The Nuts and Bolts of Computational Pathology: Considering costs, resources, infrastructure needs, and barriers to adoption

David McClintock, MD

Digital Pathology Association Companion Meeting

May 21, 2018

DISCLOSURES

Philips Digital Pathology: Member, Scientific Advisory Board

XIFIN: Member, Medical Advisory Board

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Surgical Pathology Signout - 2025

You arrive at your desk, ready to start your day's work, hot cup of coffee in hand

You open your browser on your dual 45" 8K displays

Your case list appears before you - triaged by priority

You open the first case - a new prostate biopsy, patient due to see his clinician tomorrow at 8AM for the standard second day follow-up appointment

Surgical Pathology Signout - 2025

You turn to screen #1, where you review the patient's relevant clinical history, surgical notes, lab results, prior pathology results, radiology imaging, and pertinent demographic information

You turn to screen #2, where you see multiple digital slides, arranged by diagnostic importance with multiple regions of interest flagged for review

Surgical Pathology Signout - 2025

You review the flagged ROIs and, for the challenging areas, review the correlative IHC stains

You navigate back to screen #1, review the prefilled report, make the appropriate edits, and signout the case

Five minutes have passed - you take a sip of your nice hot coffee and move on to the next case...

How Did This Happen??

Computational Pathology!!

Session Goals

1. Describe the infrastructure and resource needs required to begin doing computational pathology within your pathology practice or department
2. Consider potential high costs associated with implementing computational pathology
3. Describe potential barriers to adoption for computational pathology

Computational Pathology - Infrastructure and Resources

What is Computational Pathology?

Editorial

Computational Pathology

An Emerging Definition

David N. Louis, MD; Georg K. Gerber, MD, PhD; Jason M. Baron, MD; Lyn Bry, MD, PhD; Anand S. Dighe, MD, PhD; Gad Getz, PhD; John M. Higgins, MD; Frank C. Kuo, MD, PhD; William J. Lane, MD, PhD; James S. Michaelson, PhD; Long P. Le, MD, PhD; Craig H. Mermel, MD, PhD; John R. Gilbertson, MD; Jeffrey A. Golden, MD

Arch Pathol Lab Med—Vol 138, September 2014

- An approach to diagnosis that:
  - Incorporates multiple sources of data (e.g., pathology, radiology, clinical, molecular and lab operations)
  - Uses mathematical models to generate diagnostic inferences
  - Presents clinically actionable knowledge to customers

Building Blocks of Computational Pathology

- Whole slide imaging system(s)
- Image repository / VNA
- High speed networks (Gigabit)
- Workflow engine
- Computational Pathology platform
- Connected health information systems
- ENGAGED PATHOLOGISTS!!

Got Scanners?

Components of a WSI System

- Slide scanning instrument
- Workstation
- Monitor
- Image management system
- Digital slide repository
- Pixel data pathway

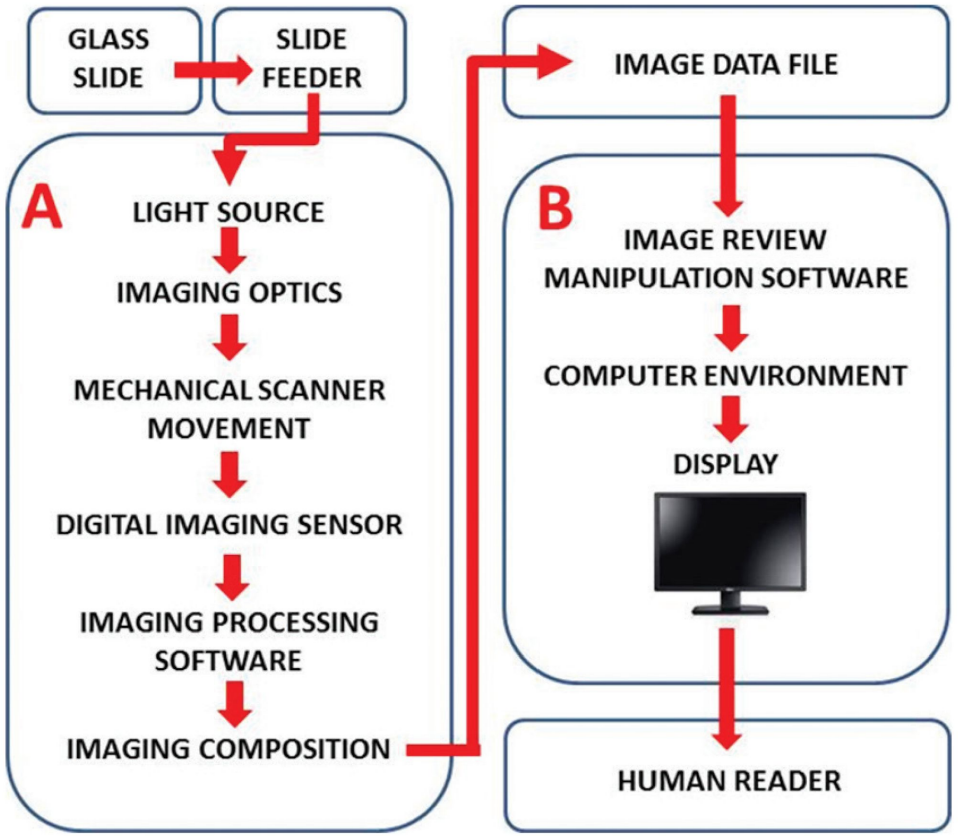

Image from: Abels E, Pantanowitz L. Current state of the regulatory trajectory for whole slide imaging devices in the USA. J Pathol Inform. 2017;8(1):23-25

The “Complete” Whole Slide Imaging System

Red arrows = Pixel Pipeline

Per FDA - Two subsystems married together

From: Abels E, Pantanowitz L. Current state of the regulatory trajectory for whole slide imaging devices in the USA. J Pathol Inform. 2017;8(1):23-25

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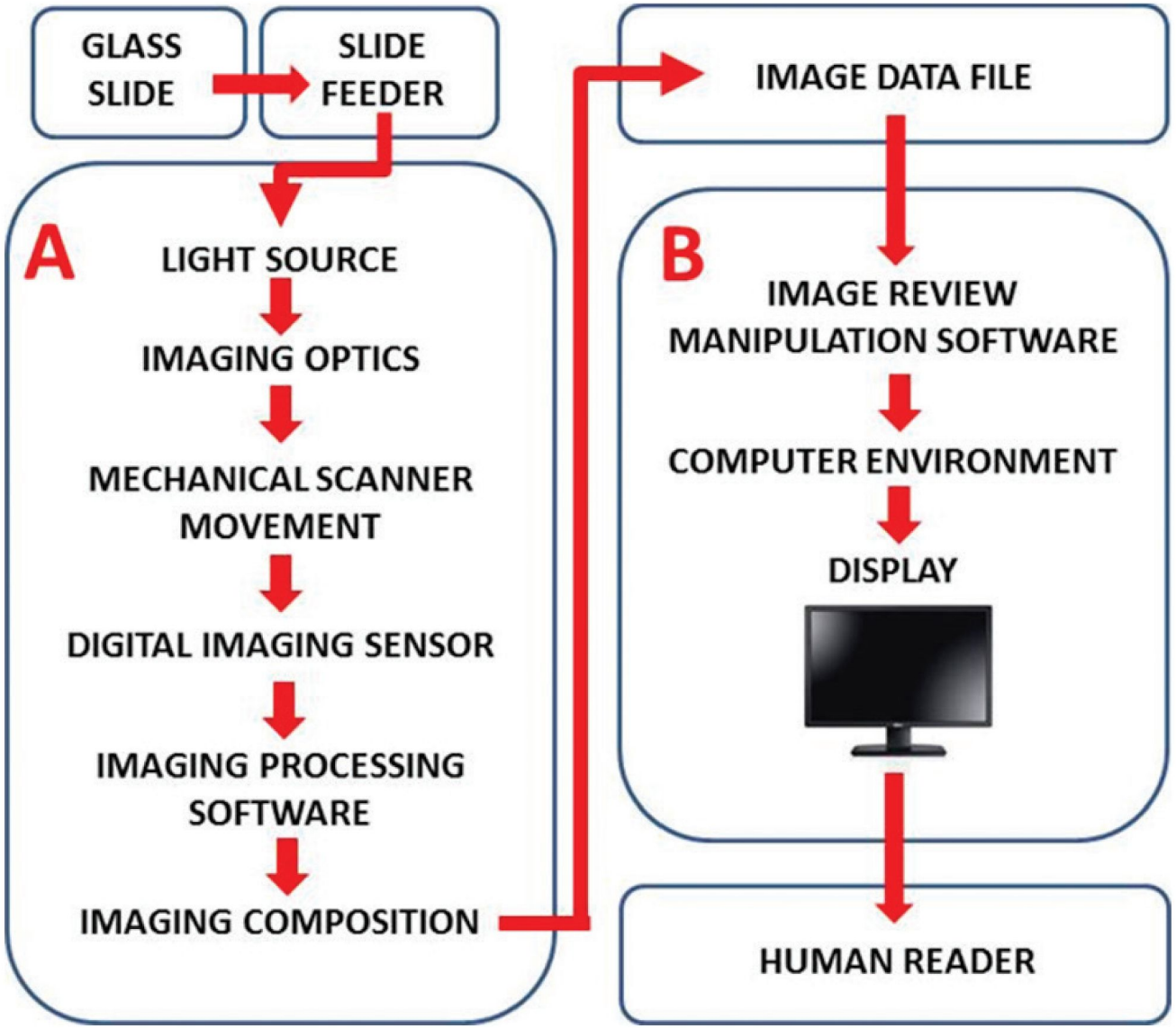


Figure 1: Overview of a digital pathology system. A digital pathology system is composed of two subsystems: (A) Image acquisition and (B) workstation environment. The arrows depict the pixel data pathway[15]

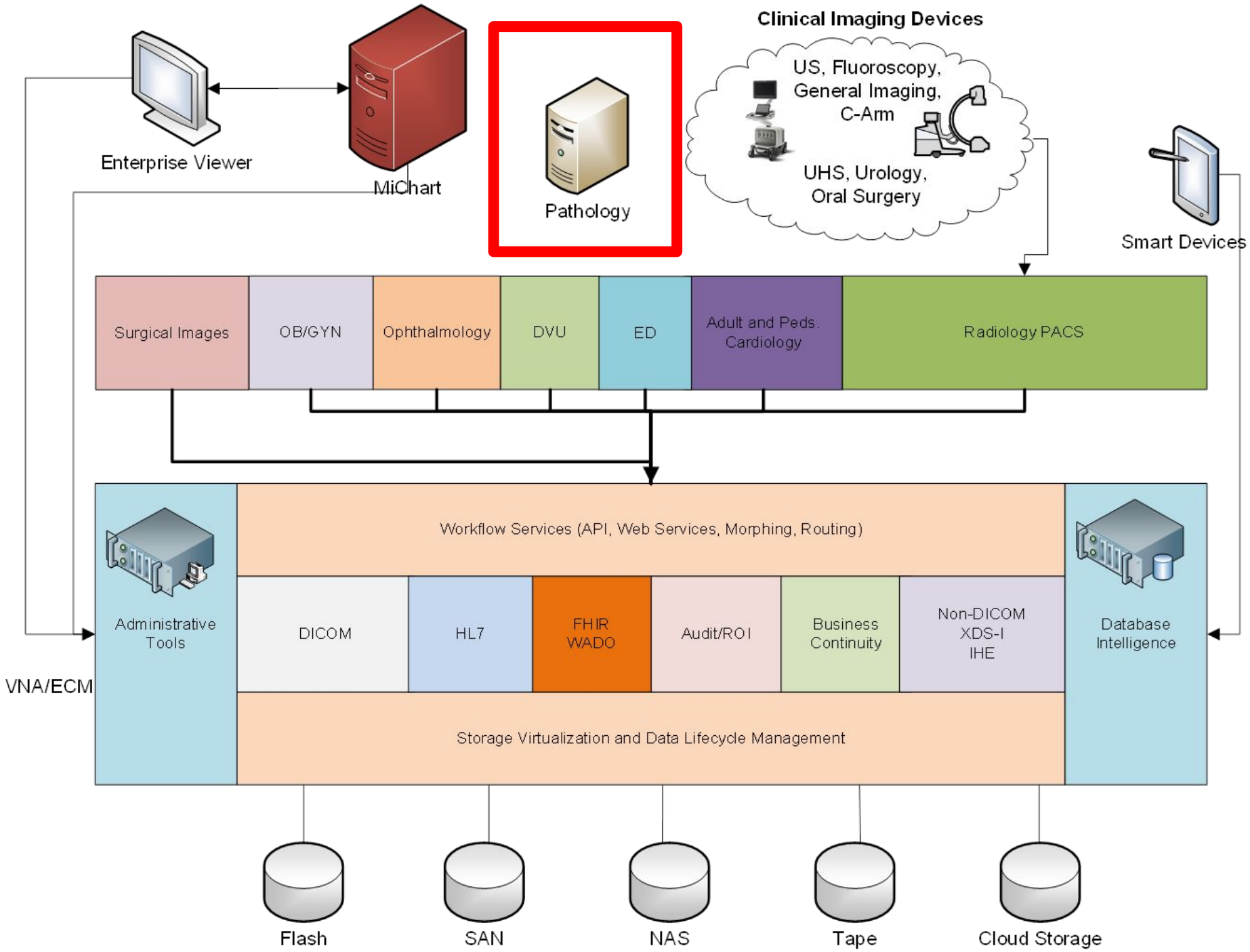
Pathology Image Repository

- NOT included in the FDA pixel data pathway
- Technically can be separate from your image management system
- Current State
  - Typically included with your whole slide imaging system
  - Typically tied to your image management system
  - Variable degrees of DICOM compliance

- Black box to your enterprise...

Academic Clinical Imaging

Do you see Pathology?



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Understanding Workflow

- For computational pathology, workflow begins BEFORE the specimen is acquired!!
  - Increased available data = improved, more efficient specimen management

- Key → CONTEXTUALLY-DRIVEN pathology processes!!
  - Patient, specimen, and clinical information drive the workflow
    - Prior clinical history, imaging findings,biopsy results, etc.
    - Future patient encounters, follow-up, procedures etc.
    - Specimen part type, tissue type, gross examination findings, etc.

Sign out Workflow: Before Computational Pathology

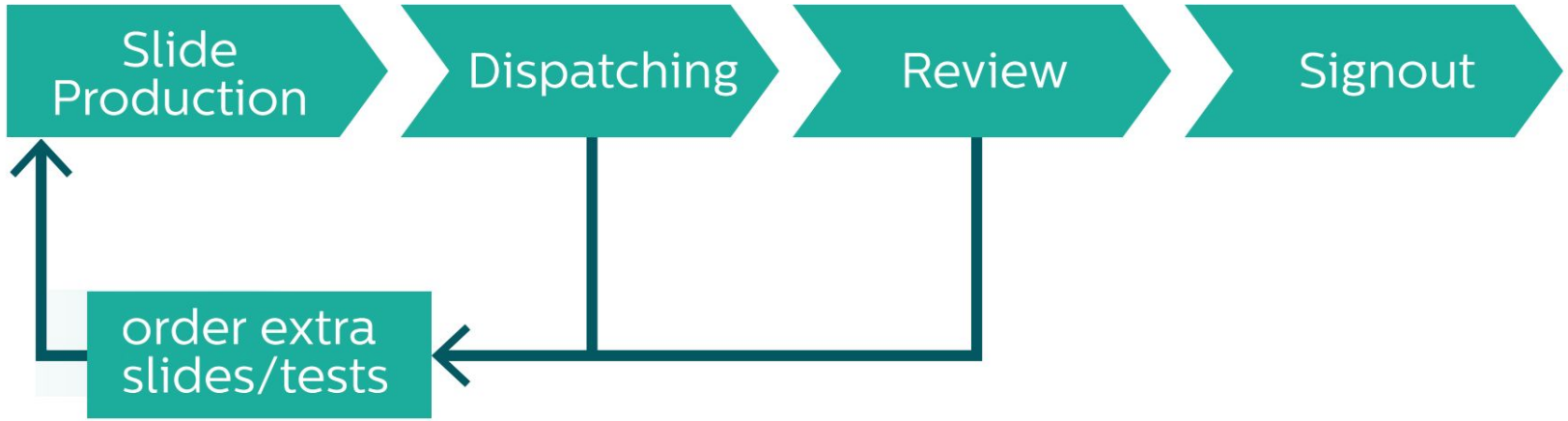

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Figure modified from: Hulsken, B. Seamless Computation Pathology (White Paper). 2018. Philips Digital Pathology

Sign out Workflow: After Computational Pathology

Computation Pathology AUGMENTS pathologist signout workflow!!

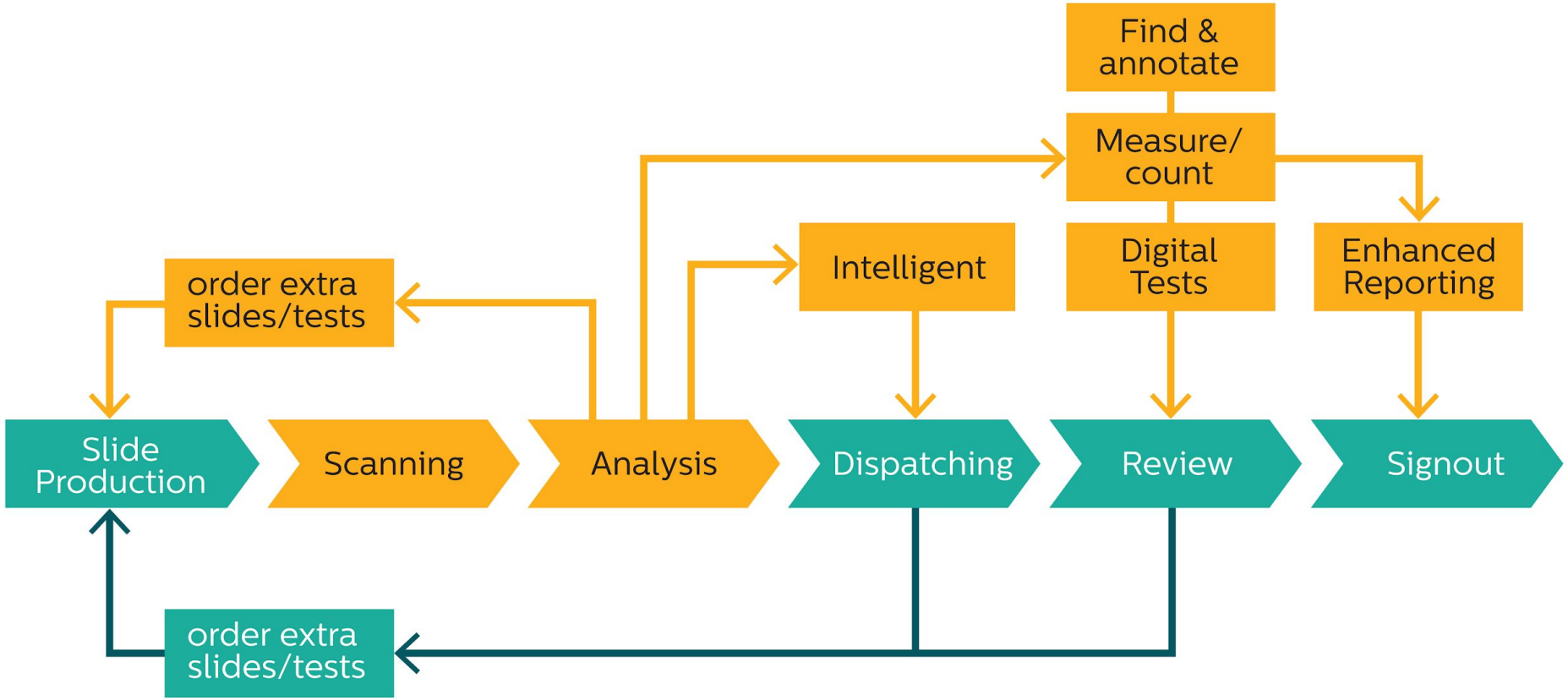

Figure from: Hulsken, B. Seamless Computation Pathology (White Paper). 2018. Philips Digital Pathology

Computational Pathology Platform

- ADDITIONAL system that interacts with your:
  - AP LIS and EHR
  - Whole slide imaging system (scanner, IMS, viewer)
  - Tracking and routing system (if separate)

- Uses multiple machine learning algorithms to provide image analysis for specific pathology use cases
- Group of integrated apps, working together to provide a seamless computational experience for the pathologist
  - Can be an on-premises or cloud based solution

Computational Pathology Platform - Vendor Example

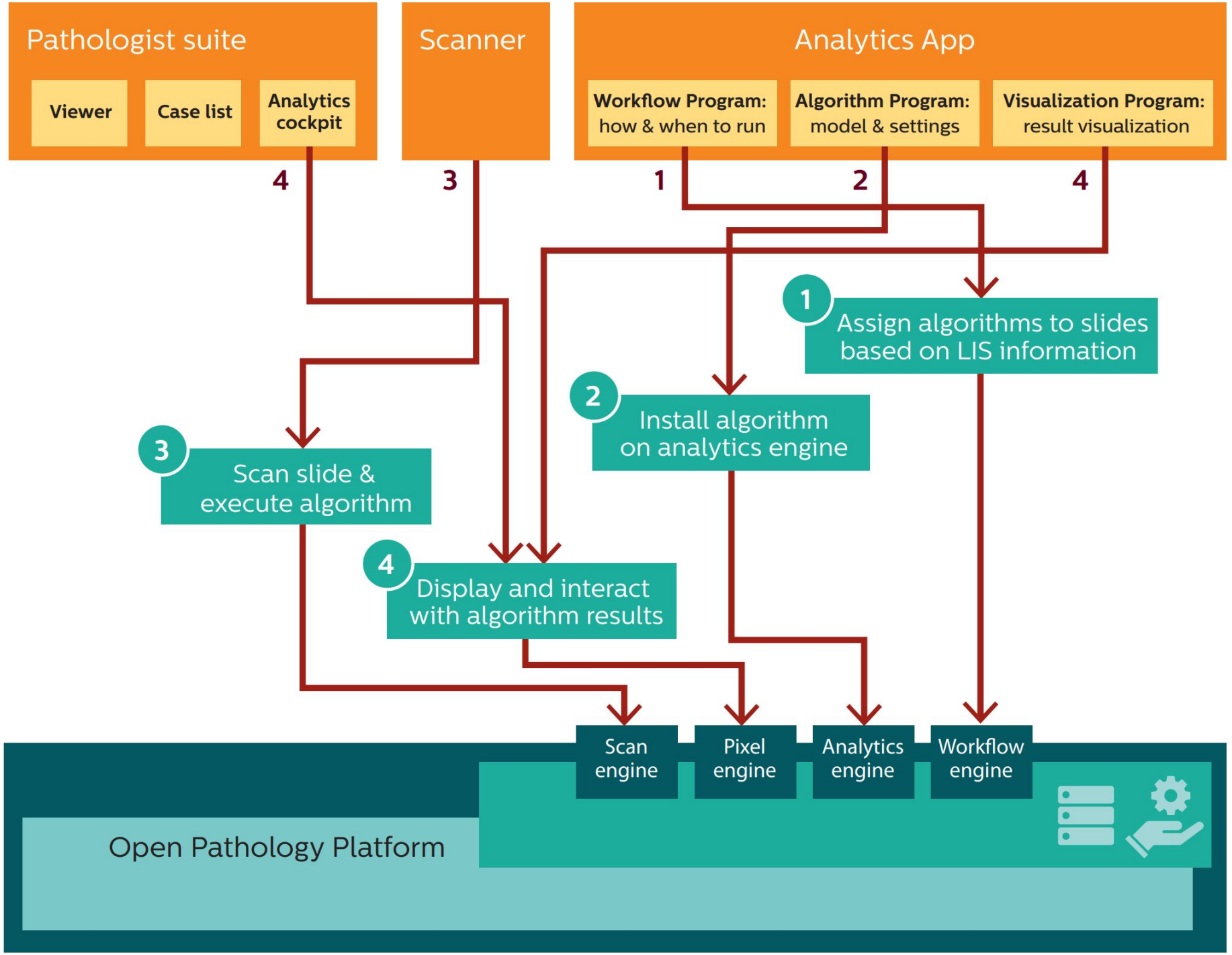

Figure from: Hulsken, B. Seamless Computation Pathology (White Paper). 2018. Philips Digital Pathology

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Parallel Computational Tasks

- Many “common” pathologist-based tasks require simultaneous, parallel processing of computational tasks

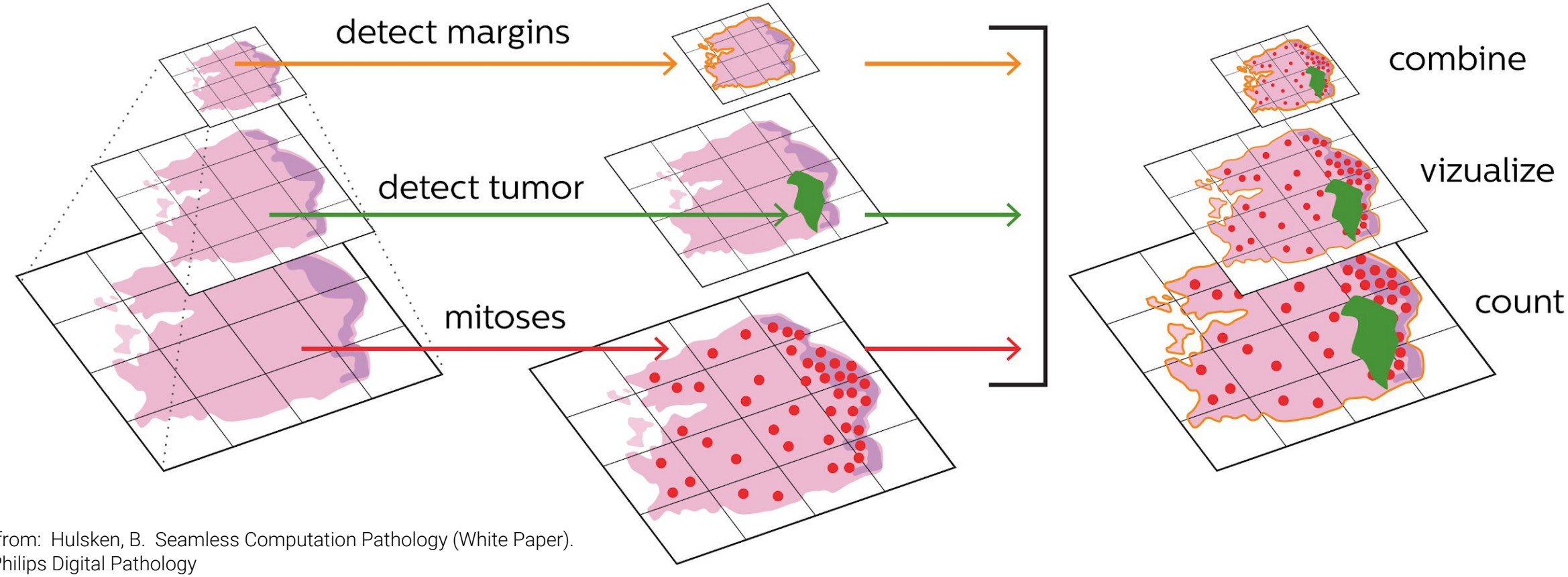


Figure from: Hulsken, B. Seamless Computation Pathology (White Paper). 2018. Philips Digital Pathology

Parallel Processing is KEY!

- Scalable, GPU-based image processing with multiple nodes needed to fulfill pathologist computational requests

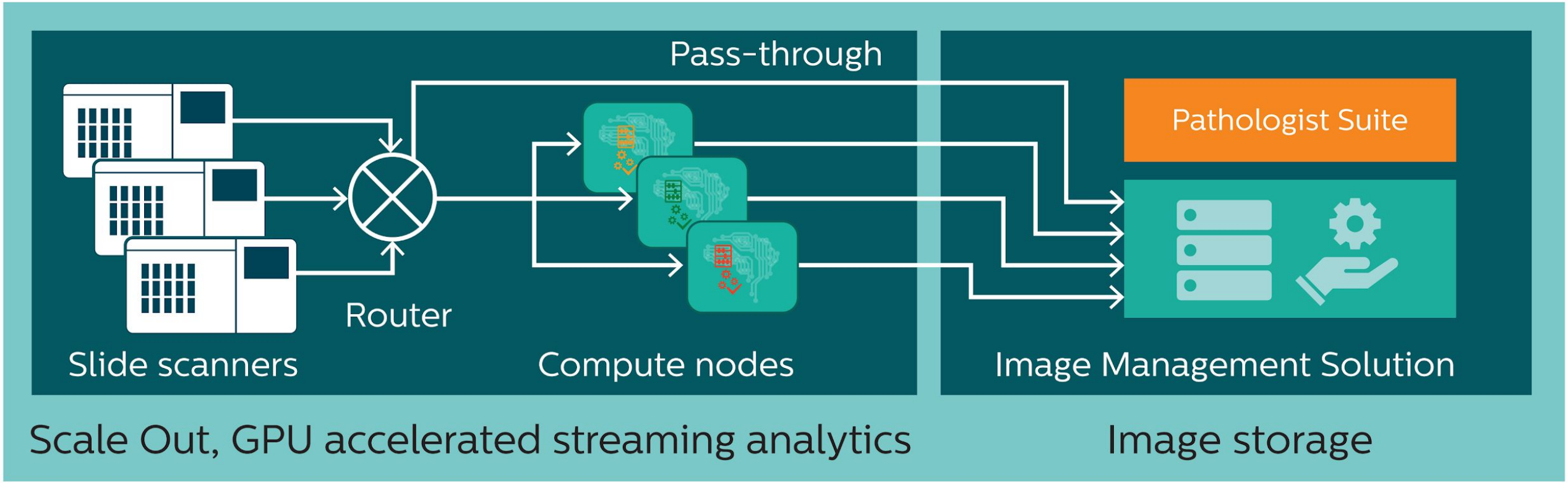
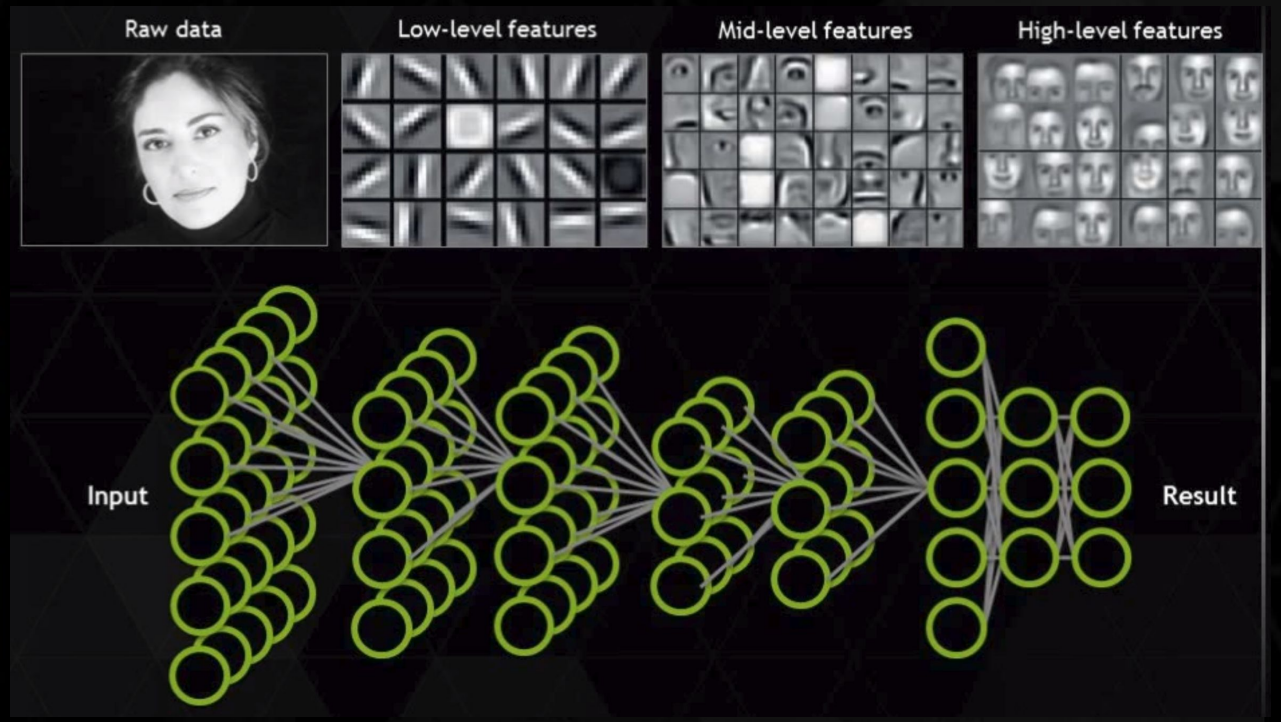


Figure from: Hulsken, B. Seamless Computation Pathology (White Paper). 2018. Philips Digital Pathology

WHY ARE GPUs GOOD FOR DEEP LEARNING?

	Neural Networks	GPUs
Inherently Parallel	✓	✓
Matrix Operations	✓	✓
FLOPS	✓	✓
Bandwidth	✓	✓



GPUs deliver --

- *same or better prediction accuracy*
- *faster results*
- *smaller footprint*
- *lower power*
- *lower cost*

GPUS MAKE DEEP LEARNING ACCESSIBLE

Deep learning with COTS HPC systems

A. Coates, B. Huval, T. Wang, D. Wu, A. Ng, B. Catanzaro

ICML 2013

"Now You Can Build Google's $1M Artificial Brain on the Cheap"

WIRED

GOOGLE DATACENTER

1,000 CPU Servers
2,000 CPUs • 16,000 cores

600 kWatts
$5,000,000

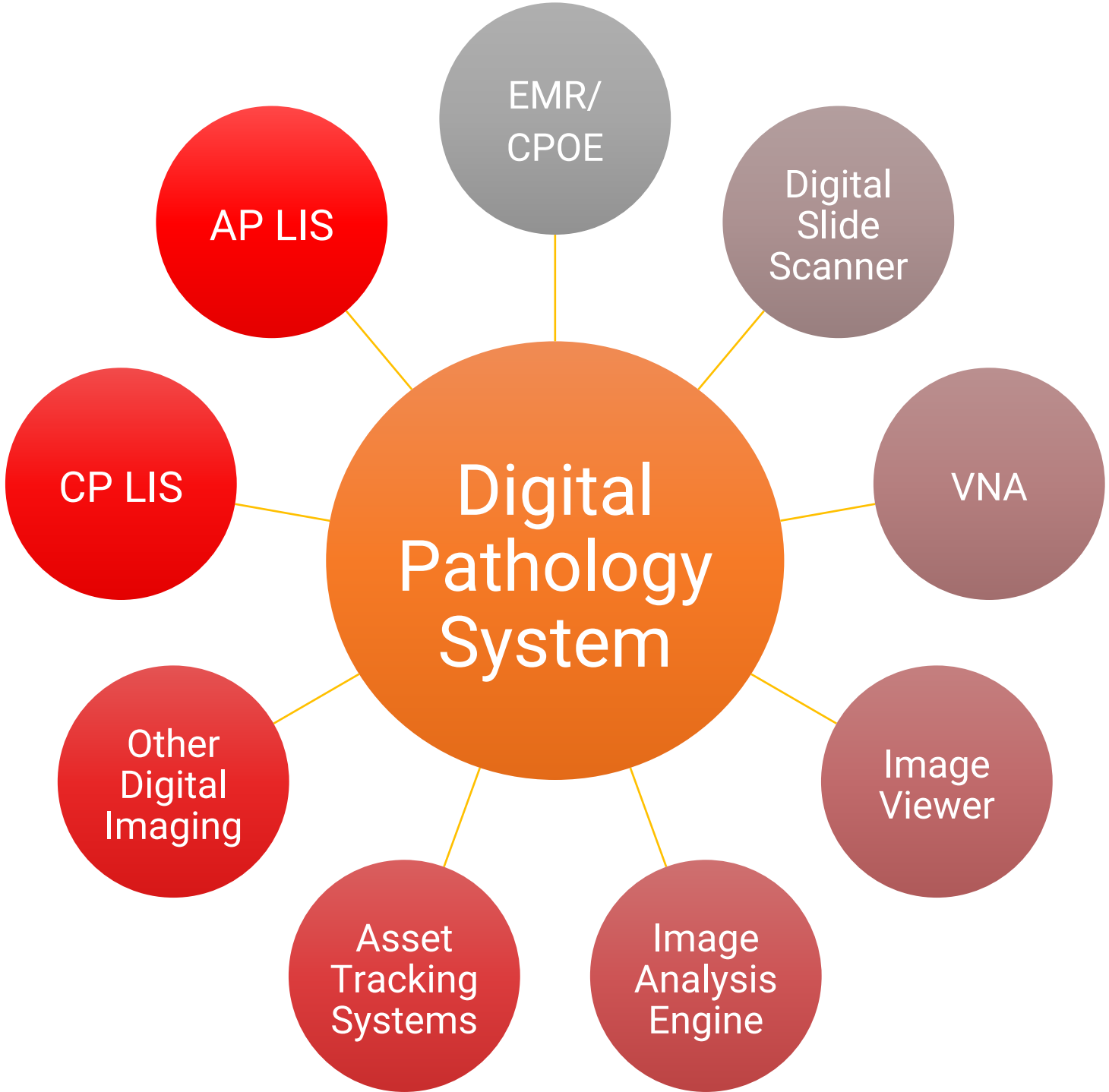
STANFORD AI LAB

3 GPU-Accelerated Servers
12 GPUs • 18,432 cores

4 kWatts
$33,000

https://www.youtube.com/watch?v=6eBpjEdgSm0&t=1600s

Connected Systems are a MUST



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Computational Pathology - Cost and Barriers to Adoption

Primary Cost Considerations for Computational Pathology

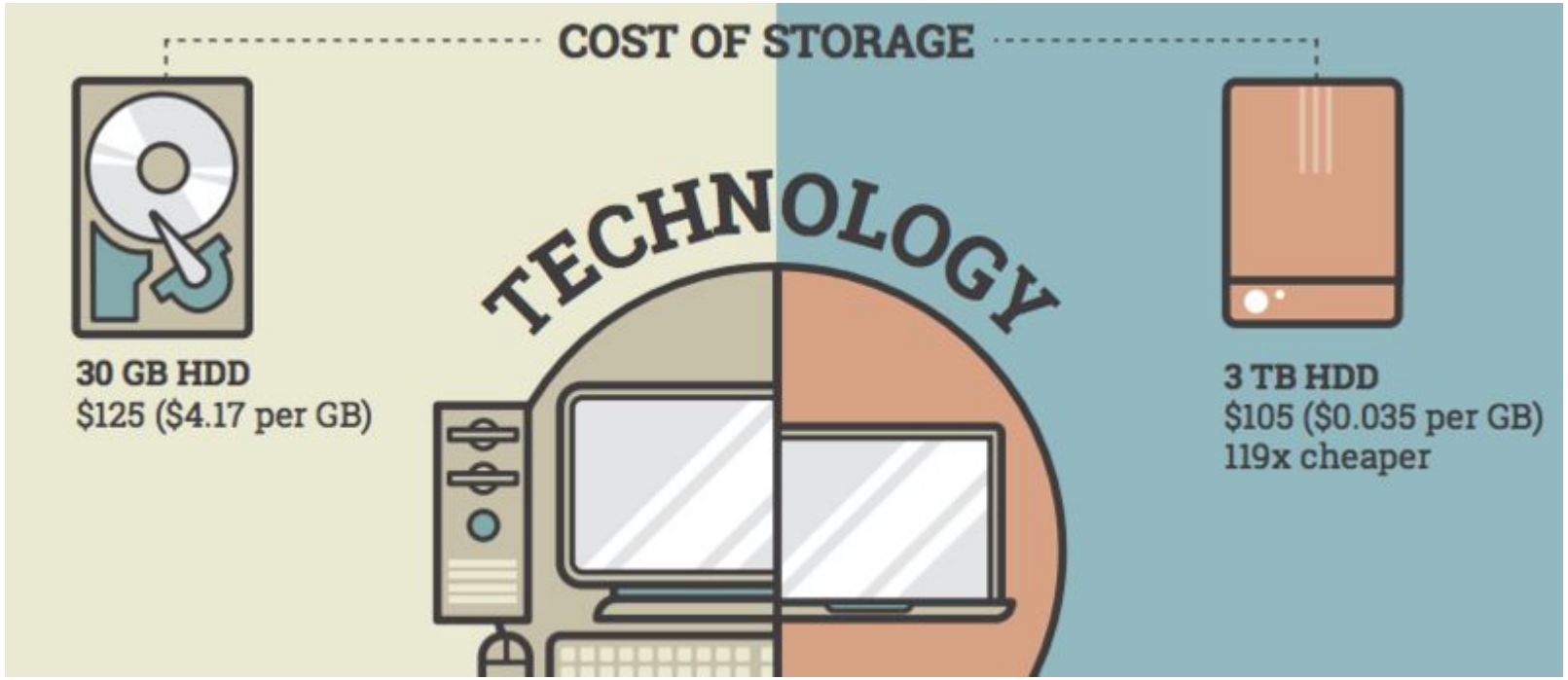
- Whole slide imaging system costs
- Digital pathology storage costs
- Vendor computational pathology platforms
- Additional servers, licenses, maintenance
- Additional FTEs

DP - Storage as the Limiting Factor

Symbol	Name	Factor
Y	yotta	10^{24}
Z	zetta	10^{21}
E	exa	10^{18}
P	peta	10^{15}
T	tera	10^{12}
G	giga	10^{9}
M	mega	10^{6}

- Current estimates with FDA-cleared system:
  - For primary dx: ~1.25 GB/slide
- Michigan Medicine creates ~11,000 slides per week
  - Annual slide volume ~570,000
  - Average estimated storage for clinical use ~715,000 GB = 715 TB
  - Requires production system redundancy…so yotta, yotta, yotta…
- GRAND TOTAL PER YEAR: ~1.43 PB required

Storage Costs are the Lowest Ever!



30 GB in 2000 → $125

3TB in 2015 → $105

350 TB in 2030 → $100-$125 ????

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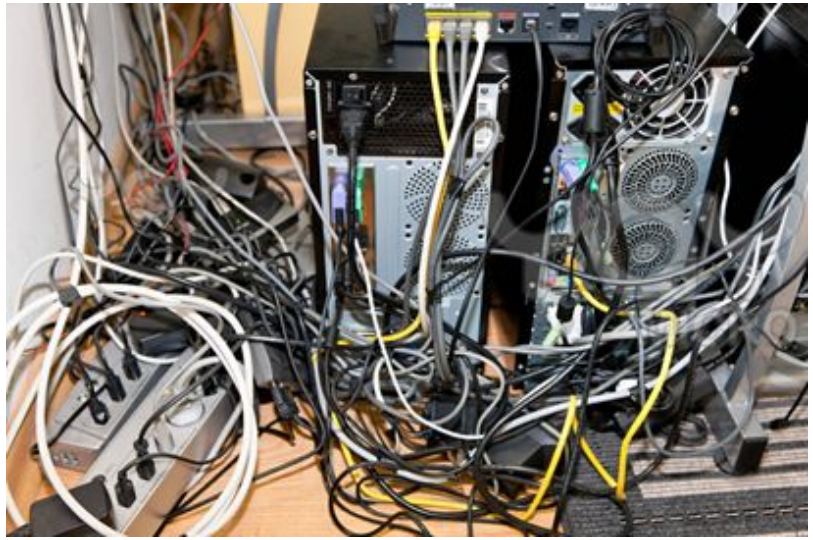
Image from : https://community.spiceworks.com/topic/1993877-future-tech-storage-capacity-in-the-year-2030-and-beyond

The Michigan Medicine Example - Costs

- Minimally:
  - Assuming $0.025/GB currently
  - 1,430,000 GB x $0.025/GB = $37,500/year

- CHEAP!!!
  - Except…that is assuming I am buying my storage from Costco…
  - And setting it up in my office???



Data Center Storage Costs

- Data center costs include:
  - Building space
  - Cooling
  - Power (UPS + Generator)
  - Fire Suppression
  - Security
  - Equipment maintenance (hard drives/servers ~5 year lifespan)
  - FTE maintenance (need people to run the data center, 24x7x365)
  - Networking (Can I have a 10Gb/s line please??)

Actual Storage Costs are MUCH MORE

- Low estimates of cost in a data center are ~$0.15 - $0.25/GB (industry estimate)
  - ~$215,000 to $375,000 per year AT A MINIMUM
  - Not so cheap anymore
- Networking speeds from data center may need upgrading
  - Also need to look at physical cabling in building where signout will occur
  - Laying fiber ain't cheap either…

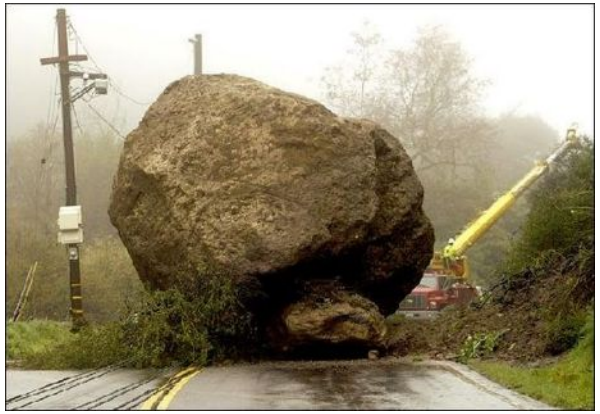
Additional FTEs cost money!!

- Anyone else going through a hiring slowdown/pause/freeze?
- FTEs recommended:
  - Computational pathologist / informaticist
  - Additional techs to run the actual slide scanning processes
    - Slide loading, WSI device maintenance
  - Programmers
  - Business analysts to support changes in LIS
  - Business analysts to support digital pathology and computational pathology systems
  - More I probably forgot...

Common Barriers to Adoption

- Cost (as previously discussed)
- The FDA...yet again
- Lack of billing codes for Computational Pathology
- Complexity of the practice of pathology
- Computational Pathology will REPLACE pathologists

Digital Pathology and the FDA



- A long, somewhat rocky road
  - Multi-year timeline…
  - Plagued by idea of the FDA trying to “back-regulate” into surgical pathology
  - WSI as Class 2 (please!) → Class 3 (NO!!!) → de novo (we can live with that)
  - FDA and LDTs…
- Kudos to the DPA, DP vendors, and pathology (WSI) experts
  - First WSI system cleared April 2017

Computational Pathology the FDA

- Vendors are JUST BEGINNING to look at the FDA process for getting algorithms approved for clinical use
  - However…

FDA Statement

Statement from FDA Commissioner Scott Gottlieb, M.D., on advancing new digital health policies to encourage innovation, bring efficiency and modernization to regulation

For Immediate Release December 7, 2017

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm587890.htm

Draft Guidance: Clinical and Patient Decision Support Software

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm587890.htm

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- **Outlines FDA approach to clinical decision support software (CDS)**
- "We want to **encourage developers to create, adapt and expand the functionalities of their software to aid providers** in diagnosing and treating old and new medical maladies."

- **Intended to make clear what types of CDS are no longer defined as a medical device**→ i.e. not regulated by FDA
  - Generally - **CDS allowing provider to independently review the basis for the recommendations are excluded**
  - Example - software that suggests a provider order liver function tests before starting statin medication, consistent with clinical guidelines and approved drug labeling

Draft Guidance: Clinical and Patient Decision Support Software

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm587890.htm

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"**However**, **the FDA will continue to enforce oversight of software programs that are intended to process or analyze medical images**, signals from in vitro diagnostic devices or patterns acquired from a processor like an electrocardiogram that use analytical functionalities to make treatment recommendations, **as these remain medical devices under the Cures Act**."

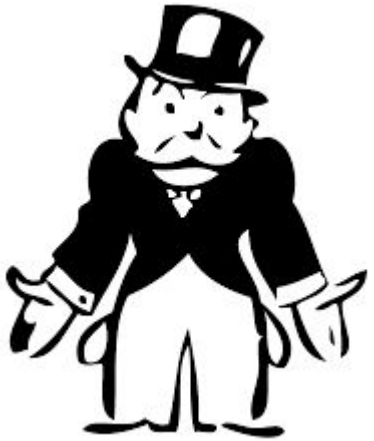
The FDA - Good News & Bad News

- The good news:
  - Computational pathology **is not called out** in the list of examples of CDS and other software functions for Health Care Professionals that remain devices

- The bad news:
  - Computational pathology **is composed of software programs that are intended to process or analyze medical images**... and thus, we start another journey with the FDA

https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM587819.pdf

Billing Codes for Computational Pathology



- There aren’t any yet
- If you can’t bill for it, then how do we pay for it?
  - No natural source of income to offset costs
  - Improving efficiency can only goes so far...
- Future efforts for computational pathology MUST include a way to bill for it to be successful

Pathology is COMPLEX!!

- Our initial use case - prostate biopsies
  - Single tissue type
  - Binary diagnosis type (cancer vs. no cancer)
  - Easy synoptic reporting with (generally) standardized criteria
  - Few exceptions to the rule
- Many thousands of additional use cases exist!
  - Varying degree of complexity
  - Multiple deep learning opportunities per use case
  - New use cases constantly appearing

Computational Pathology Replacing Pathologists??

- Common MISFOUNDED fear amongst pathologists
- Designed to AUGMENT and IMPROVE diagnostic care provided by pathologists, not replace their care

- Pathologists represent thousands to millions of hours of collective pathology expertise…
- Immense breadth of the field (see Dr. Fuch's slides)

Adding Value to Pathology

Table 1: Operational definition of "Value added"

Is defined broadly by the following
Cost savings
Time savings
Improved quality of service
Can be measured along several axes
Patient care
Educational activities
Research
Things that are not intrinsically value added
Novelty
Technical feasibility

The Digital Pathology Hype Cycle

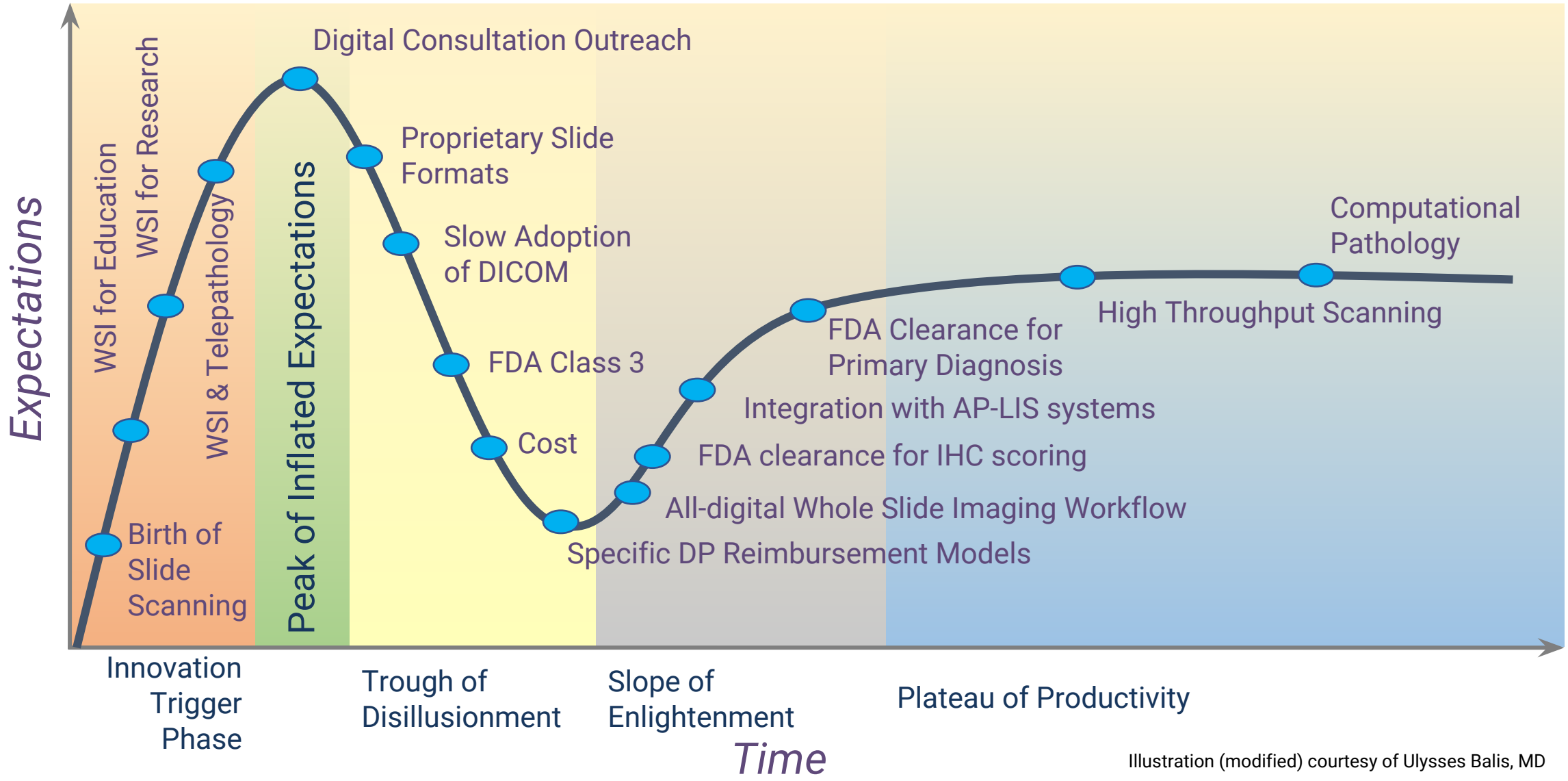


Illustration (modified) courtesy of Ulysses Balis, MD

QUESTIONS?

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Association for Pathology Informatics

https://pathologyinformatics.org

Digital Pathology Association

https://digitalpathologyassociation.org

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