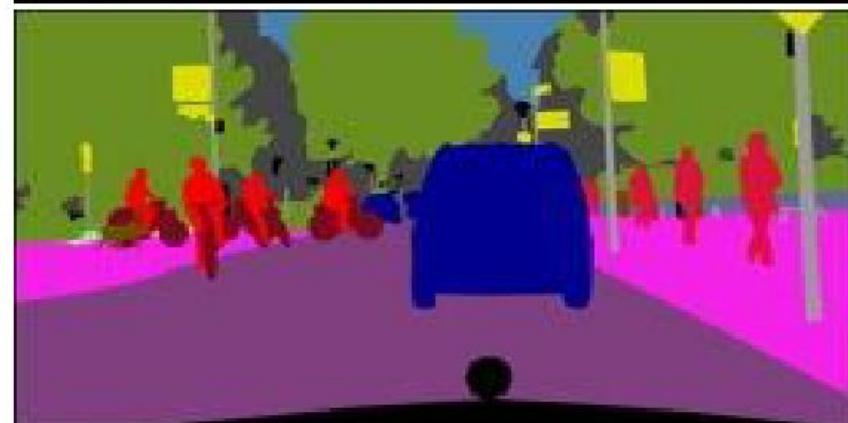
Input



Ground truth



L1



Ground truth



cGAN



L1 + cGAN



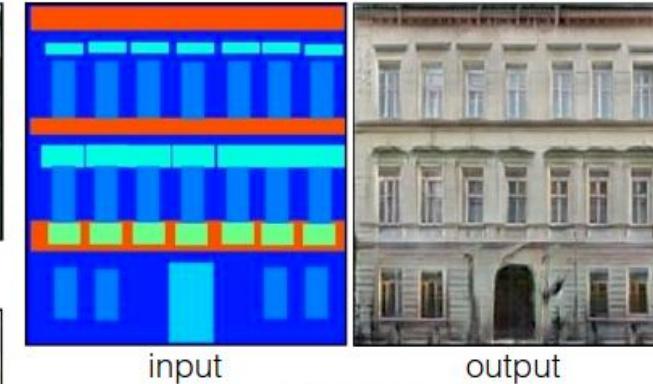
Labels to Street Scene



input

output

Labels to Facade



input

output

BW to Color



input

output

Aerial to Map



input

output

Day to Night



input

output

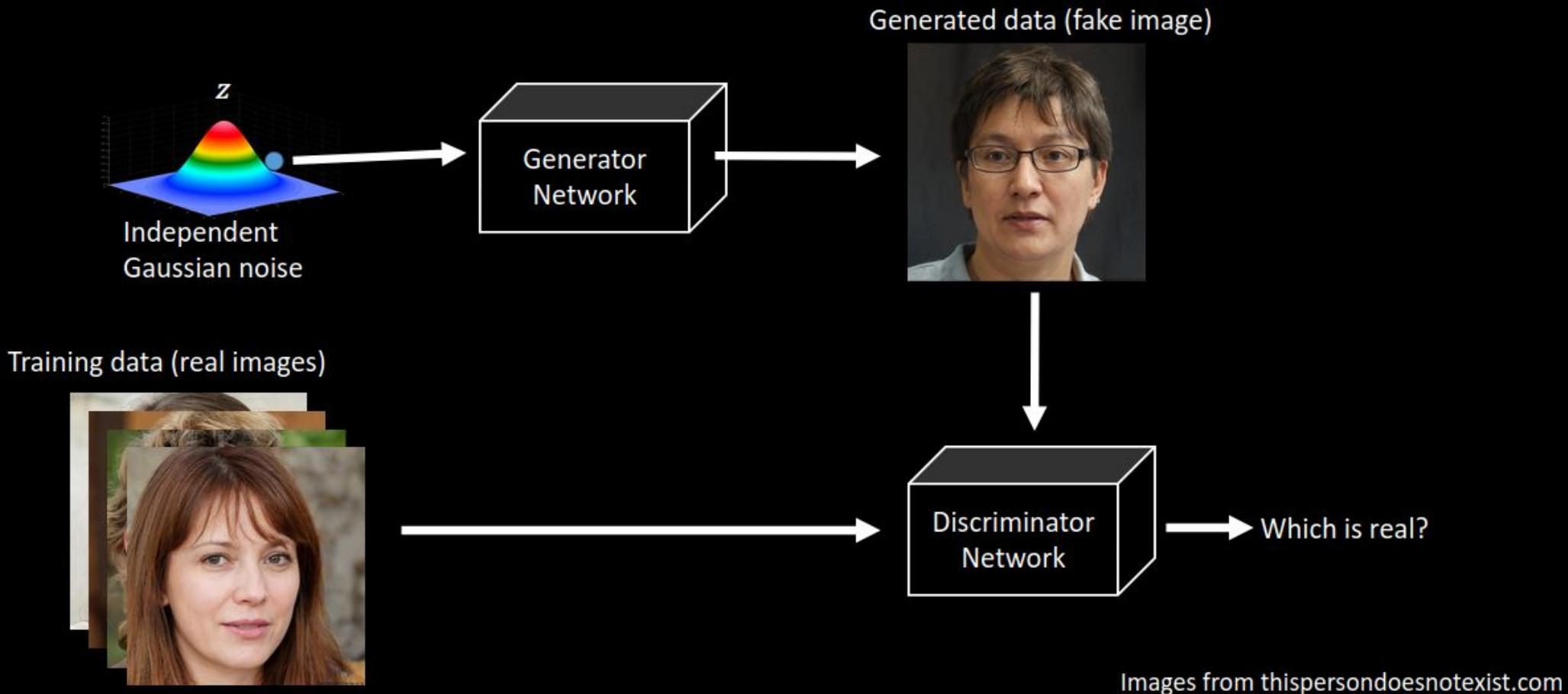
Edges to Photo



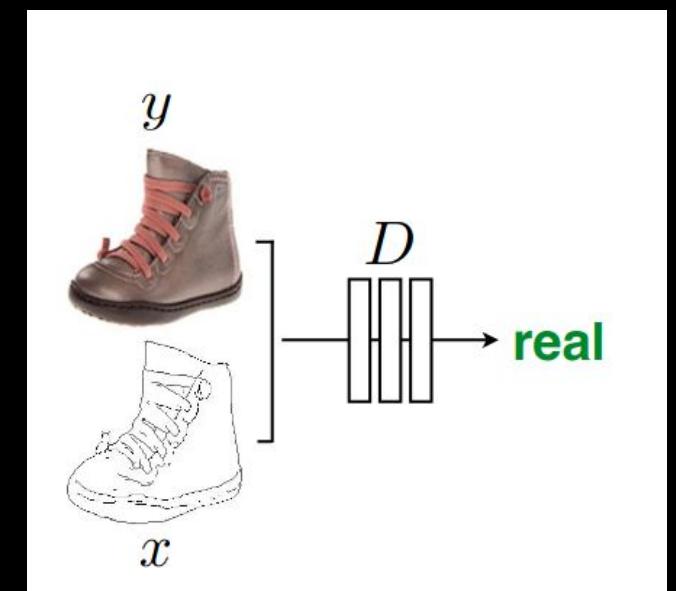
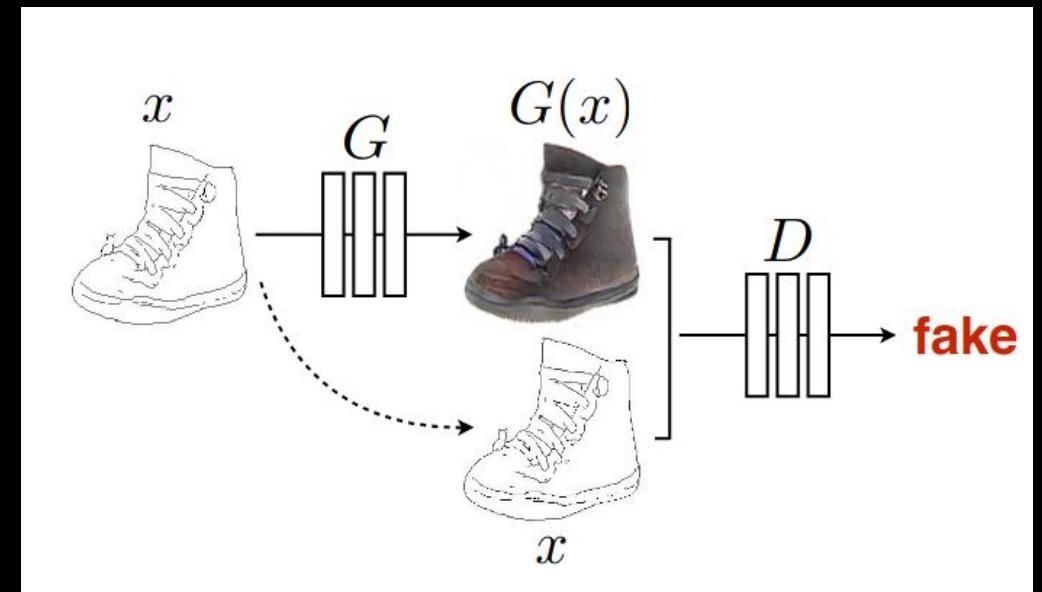
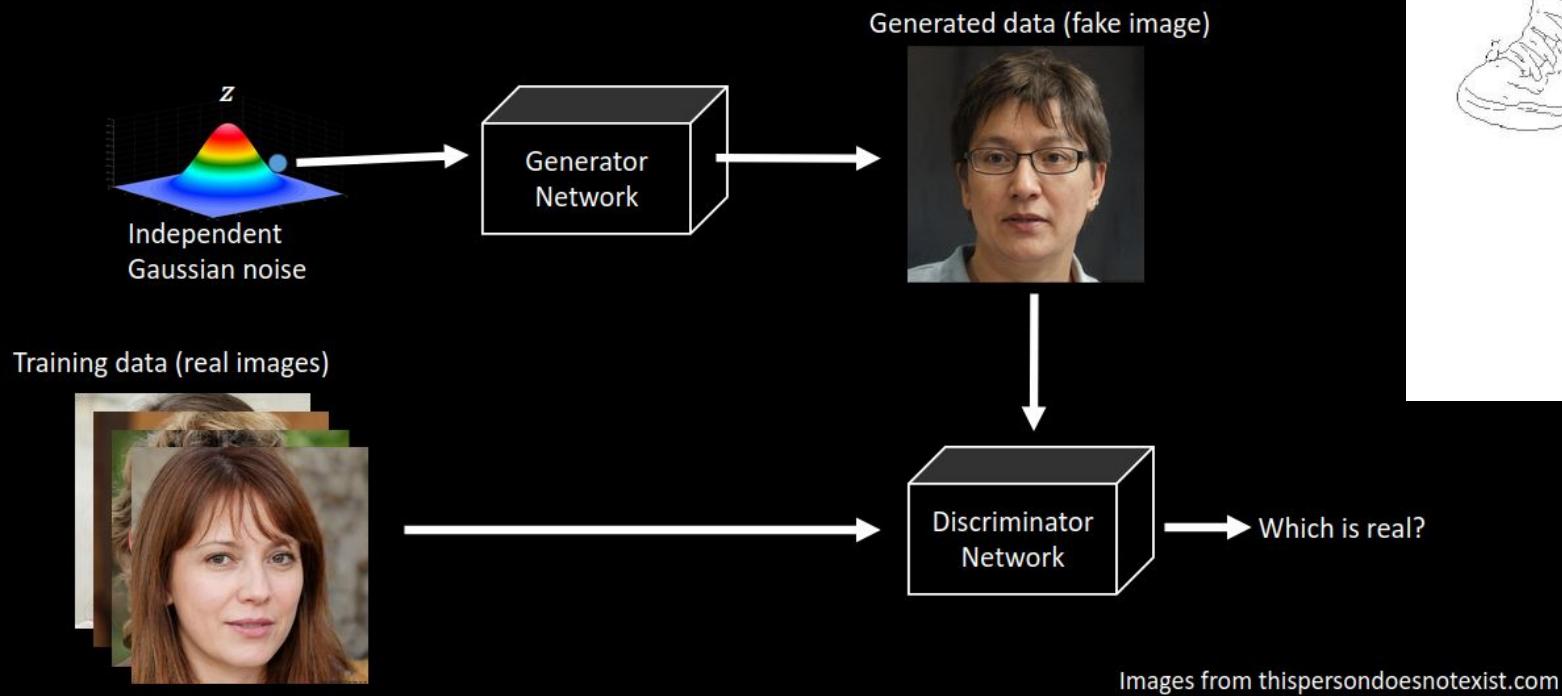
input

output

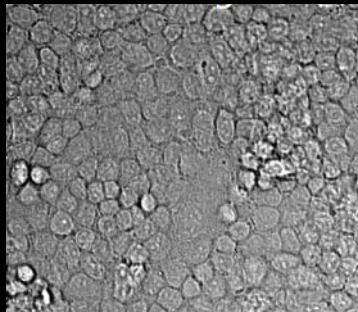
Generative Adversarial Networks- Training



Generative Adversarial Networks- Training



Evaluating virtual staining for high-throughput screenings



Bright-field



Virtual Stain



Samuel
Tonks



Chih-Yang
Hsu



Steve
Hood



Ryan
Musso



Ceridwen
Hopely



Steve
Titus



Alexander
Krull



Minh
Doan



Iain
Styles



UNIVERSITY OF
BIRMINGHAM

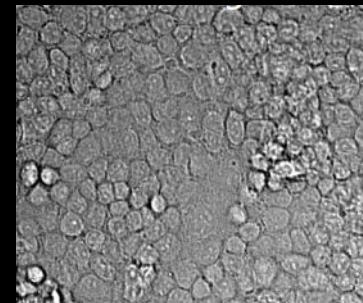
GSK

The
Alan Turing
Institute

Can we combine virtual staining with HTS?

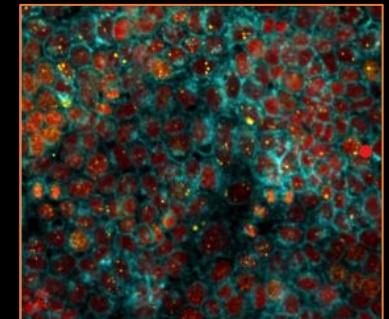
Virtual staining

- synthesis of stained cells or tissue images from unstained images



Bright-field

→ [1]



Virtual Stain

High-throughput screening (HTS)

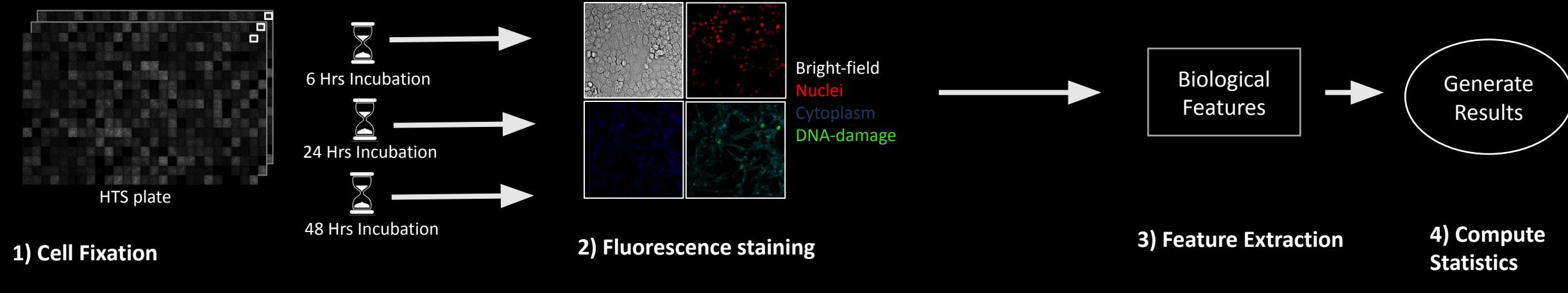
- simultaneously testing of multiple compounds for drug effect.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
1	C1				C2				C3			C4											
6	C5				C6			C7			C8												
11	C9																						
12	Positive																						
13	Control																						
14																							
15																							
16																							

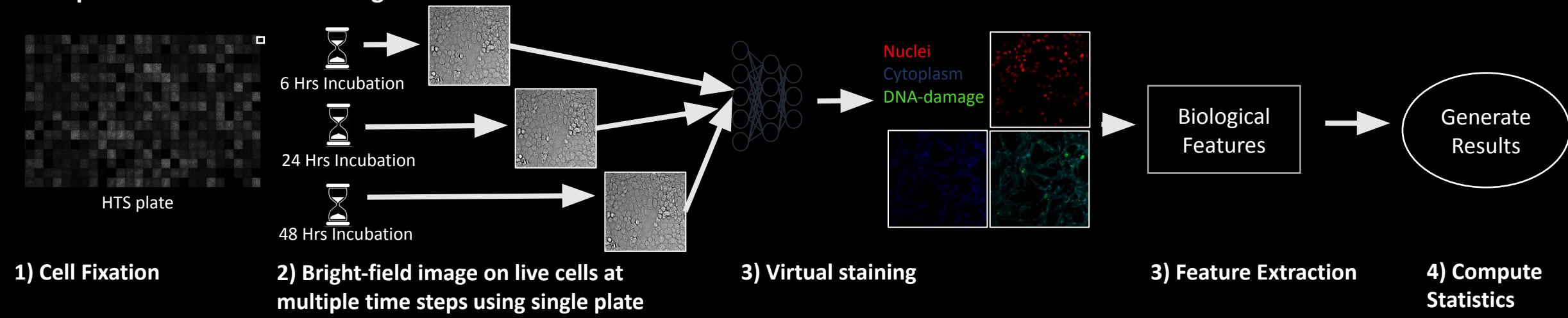
[1] Chawin Ounkomol, Sharmishtaa Seshamani, Mary M Malekcar, Forrest Collman, and Gregory R Johnson, "Label-free prediction of three-dimensional fluorescence images from transmitted-light microscopy," *Nature methods*, vol. 15, no. 11, pp. 917–920, 2018.

HTS and the promise of virtual staining

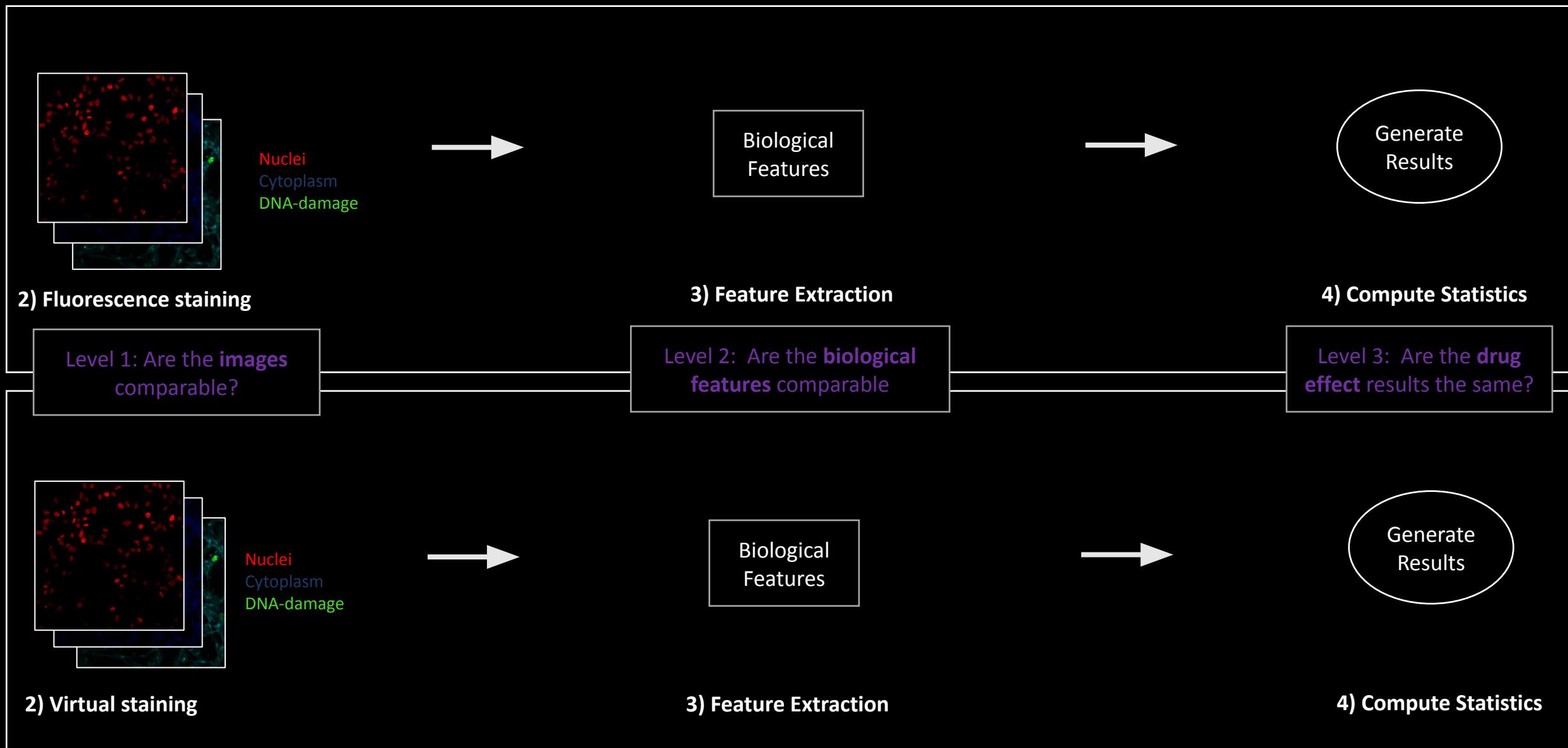
Traditional HTS Pipeline



HTS Pipeline with Virtual Staining



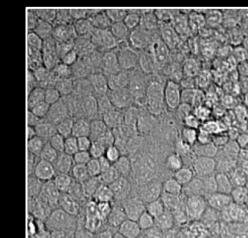
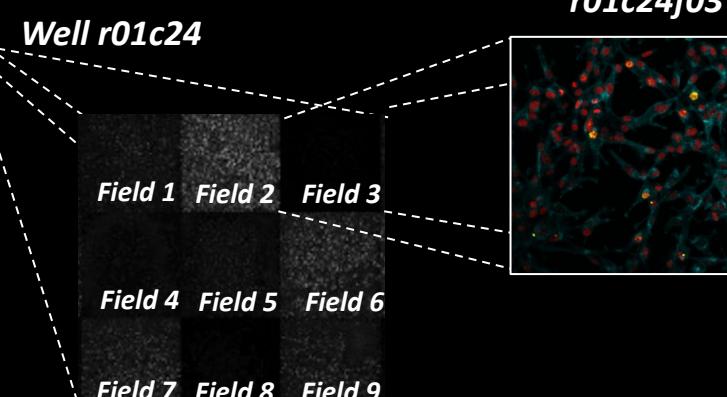
Evaluation pipeline of virtual staining consists of three levels



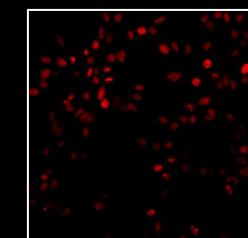
Dataset & Sampling

Cell types: Lung, Ovarian and Breast

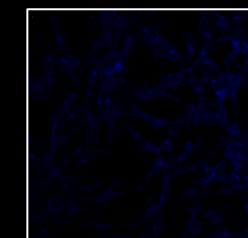
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	
1	C1	C2	C3	C4																				
2																								
3																								
4																								
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6																								
7																								
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11																								
12	C9																							
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16																								



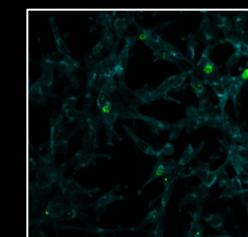
Bright-field
r01c24f03ch1



Nuclei
6-diamidino-2- phenylindole (DAPI)
r01c24f03ch2



Cytoplasm
fluorescein (FITC)
r01c24f03ch3



DNA-damage
Cyanine (Cy5)
r01c24f03ch4

1) 16x24 HTS plate with compounds & controls layout.



2) Each well contains 9 Fields of view (3x3 grid) (9 Images)

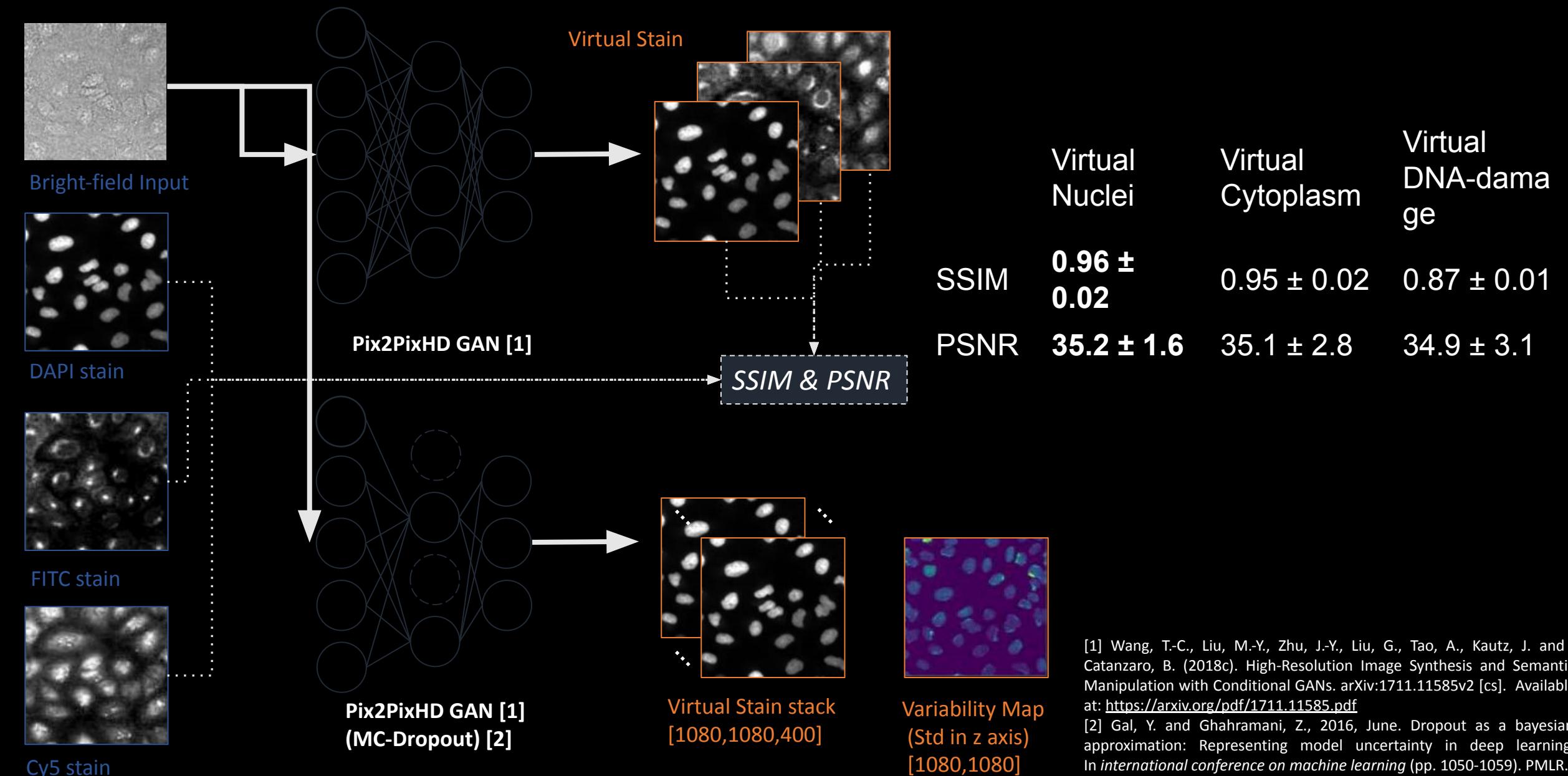


3) Each field of view has 4 channels: bright-field with three stains.

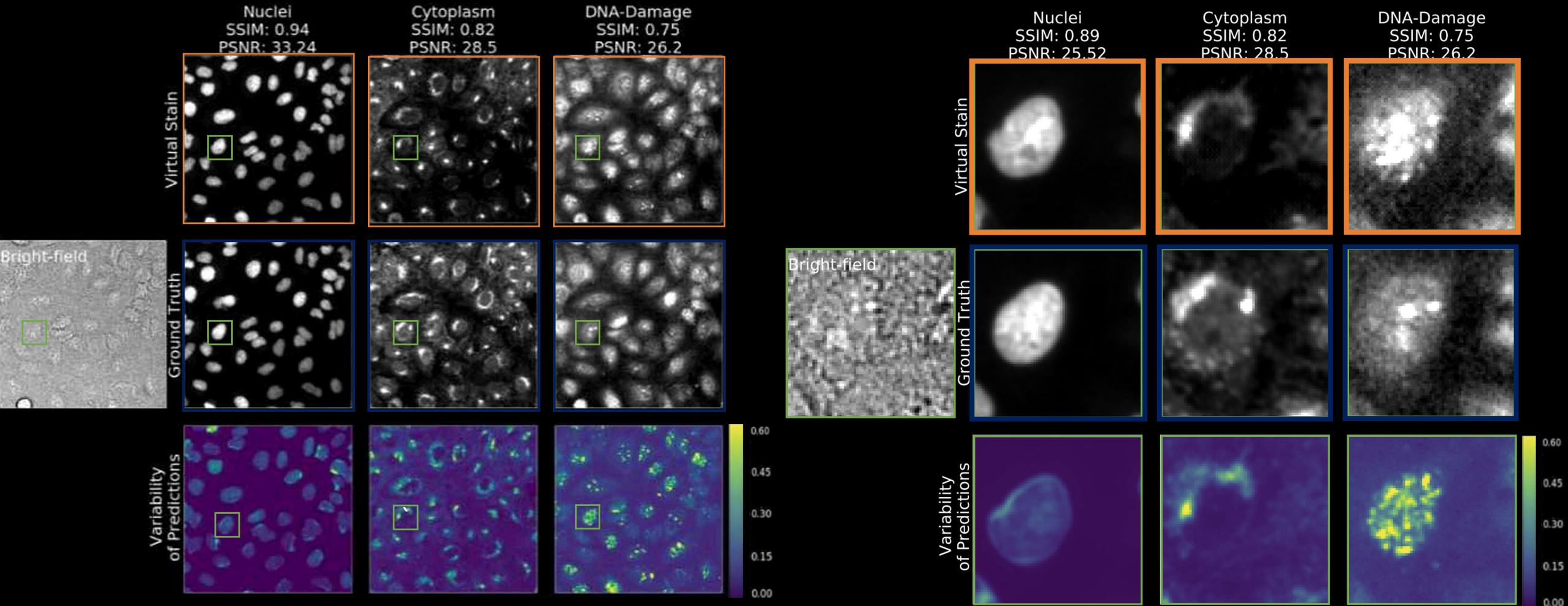
Sampling

- 30,000 bright-field and fluorescence stain image pairs were randomly sampled across plates.

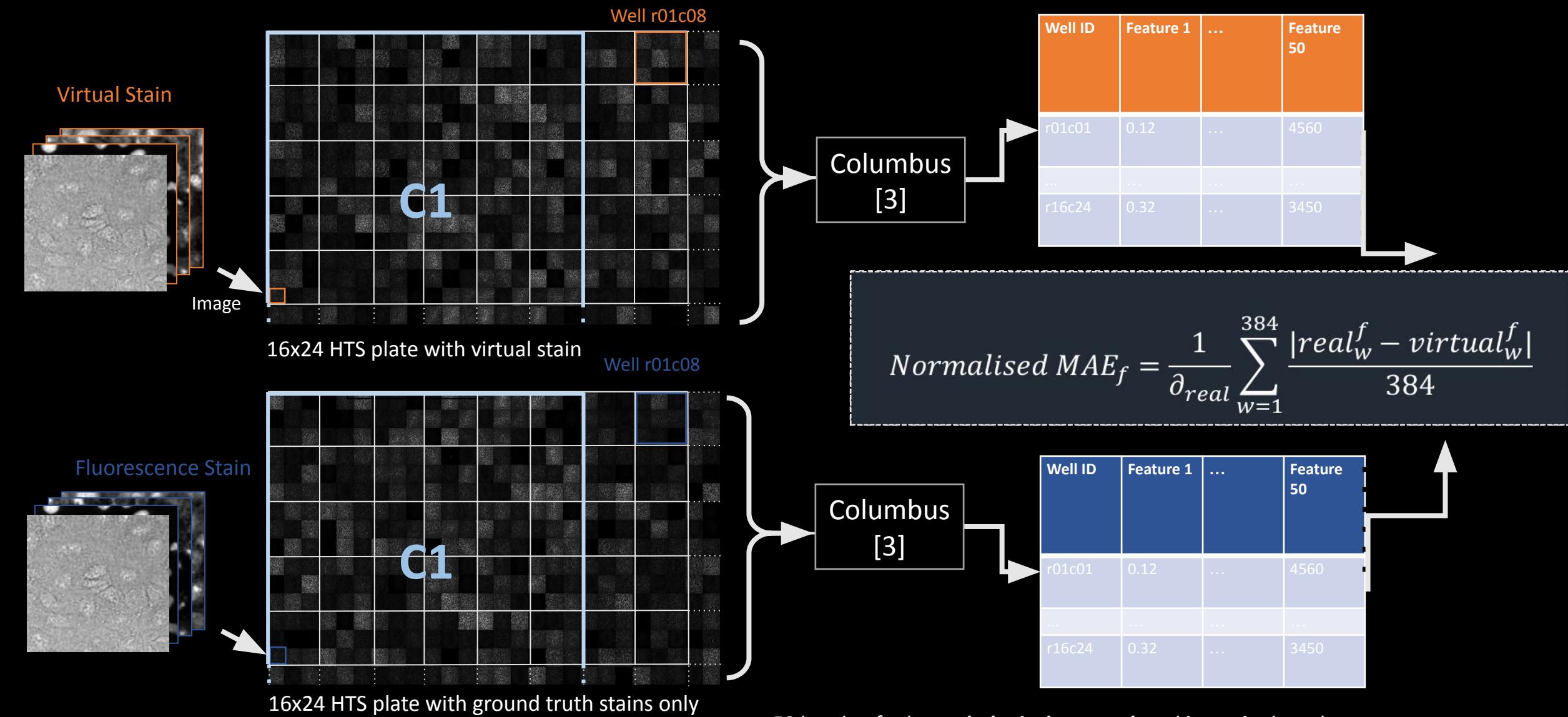
Evaluation Pipeline: Results Level 1 – Pixel Quality Metrics



Evaluation Pipeline: Results Level 1 – Pixel Quality Metrics



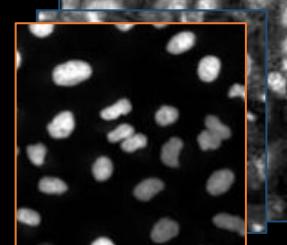
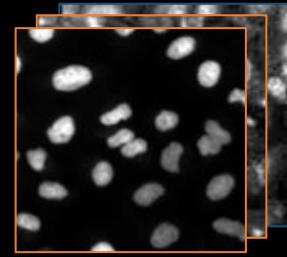
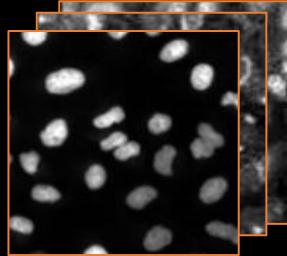
Evaluation Pipeline: Level 2 – Biological Features



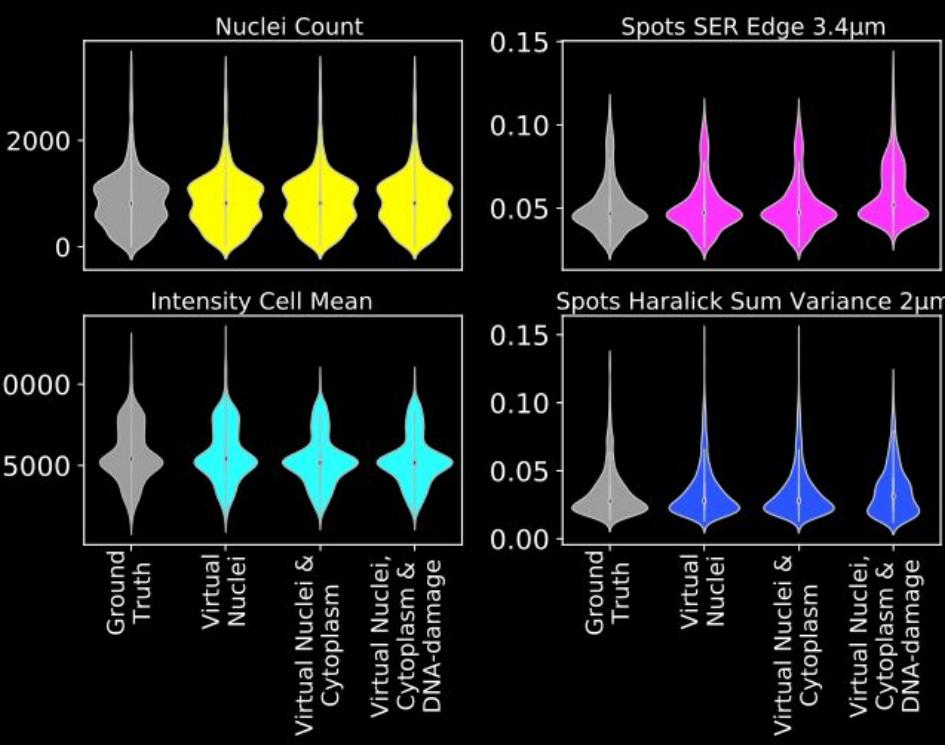
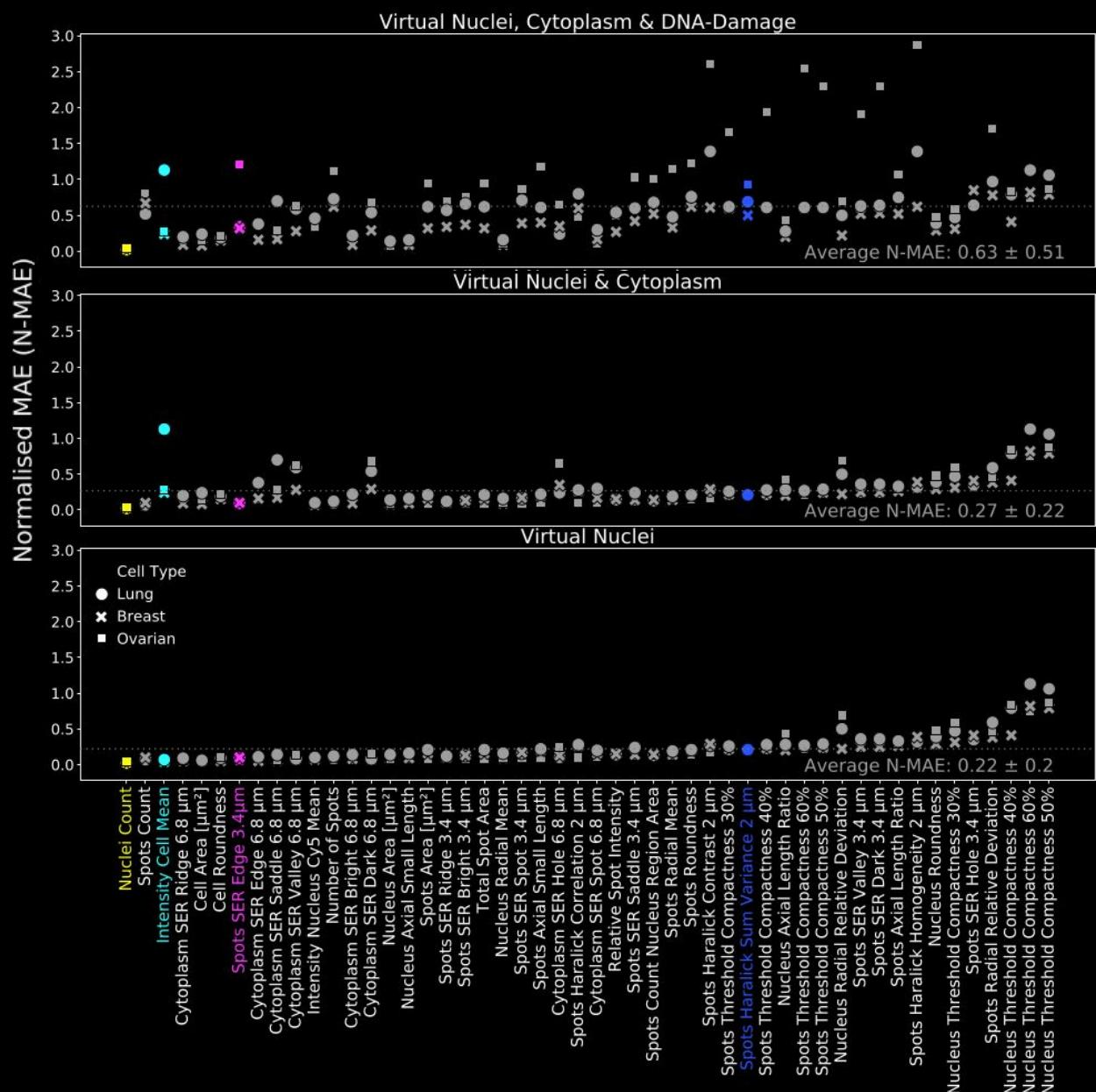
50 handcrafted morphological, textural and intensity based features across all three stained channels used for original toxicity

[3] <https://www.perkinelmer.com/uk/product/image-data-storage-and-analysis-system-columbus>

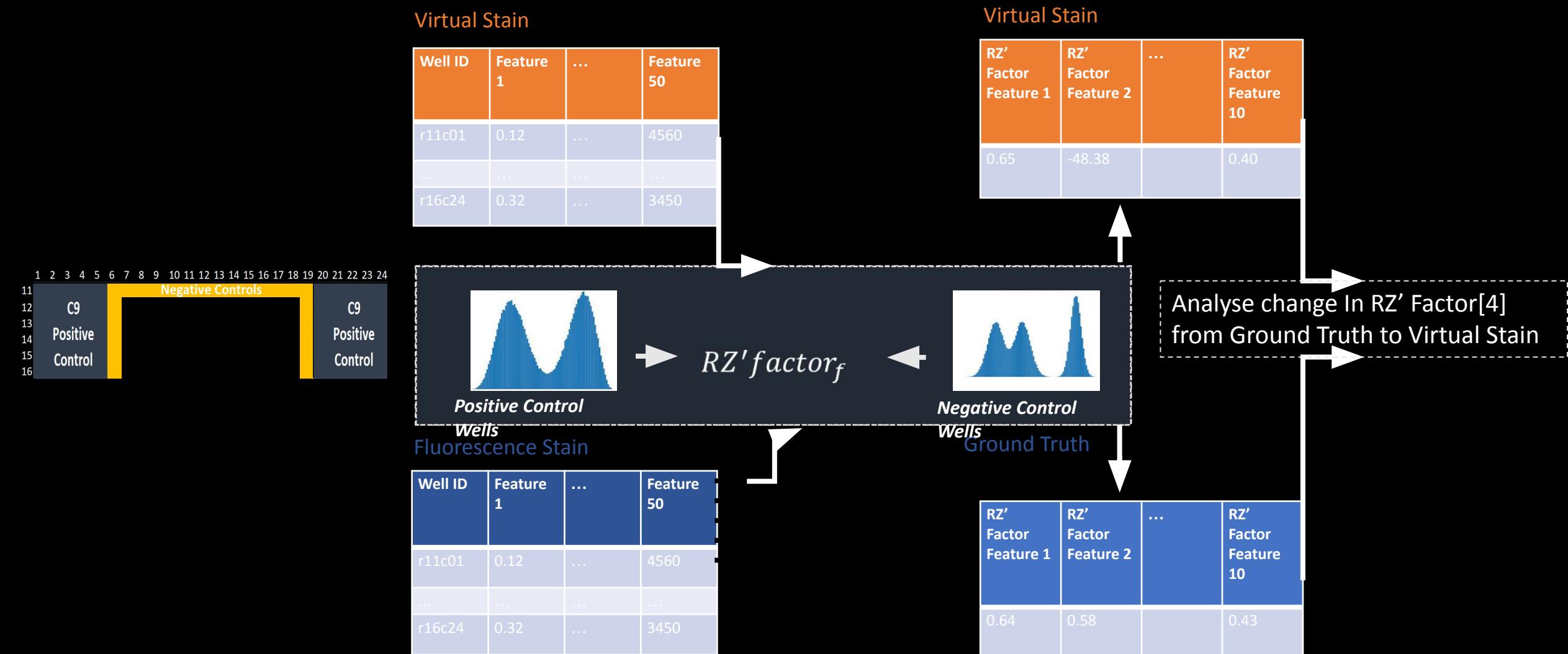
Evaluation Pipeline: Results Level 2 – Biological Features



Fluorescence Stain
Virtual Stain



Evaluation Pipeline: Level 3 – Drug Effect



1) Using feature scores for positive and negative control wells.

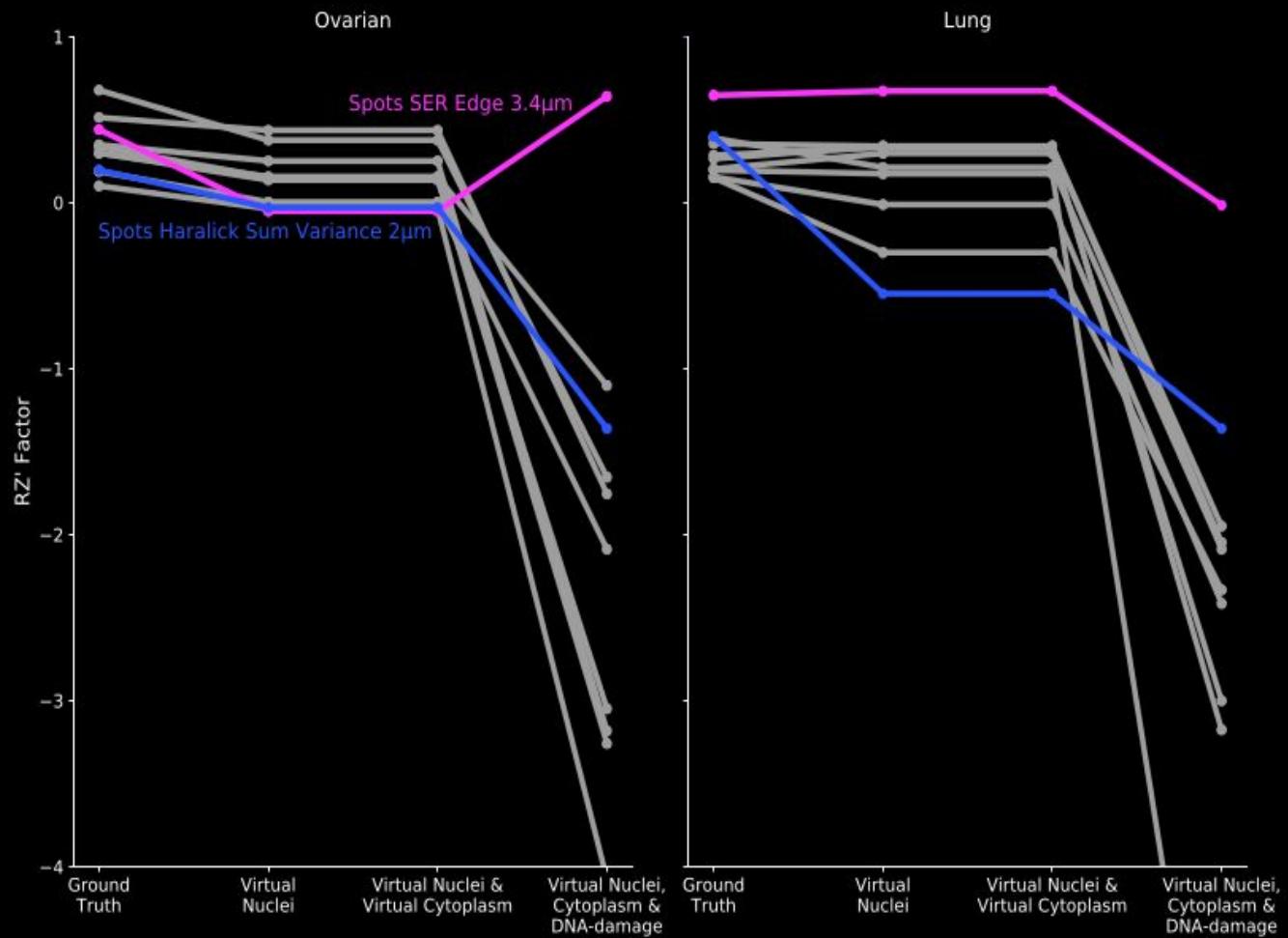
2) Compute $RZ' \text{ factor}$ per feature

3) Identify the highest 10 $RZ' \text{ factor}$ in Ground Truth

4) Compute Change in $RZ' \text{ factor}$ with the introduction of virtual staining

[4] Hu Zhang, Thomas DY Chung, and Kevin R Oldenburg, “A simple statistical parameter for use in evaluation and validation of high throughput screening assays,” Journal of biomolecular screening, vol. 4, no. 2, pp. 67–73, 1999.

Evaluation Pipeline: Results Level 3 – Drug Effect



Discussion & Conclusion

- Virtually stained nuclei and cytoplasm can be synthesized with high image quality, realistic biological features, and accurate quantification of drug effect.
- Virtually stained DNA-damage showed high variability, unrealistic biological features and notable inaccuracies in drug effect.
- These findings could reduce the time needed from days to several minutes to image these two labels and could enable new multiplex imaging combinations.
- Future work will further scrutinize the ability of I2I methods to generalize to other cell types and explore uncertainty quantification to improve virtual staining.

Thank you & Questions

Thanks to all those involved in the project:



Samuel
Tonks



Chih-Yang
Hsu



Steve
Hood



Ryan
Musso



Ceridwen
Hopely



Steve
Titus



Alexander
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Any questions?



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