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Accelerated Genomics Analysis with NVIDIA Parabricks & RAPIDS





Agenda

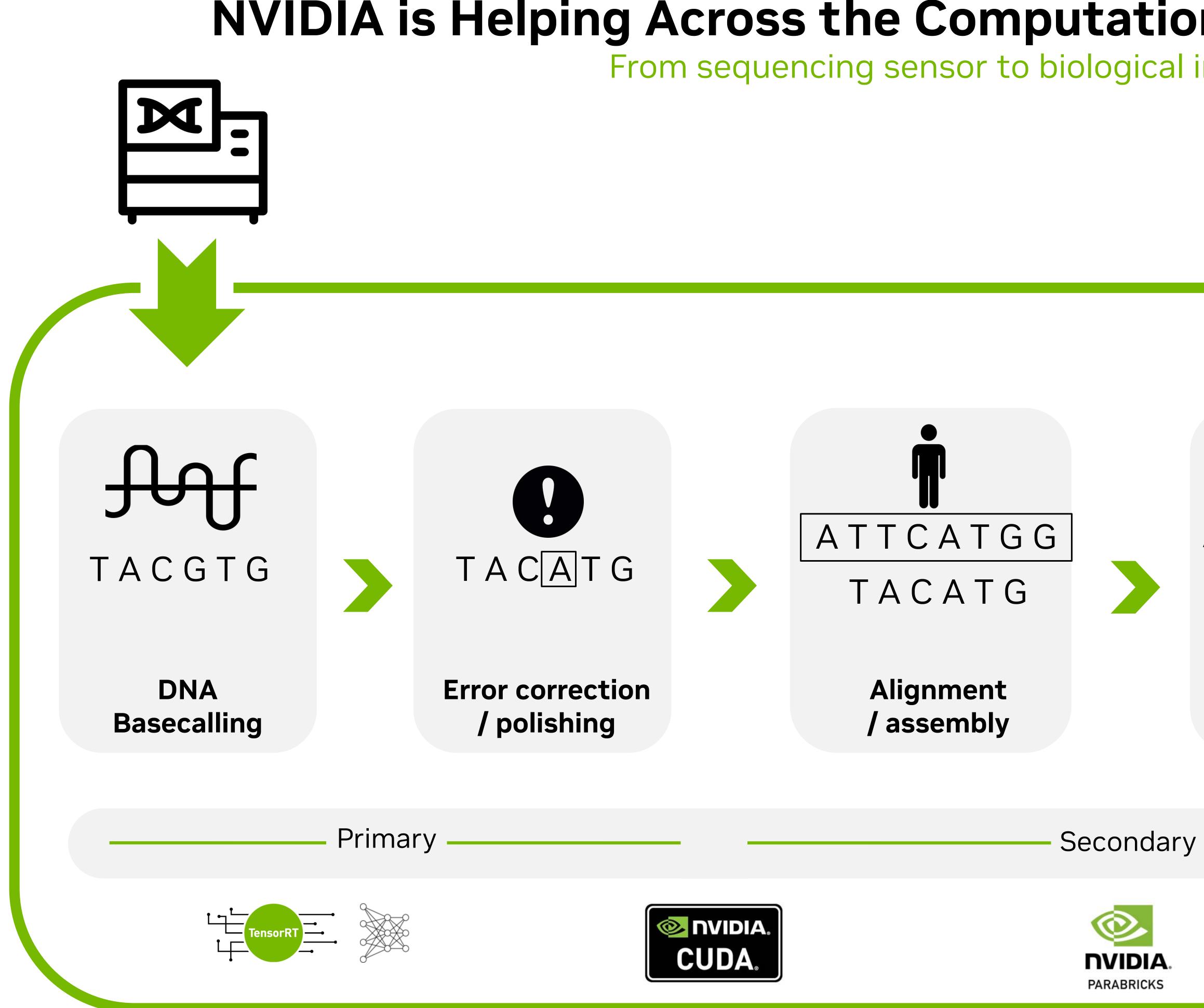
NVIDIA Parabricks for secondary analysis RAPIDS for tertiary analysis, single-cell RNAseq analysis and spacial genomics



Agenda

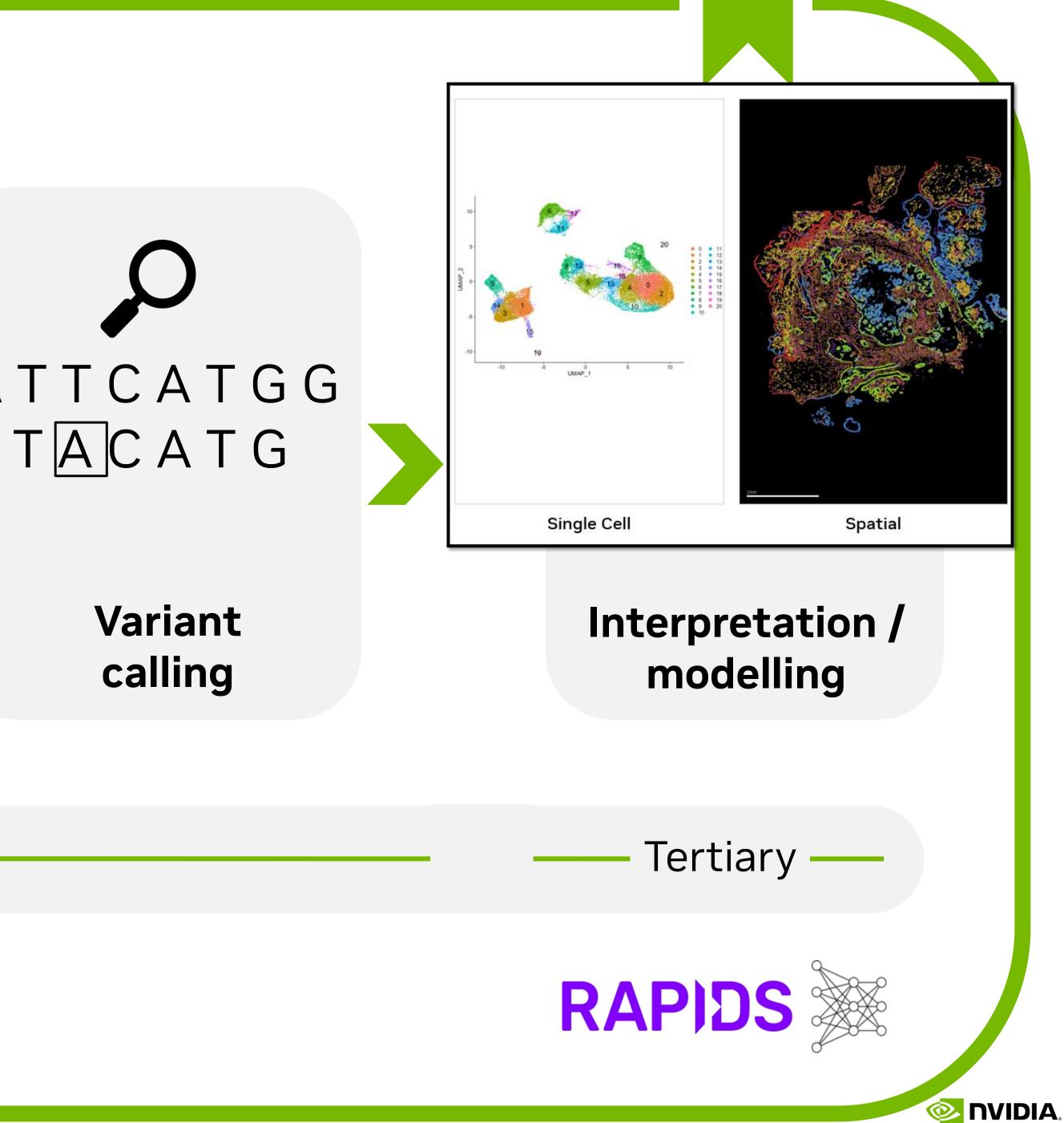
NVIDIA Parabricks for secondary analysis RAPIDS for tertiary analysis, single-cell RNAseq analysis and spacial genomics





NVIDIA is Helping Across the Computational Genomics Workflow From sequencing sensor to biological insights

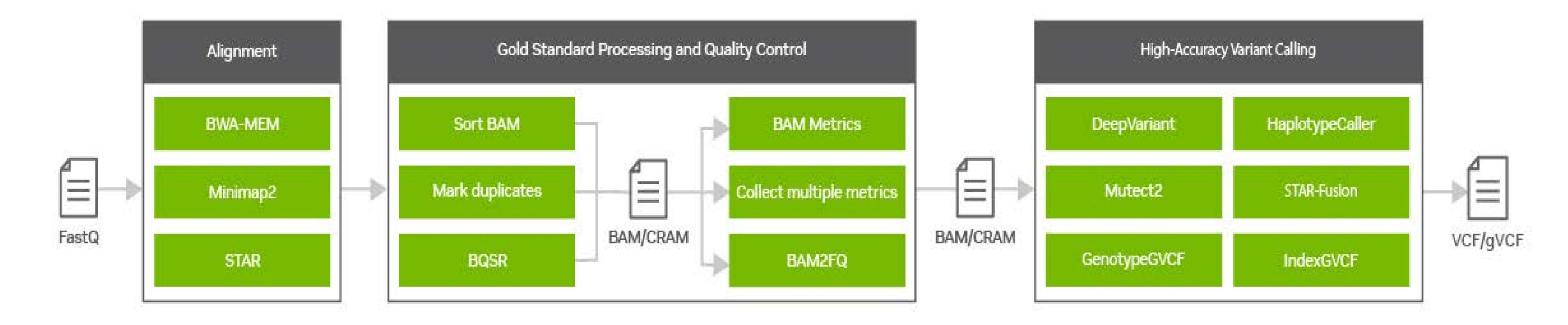


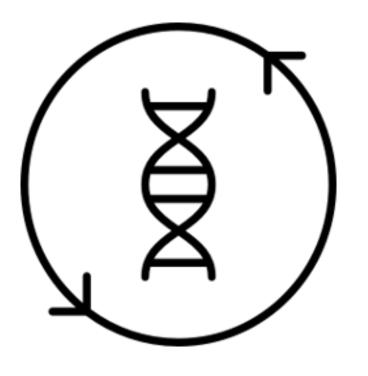






NVIDIA Parabricks for Alignment & Variant Calling Speed, Scale, Accuracy





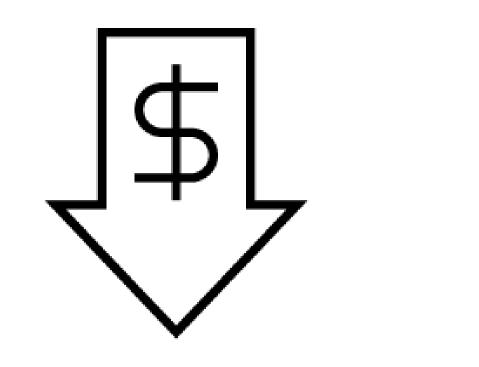
Universal Analysis

Industry-standard tools for all major sequencers, ported to GPU

Up to 100x faster for WGS compared to CPU-only



Up to 100x Acceleration



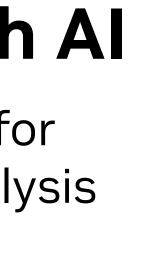
Up to 50% Lower Cost

Up to 50% lower compute cost for WGS compared to CPU-only



Higher Accuracy with AI

The power of deep learning for customized high accuracy analysis









Population Genomics

Key Applications of NVIDIA Parabricks Accelerated and Deep Learning Genomic Analysis

Cancer Genomics



RNA Sequencing

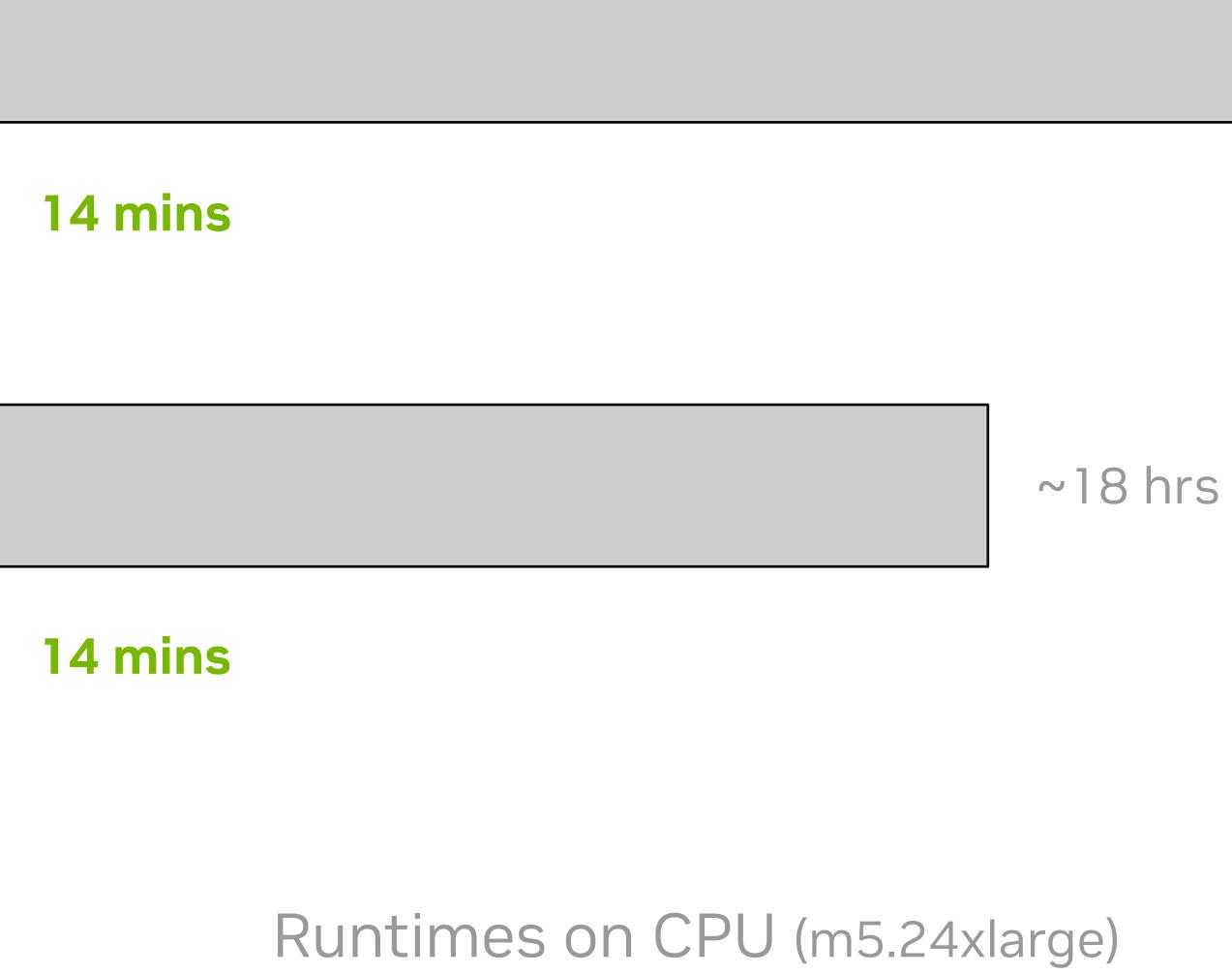


End-to-end germline sample analysis with industry-standard tools in under 15 mins on the new NVIDIA H100 GPUs

Germline GATK (FQ2BAM + HaplotypeCaller)

> Germline DeepVariant (FQ2BAM + DeepVariant)

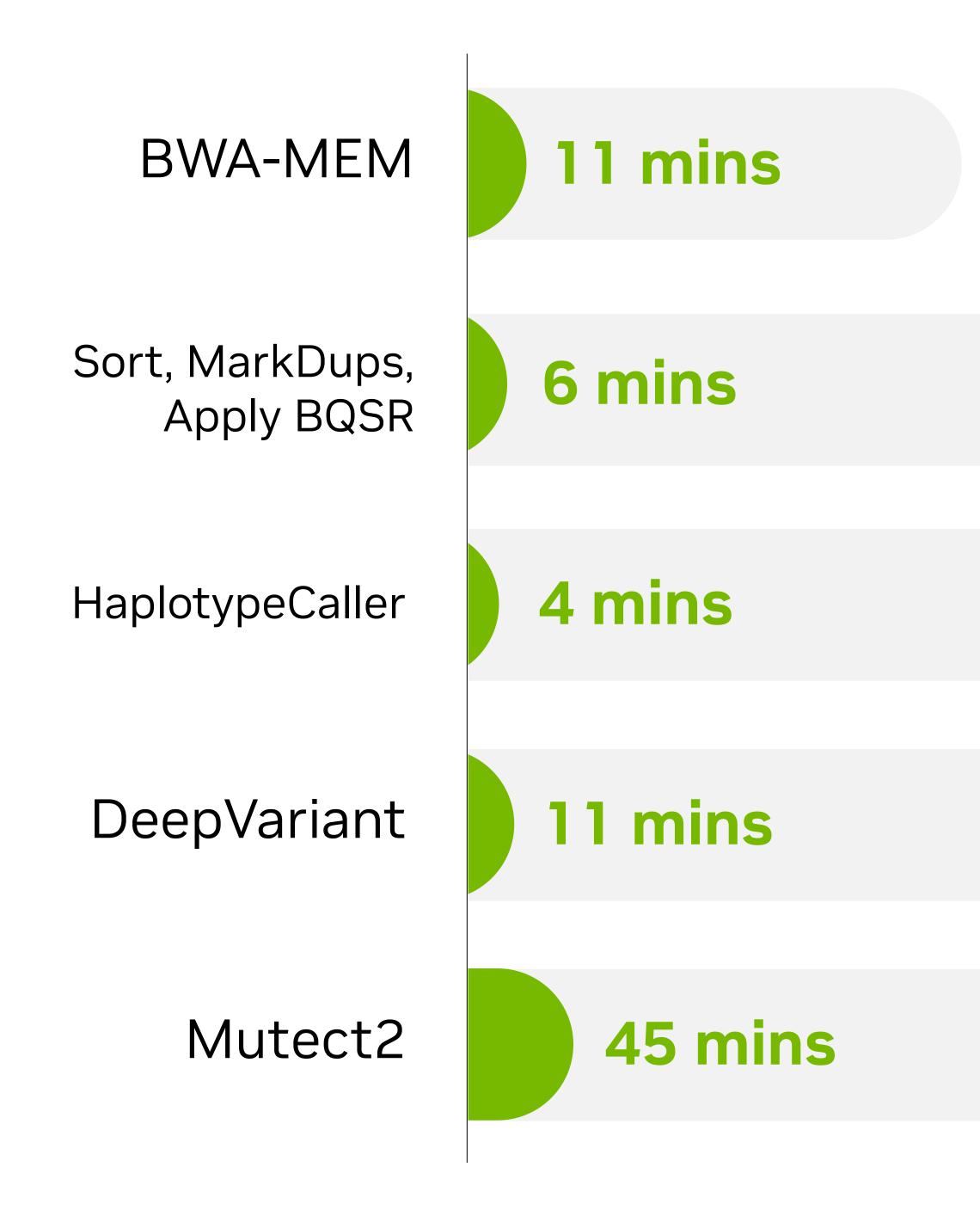
Higher Speed From hours to minutes



Runtimes on NVIDIA GPU (8xH100)

~30 hrs





v3.8 Benchmarks

Dataset: HG002 30x WGS, except Mutect2 on SEQC2 50x WGS CPU: m5.24xlarge; GPU: 8xA100, except DeepVariant & Mutect2 on 8xV100

Up to 80x Acceleration Gold-standard results, faster

~4 hrs

~9 hrs

~16 hrs





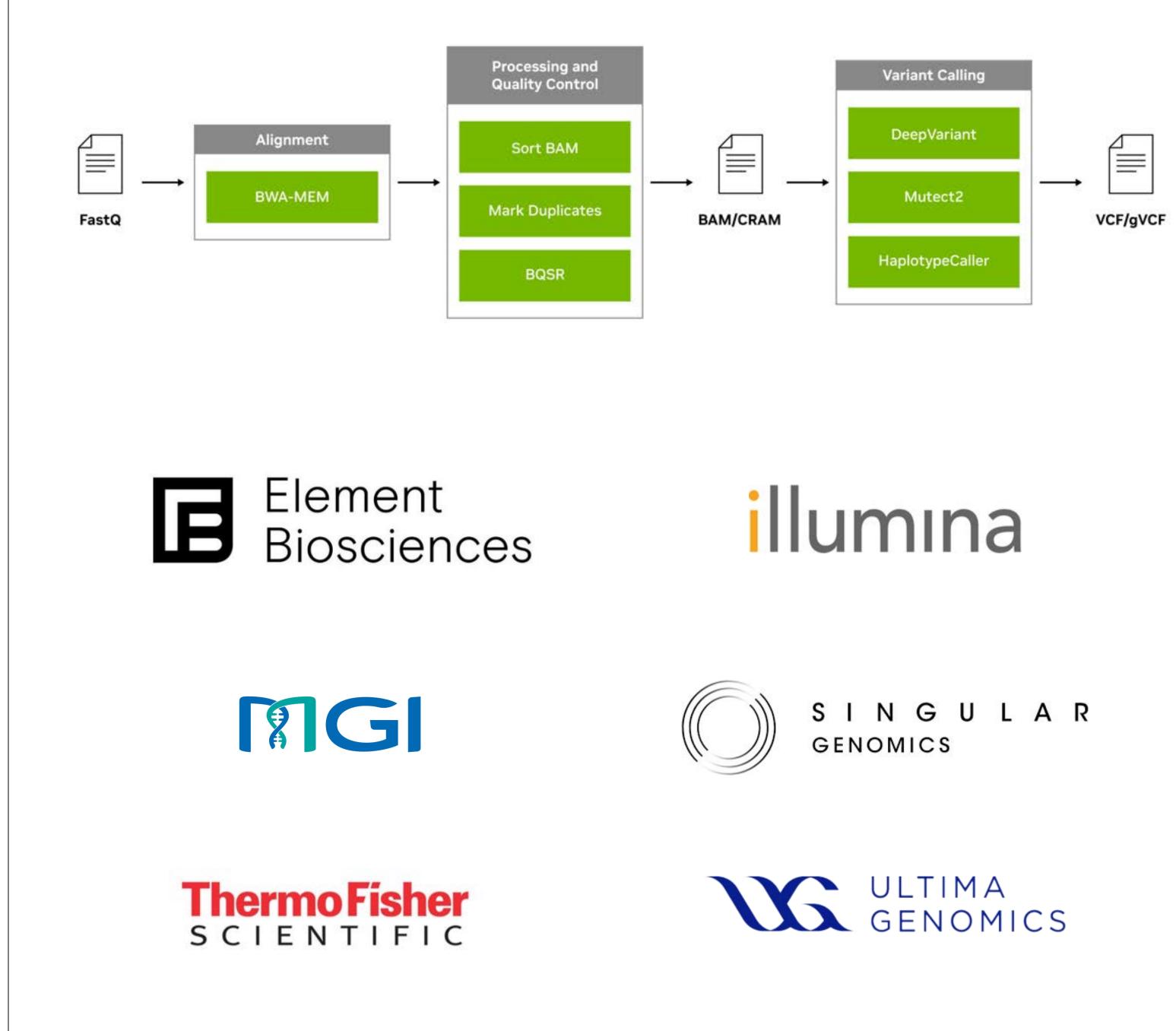


Runtimes on CPU Runtimes on NVIDIA GPU

~31 hrs



Short-Read



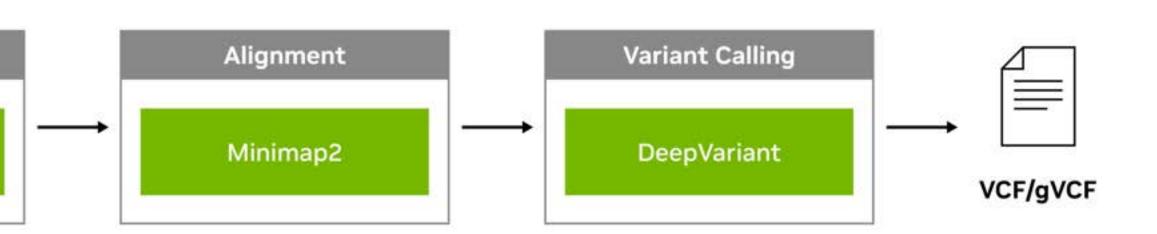
A Universal Analysis Solution

Basecalling/Polishing Dorado DeepConsensus





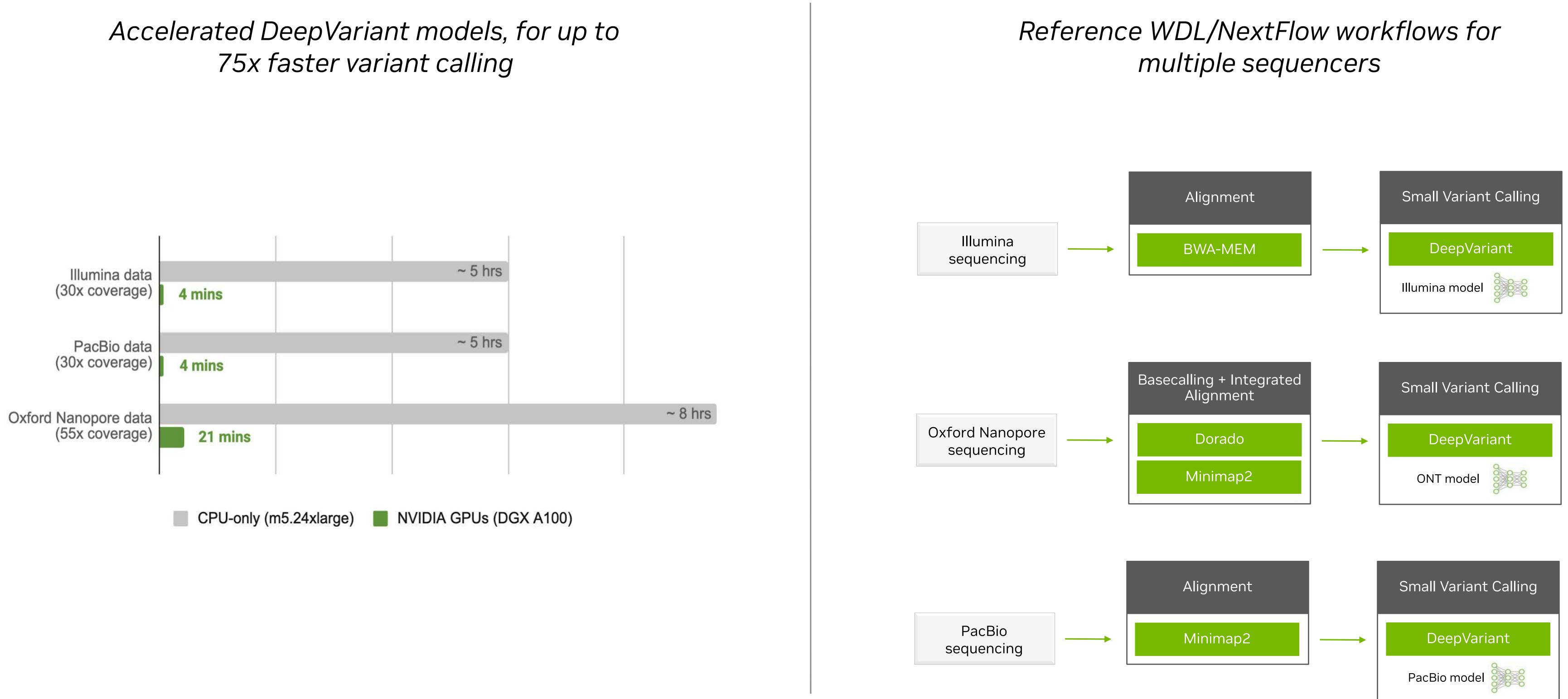
Long-Read











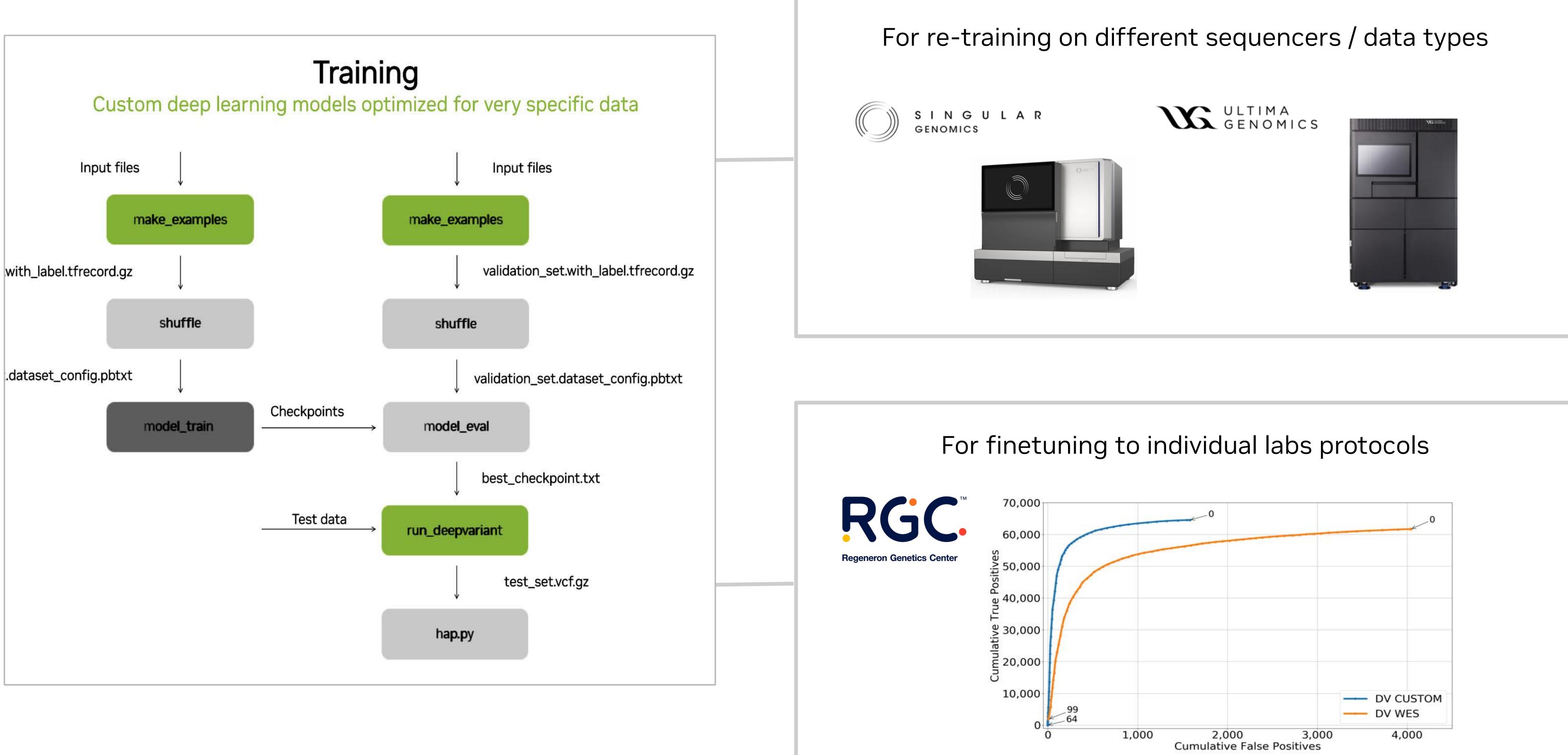
Universal Sequencing Analysis

The only hardware-accelerated solution for multiple sequencers



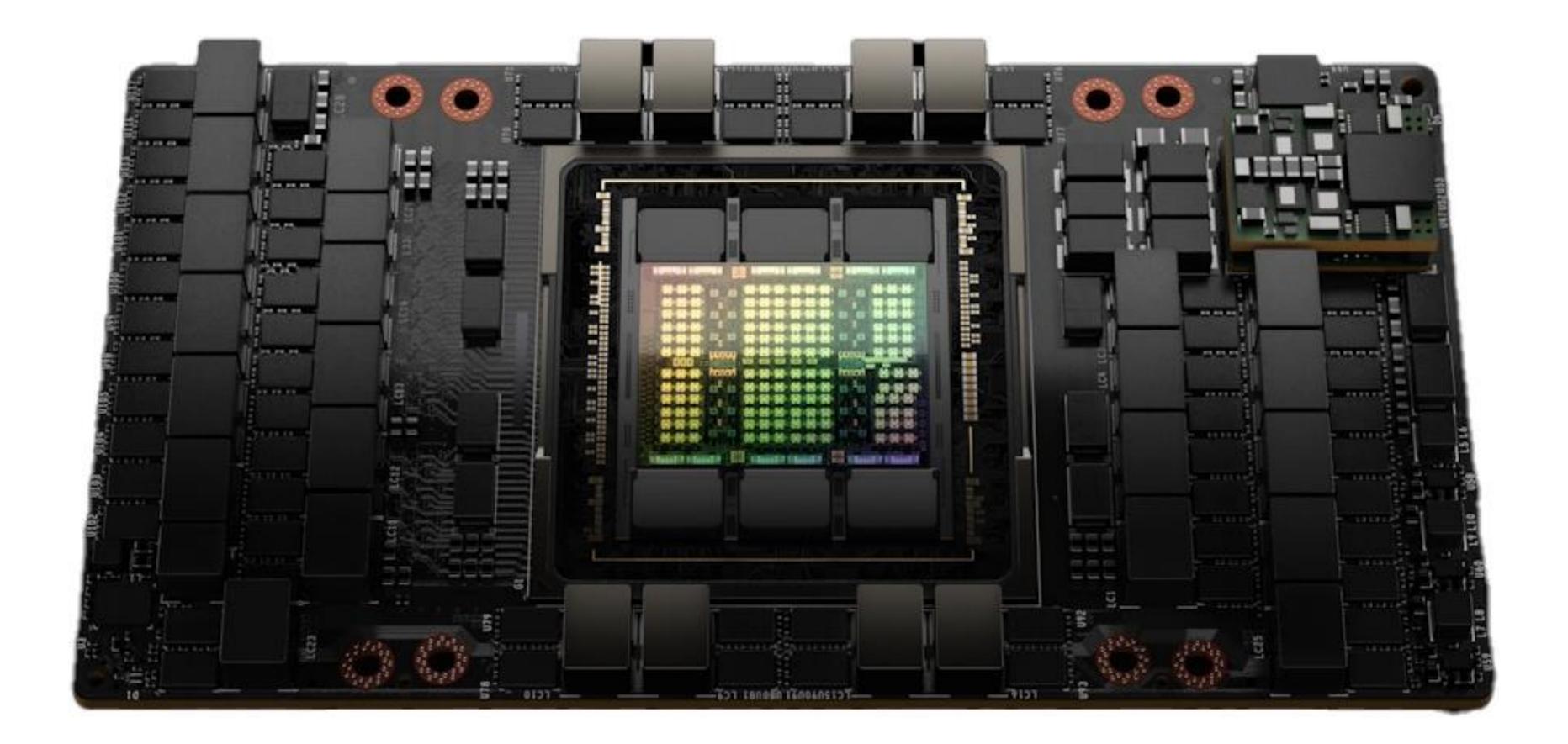


Parabricks DeepVariant Training Framework Easily Train a Custom Model for Optimal Accuracy





NVIDIA GPUs for Secondary Analysis The H100 Dynamic Programming Core



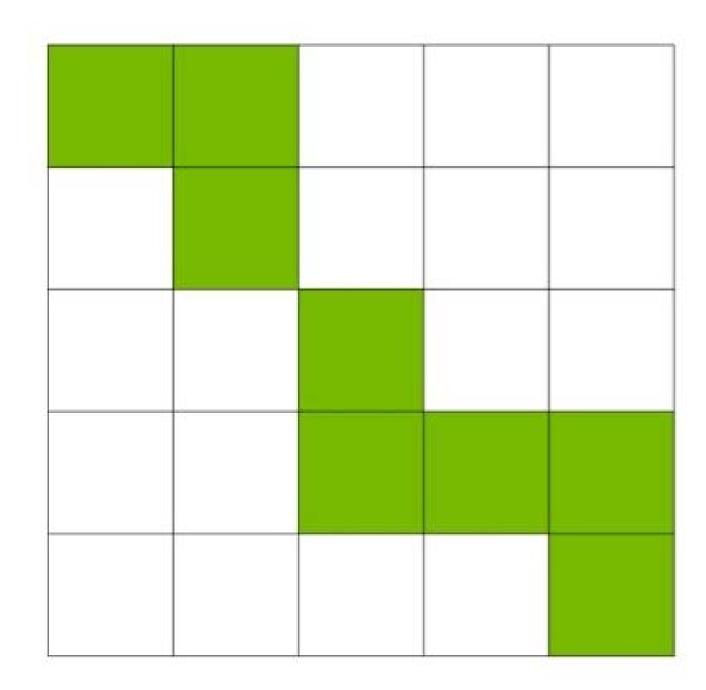
Boosting Dynamic Programming Performance Using NVIDIA Hopper GPU DPX Instructions

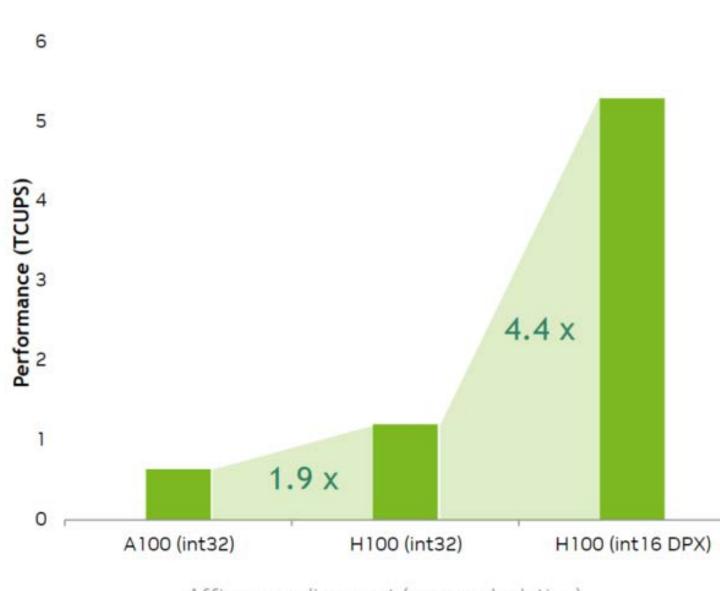
Dynamic Programming

Exponential to polynomial time problem solving

Supercharged Smith-Waterman

35x acceleration over CPU 7x acceleration over Ampere





Affine gap alignment (score calculation) Weights used from BWA.

Data: HG002 (NA24385) paired-end protocol using Illumina Sequencers.

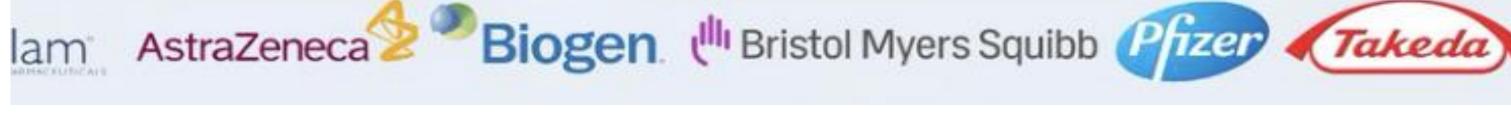


User Success Stories



Large Population Study UK Biobank's 470,000+ exomes analyzed by Regeneron as of July 2022

Word's LARGEST Whole Exome Sequencing project COMPLETED! Sequenced data on 470,000**UK Biobank participants** now available







- 500,000 Exomes
- versus 1 hour in CPUs
- alignment.

Regeneron Genetics Center Sequencing close to

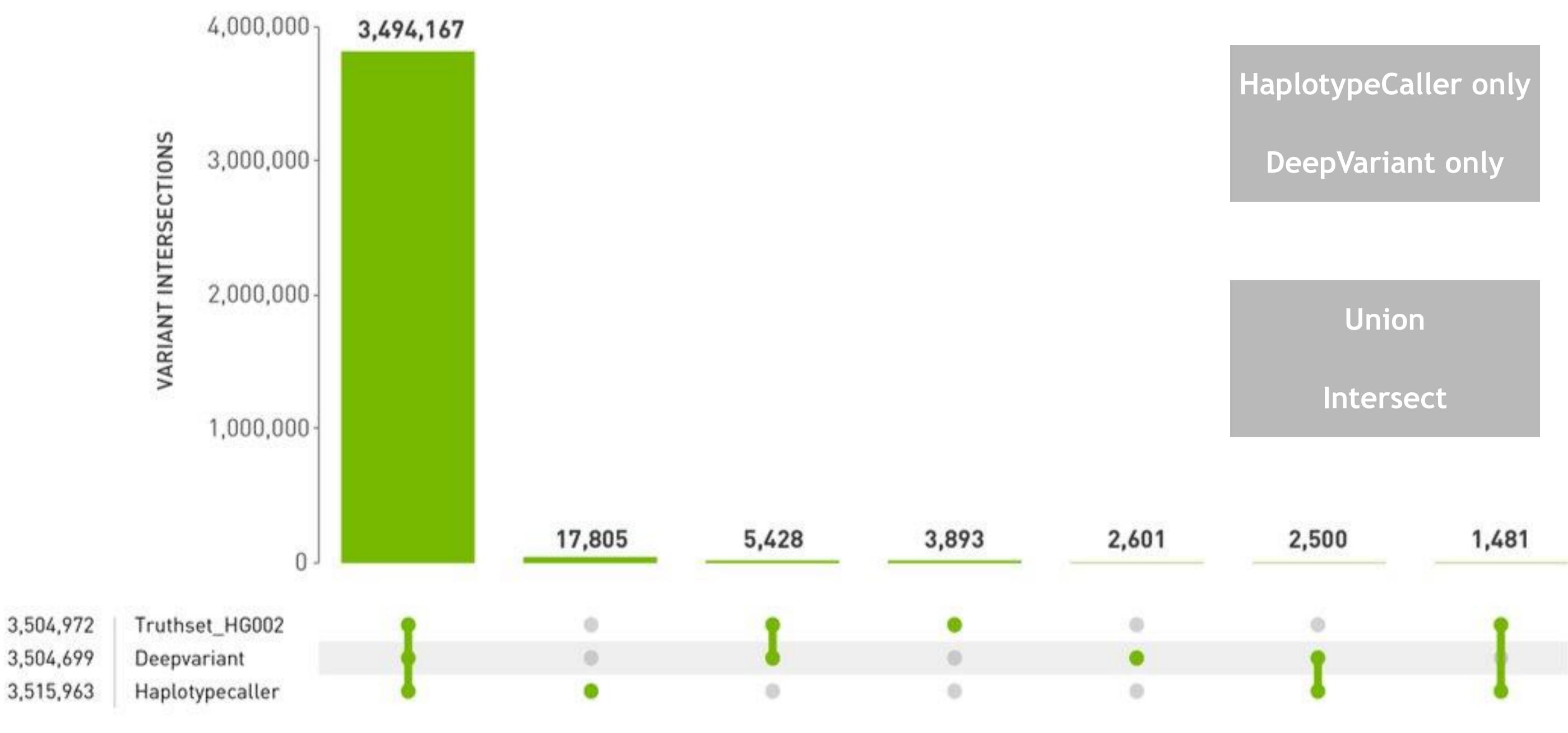
• Exomes were analyzed in 5 minutes with Clara Parabricks

• The cost went down 60% on GPUs

DeepVariant optimized for RGC outputs, especially

 Analysis of DNA given to researchers on UK Biobank which span academia, pharma and other scientists interested in genomic variants for diseases





VARIANTS CALLS PER SUBSET

MULTI-TOOL IMPLEMENTATION PROVIDES THE BEST RESULTS

Comparing germline calling between GATK Haplotype and Google's DeepVariant

HG002 Target genome, analyzing only high confidence regions

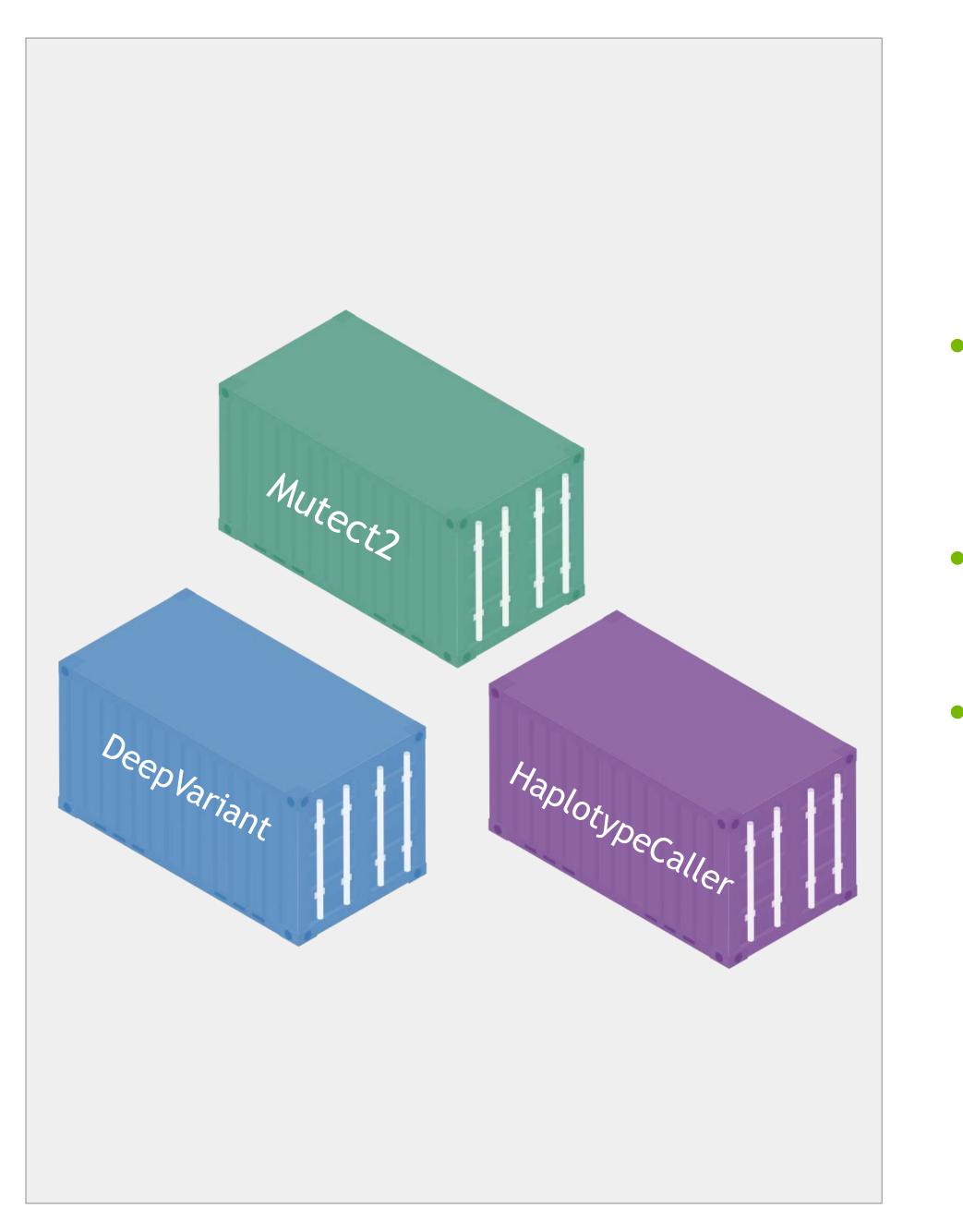
	False Positives	False Negative
HaplotypeCaller only	20,305	9,321
DeepVariant only	5,101	5,374
Union	22,906	3,893
Intersect	2,500	10,802



Getting Started with NVIDIA Parabricks



Modular Tools for Flexible Deployment With NVIDIA AI Enterprise for Production



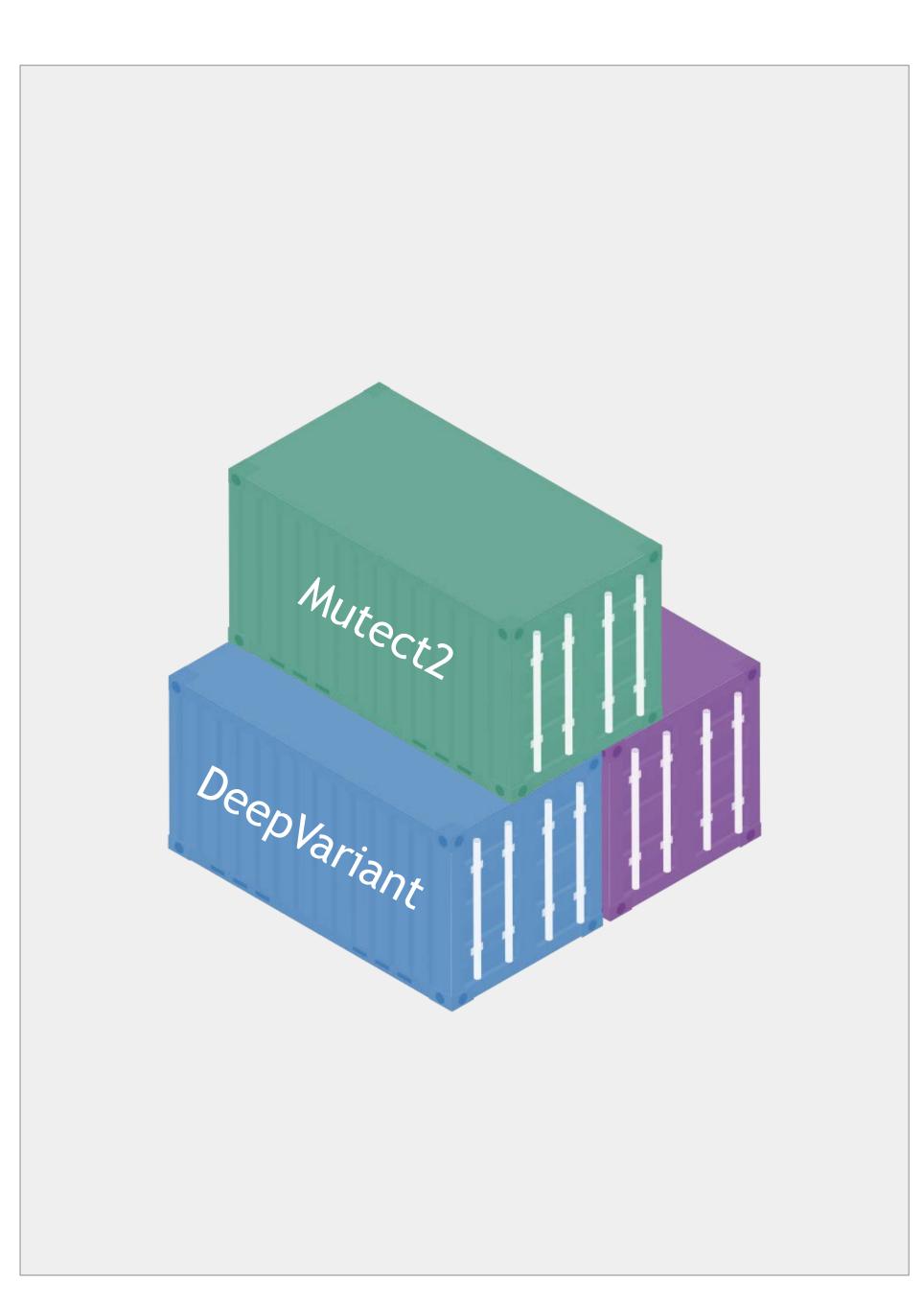
Top of Tree Individual Containers Available on NGC

All NVIDIA Parabricks Containers are available publicly in the <u>NGC Catalog</u>

 Individual Containers for Each Tool

 Agile Releases as and when required

 Lean Deployment on Sequencers or as part of custom workflows

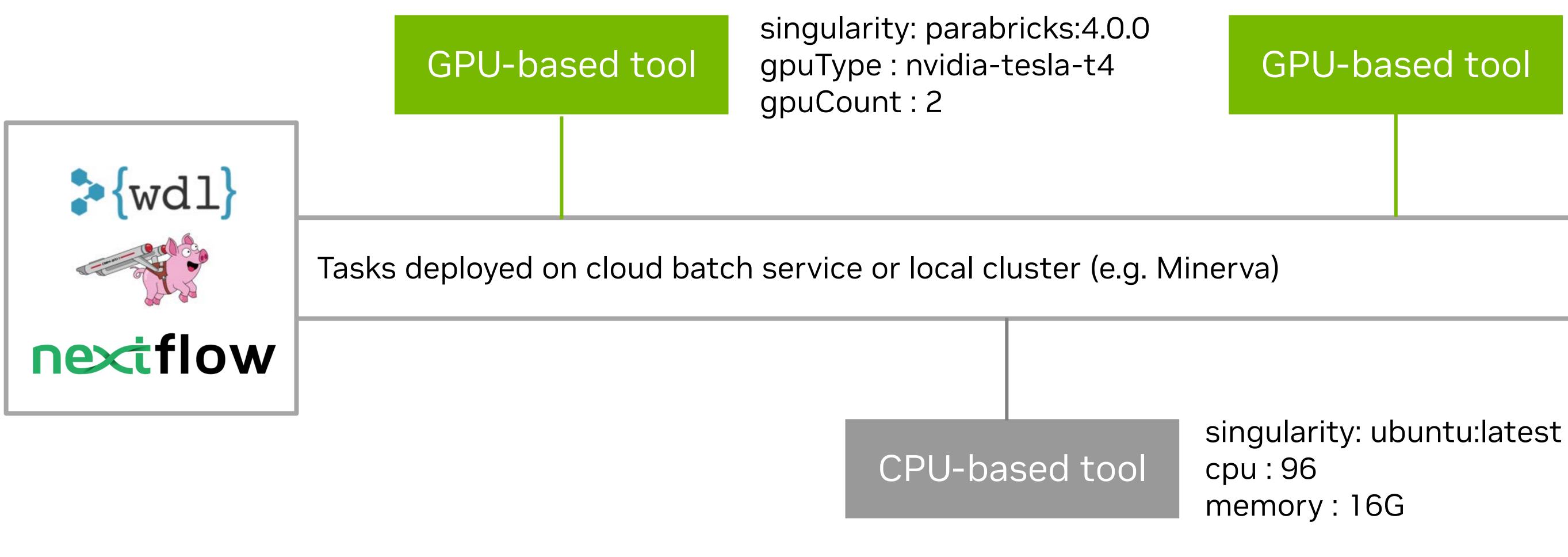


- Includes every Parabricks tool
- Regular Releases timed with NVIDIA AI Enterprise
- Option of Purchasing Enterprise Support thru **NVIDIA AI Enterprise**

Stable Unified Container

Available on NGC Enterprise Support Available





Workflow Manager Compatible Customize and deploy Parabricks at scale

Parabricks is fully compatible with common workflow managers WDL and NextFlow for deploying at scale

Intertwine GPU and CPU powered tasks with different compute requirements

• Reference workflows and recommended compute configs at: <u>github.com/clara-parabricks-workflows</u>



singularity: parabricks:4.0.0 gpuType : nvidia-tesla-v100 gpuCount:4



Hardware Requirements

- Any NVIDIA GPU that supports CUDA architecture 60, 70, 75, or 80 and has at least 16GB of GPU RAM. Parabricks has been tested on the following NVIDIA GPUs:
 - V100
 - **T4**
 - A10, A30, A40, A100, A6000
- System Requirements:
 - A 2 GPU server should have at least 100GB CPU RAM and at least 24 CPU threads.
 - A 4 GPU server should have at least 196GB CPU RAM and at least 32 CPU threads.
 - A 8 GPU server should have at least 392GB CPU RAM and at least 48 CPU threads.

Note

Clara Parabricks is not supported on virtual (vGPU) or Multi-Instance (MIG) GPUs.

Note

The Clara Parabricks deepvariant and deepvariant_germline tools ship with support for T4, V100, and A100 GPUs. See the Models for additional GPUs section for more details on downloading model files for A10, A30, A40, A100, and A6000 GPUs for the deepvariant and deepvariant_germline tools.

Software Requirements

The following are software requirements for running Clara Parabricks.

- An NVIDIA driver greater than version 465.32.*.
- Any Linux Operating System that supports nvidia-docker2 Docker version 20.10 (or higher)

Running NVIDIA Parabricks Requirements

<u>Verifying Hardware and Software Requirements</u>

Checking available NVIDIA hardware and driver

To check your NVIDIA hardware and driver version, use the nvidia-smi command:

NVID	[A-SMI	515.6	5.01 Driv	ver Ve		515.65.01			Transfer I forder of the	
	Name Temp	Perf	Pwr:Usage/C	:ap 	us-Id	Disp.A Memory-Usage	Vol GPU 	atile —Util	Uncorr. Compute MIC	ECC e M. G M.
0 N/A			-DGXS On	0(0000000	0:07:00.0 Off B / 16155MiB	1	.====== 0%	Defa	0
Proce GPU	esses: GI ID	CI ID	PID	Туре	Proce	ess name			GPU Men Usage	nory
0	N/A	====== N/A	3019	G	/usr/	======================================	====== q		=======================================	==== 5MiB

This shows the following important information:

- The NVIDIA driver version is 515.65.01.
- The supported CUDA driver API is 11.7.
- The GPU has 16 GB of memory.

<u>Checking available CPU RAM and threads</u>

To see how much RAM and CPU threads in your machine, you can run the following:

- # To check available memory
- \$ cat /proc/meminfo | grep MemTotal

Doc for NVIDIA Parabricks 4.3.0

```
# To check available number of threads
$ cat /proc/cpuinfo | grep processor | wc -l
```



Run Parabricks on Minerva

```
singularity exec \
    --nv \
    --bind ${DATA_DIR}:${DATA_DIR} \
    ${SINGULARITY_IMAGE} \
    pbrun fq2bam \
    --ref /workdir/${REFERENCE_FILE} \
    --in-fq /workdir/${INPUT_FASTQ_1} /workdir/${INPUT_FASTQ_2} `
    --knownSites /workdir/${KNOWN_SITES_FILE} \
    --out-bam /outputdir/${OUTPUT_BAM} \
    --out-recal-file /outputdir/${OUTPUT_RECAL_FILE}
```

Running NVIDIA Parabricks Drop-in Command Line Replacements

Compatible CPU-based BWA-MEM, GATK4 Commands

The commands below are the bwa-0.7.15 and GATK4 counterpart of the Parabricks command above. The output from these commands will be identical to the output from the above command. See the Output Comparison page for comparing the results.

```
# Run bwa-mem and pipe the output to create a sorted BAM.
S bwa mem
    -t 32 \
    -K 1000000
  gatk SortSam \
    --java-options -Xmx30g \
    --MAX_RECORDS_IN_RAM 5000000
    -I /dev/stdin \
    -0 cpu.bam \
    --SORT_ORDER coordinate
# Mark duplicates.
$ gatk MarkDuplicates \
    --java-options -Xmx30g
   -I cpu.bam \
    -0 mark_dups_cpu.bam
    -M metrics.txt
# Generate a BQSR report.
$ gatk BaseRecalibrator
    --java-options -Xmx30g \
    --input mark_dups_cpu.bam \
    --output <OUTPUT_DIR>/${OUTPUT_RECAL_FILE} \
    --known-sites <INPUT_DIR>/${KNOWN_SITES_FILE} \
    --reference <INPUT_DIR>/${REFERENCE_FILE}
```

Doc for NVIDIA Parabricks 4.3.0



```
-R '@RG\tID:sample_rg1\tLB:lib1\tPL:bar\tSM:sample\tPU:sample_rg1' \
<INPUT_DIR>/${REFERENCE_FILE} <INPUT_DIR>/${INPUT_FASTQ_1} <INPUT_DIR>/${INPUT_FASTQ_2} | \
```





Dace		Tute
DOCS	n	Tuto

The tutorials walk you through a simple use case for Clara Parabricks, giving a brief introduction of how it worl You will start by downloading some sample data:

The tutorials then walk through the following steps:

The tutorials are meant to be simple and straightforward and to only cover a single, specific use case. You shou be able to copy and paste the commands into a terminal window and get the same results as shown. The How Tos cover more general problem solving using Clara Parabricks.

Steps in the Tutorial

G Previous

Running NVIDIA Parabricks Demo: run tutorials on Minerva

orials

Tutorials

• A reference file (Homo_sapiens_assembly38.fasta) and its index

• A 'known indels' file and its index

Two FASTQ files

Associated index files

 Alignment (FASTA + FASTQ ==> BAM) Variant calling (BAM ==> VCF)

 Getting The Sample Data FQ2BAM Tutorial HaplotypeCaller Tutorial

Doc for NVIDIA Parabricks 4.3.0

Next



GTC DLI Workshop - Training DeepVariant Models using Parabricks - Recording: <u>https://www.nvidia.com/en-us/on-demand/session/gtc24-dlit61813/</u> or search for the title on NVIDIA On-Demand

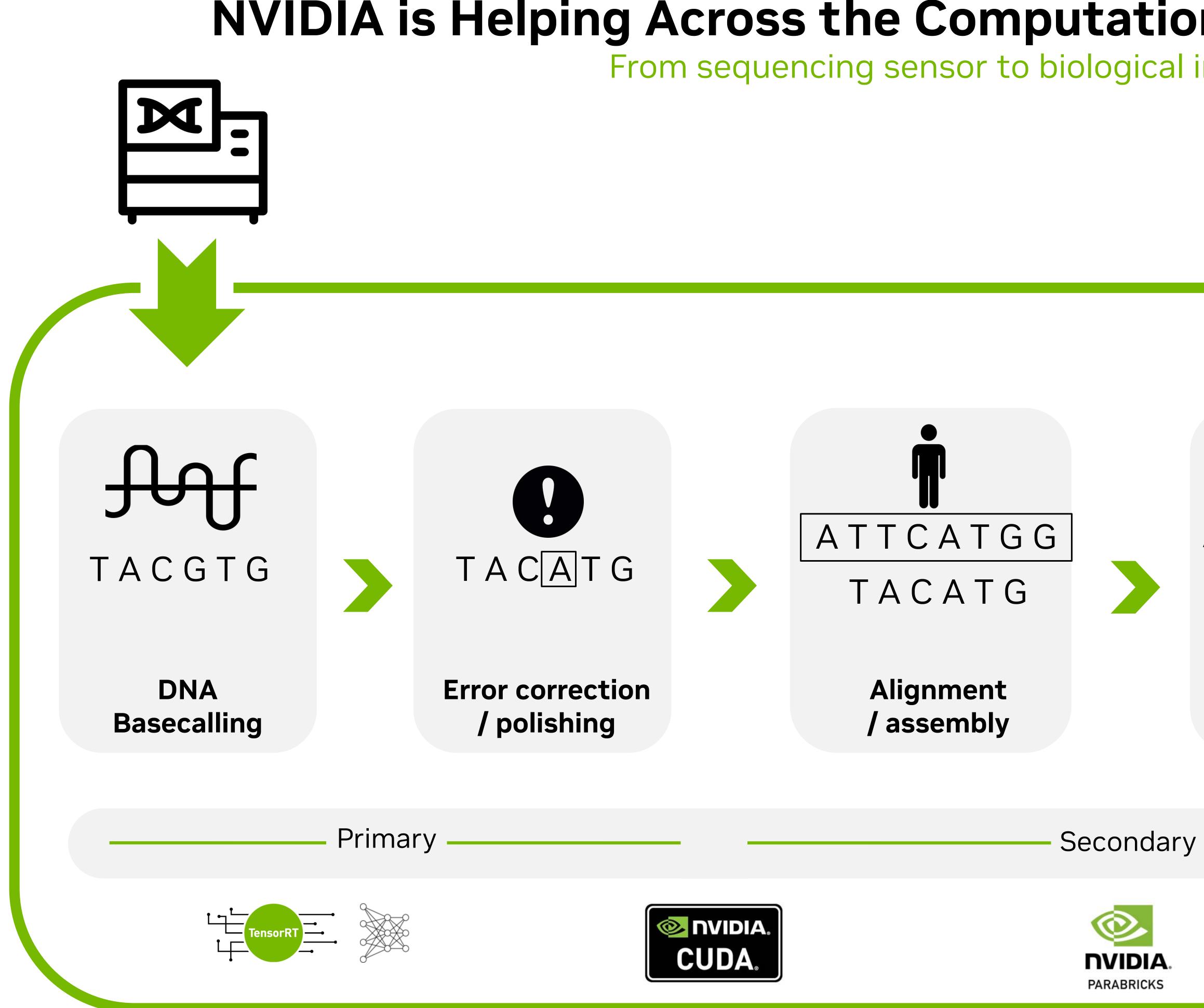
Resources



Agenda

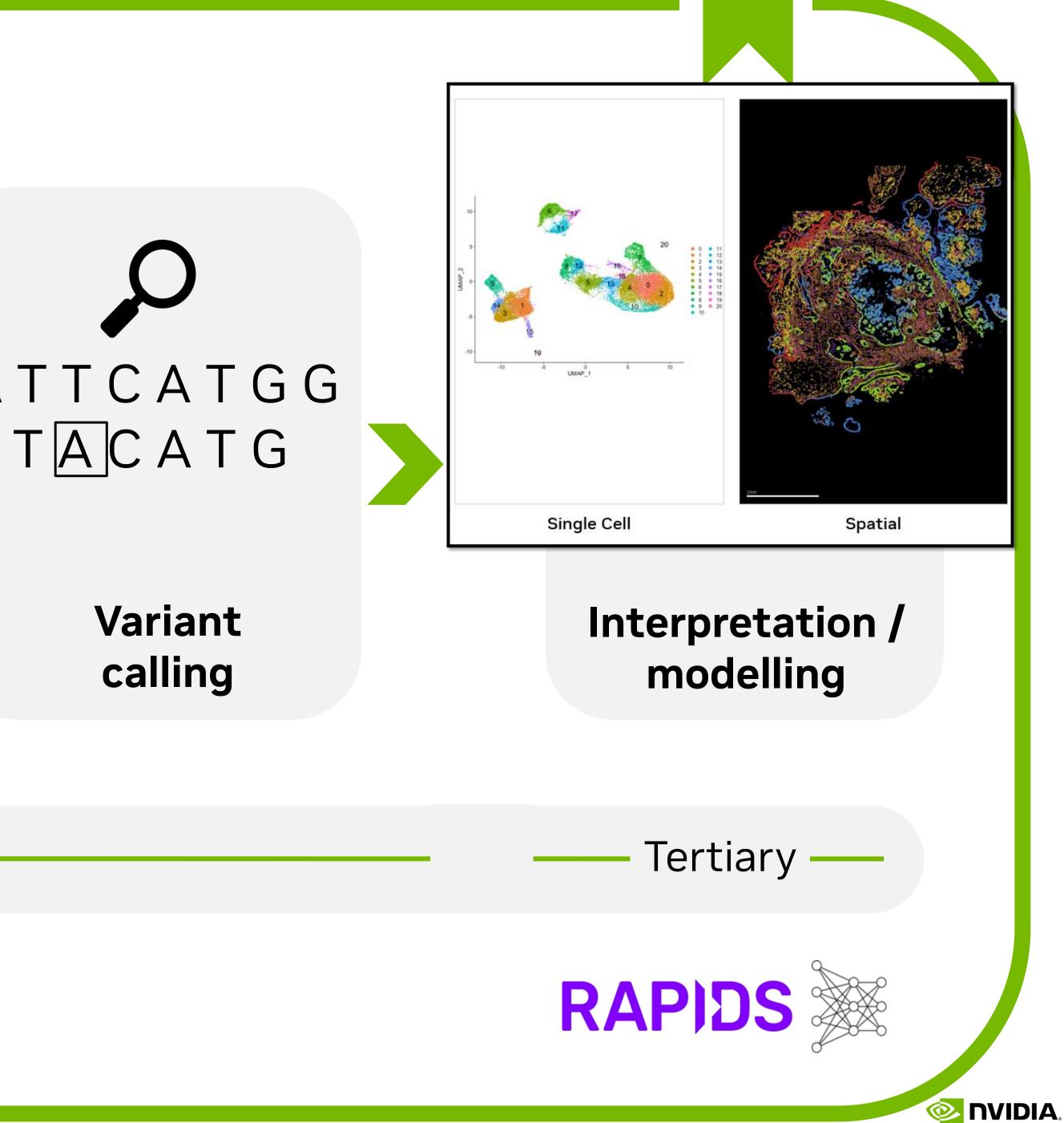
NVIDIA Parabricks for secondary analysis RAPIDS for tertiary analysis, single-cell RNAseq analysis and spacial genomics





NVIDIA is Helping Across the Computational Genomics Workflow From sequencing sensor to biological insights









(i) ACCELERATED DATA SCIENCE

The RAPIDS suite of open source software libraries gives you the freedom to execute end-to-end data science and analytics pipelines entirely on GPUs. Learn about RAPIDS >>

TOP MODEL ACCURACY

Increase machine learning model accuracy by iterating on models faster and deploying them more frequently. Learn about RAPIDS for model optimization >>

RAPDS

GPU DATA SCIENCE

SCALE OUT ON GPUS

Seamlessly scale from GPU workstations to multi-GPU servers and multi-node clusters with Dask. Learn about Dask >>

O REDUCED TRAINING TIME

Drastically improve your productivity with more interactive data science tools like XGBoost.

Learn about XGBoost >> Learn about accelerated ML with cuML >>



PYTHON INTEGRATION

Accelerate your Python data science toolchain with minimal code changes and no new tools to learn.

Learn about our libraries >>

POPEN SOURCE

RAPIDS is an open source project. Supported by NVIDIA, it also relies on Numba, Apache Arrow, and many more open source projects.

Learn about our projects >>



	CPU
Data handling	pandas
Machine learning	scikit-learn
Graph analytics	NetworkX

DATA SCIENCE TOOLSETS

GPU/RAPIDS

cuDF

cuML

cuGraph

Viz

Geospati

Signals

Cyber

	CPU	GPU/RAPI
	Bokeh/ Datashader	cuXfilter
ial	GeoPandas/ SciPy.spatial	cuSpatial
	SciPy.signal	cuSignal
	cyberpandas	CLX

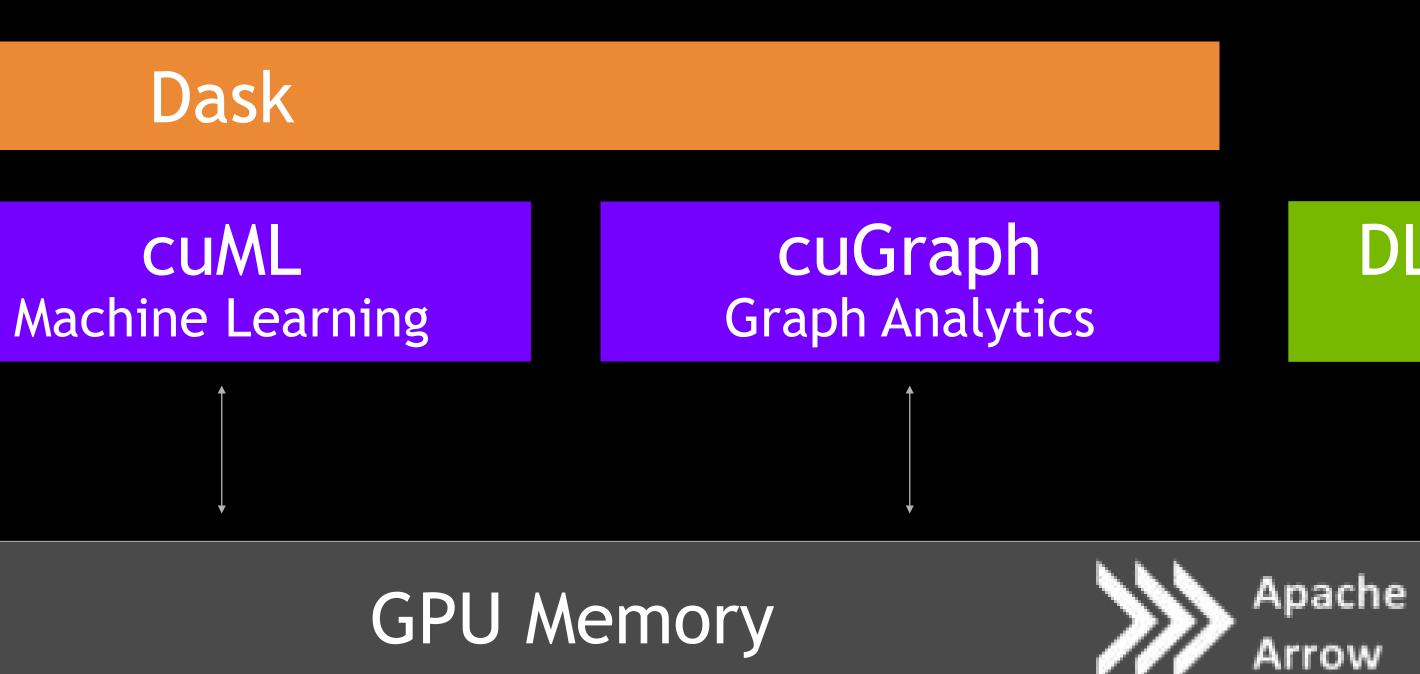




cuDF Data Prep/Handling

cuSignal cuSpatial **Geospatial Analytics** Signal Processing

RAPIDS PLATFORM



Specialized package examples

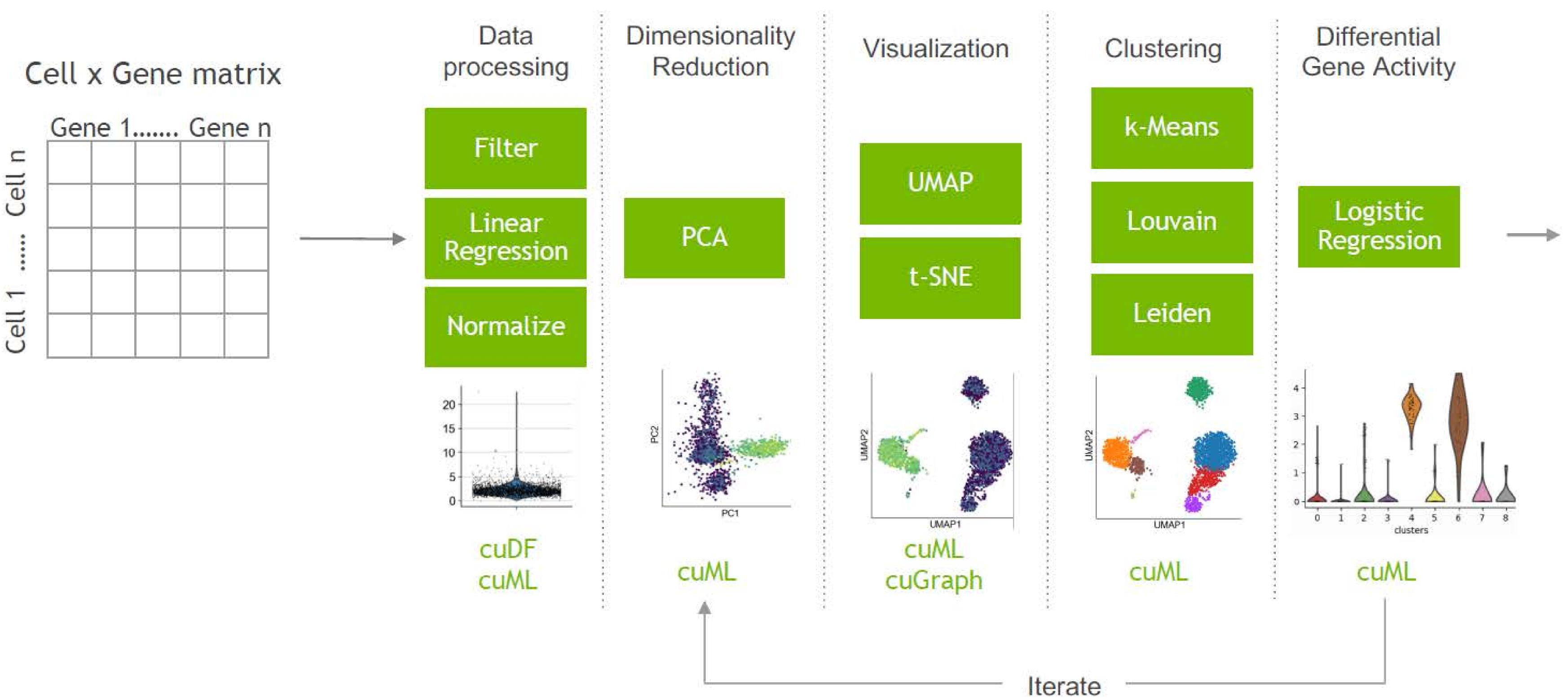
DL Frameworks Deep Learning

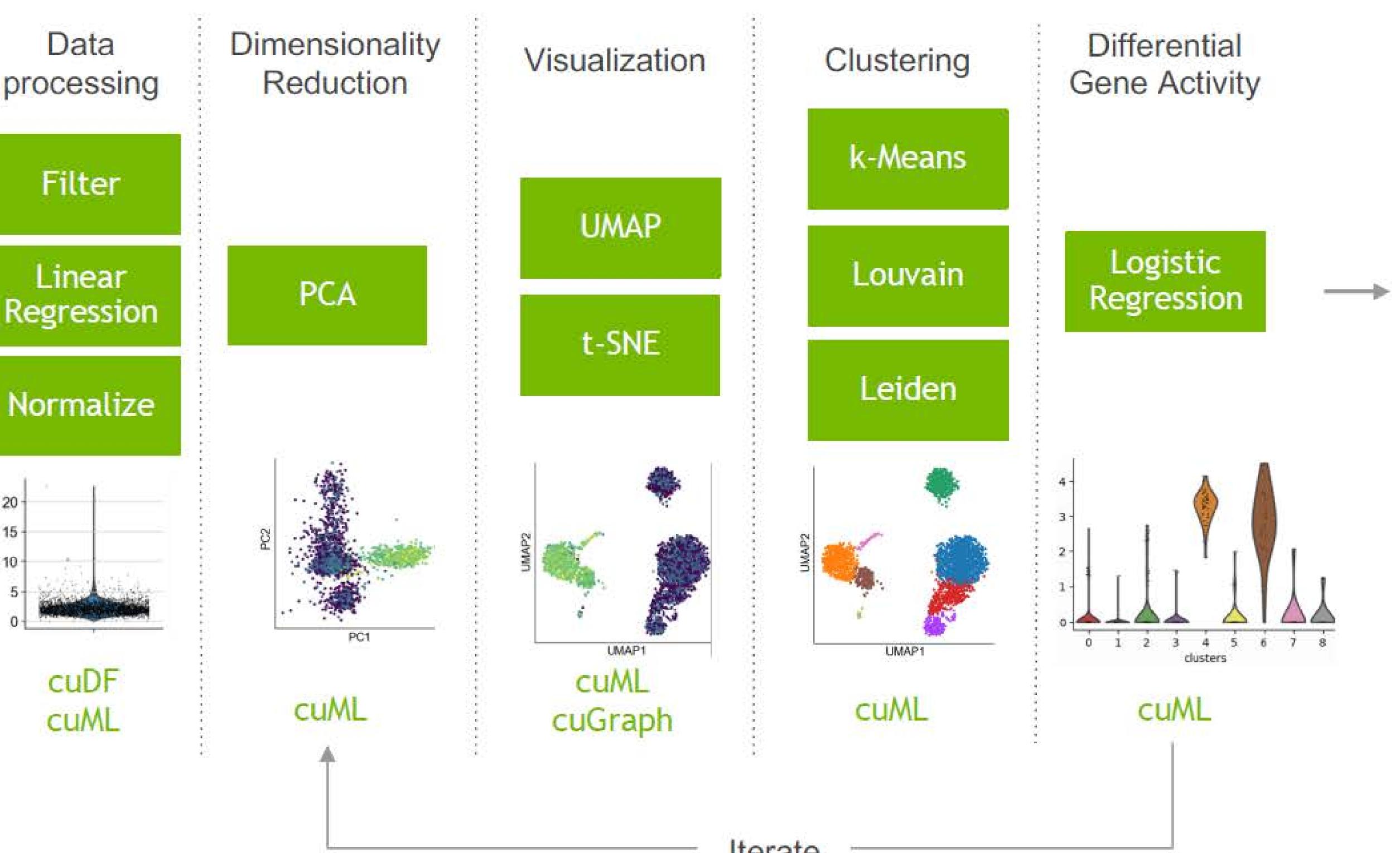
cuXfilter Visualization

CLX Cyber Analytics



SINGLE-CELL RNA-SEQ ANALYSIS USING RAPIDS





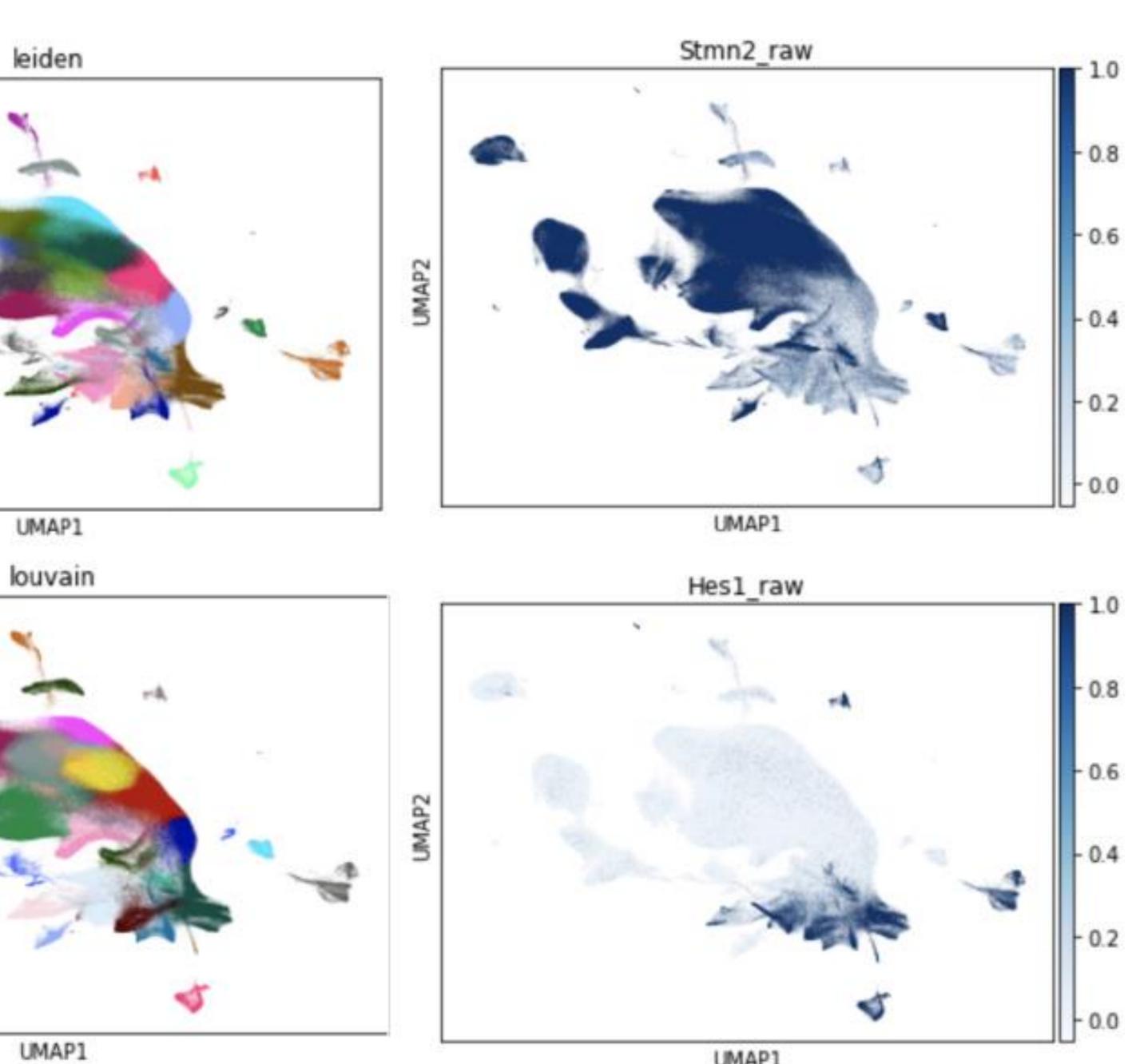


🕺 NVIDIA.

GPU ANALYSIS OF 1 MILLION CELLS From 3.5 hours to 8 minutes

				1
	CPU Runtime n1-highmem-32 32 vCPUs	GPU runtime a2-highgpu-1g Tesla A100 40GB GPU	GPU acceleration	
Preprocessing	28m35s	3m21s	9x	~
PCA	29.2s	11.4s	2.6x	UMAP2
t-SNE	1hr23m10s	28s	178x	
KNN	3m5s	46s	4x	
UMAP	21m47s	13.4s	98x	
k-means clustering	2m6s	1.9s	66x	
Louvain clustering	1 <mark>5m</mark> 5s	1.9s	476x	2
Leiden clustering	51m1s	1.4s	2186x	UMAP
End-to-end runtime	3hr31m48s	8m22s	25x	
End-to-end cost	\$6.682	\$0.553		

Repository for example jupyter notebooks: <u>https://github.com/NVIDIA-Genomics-Research/rapids-single-cell-examples</u>



UMAP1

- A new library drawing inspiration from the rapids-single-cell-examples library and the ScanPy library
- Introduces GPU-optimized versions of lacksquarethe ScanPy (single cell) and SquidPy (spatial) functions
- The library's primary objective is to blend the computational strength of GPUs with the user-friendly nature of the scverse ecosystem.

RAPIDS-SingleCell Part of the Scverse ecosystem

Function

Whole notebook(excluding PR functions)

Preprocessing

HVG (Seurat v3)

Regress out

scale

PCA

Neighbors

UMAP

TSNE

Louvain

Leiden

Logistic regression

Diffusion map

HVG (PR)

Normalize (PR)

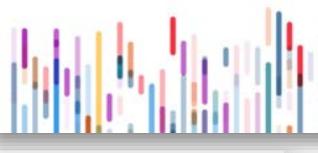
Table 2. Server node and consumer system benchmark for a dataset of 500,000 cells

https://developer.nvidia.com/blog/gpu-accelerated-single-cell-rna-analysis-with-rapids-singlecell/

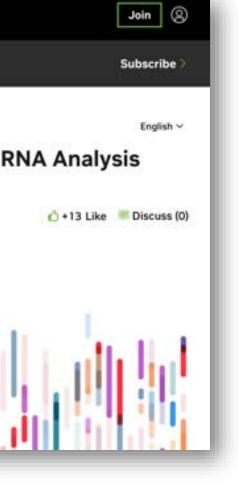
Technical Blog Q

Data Science

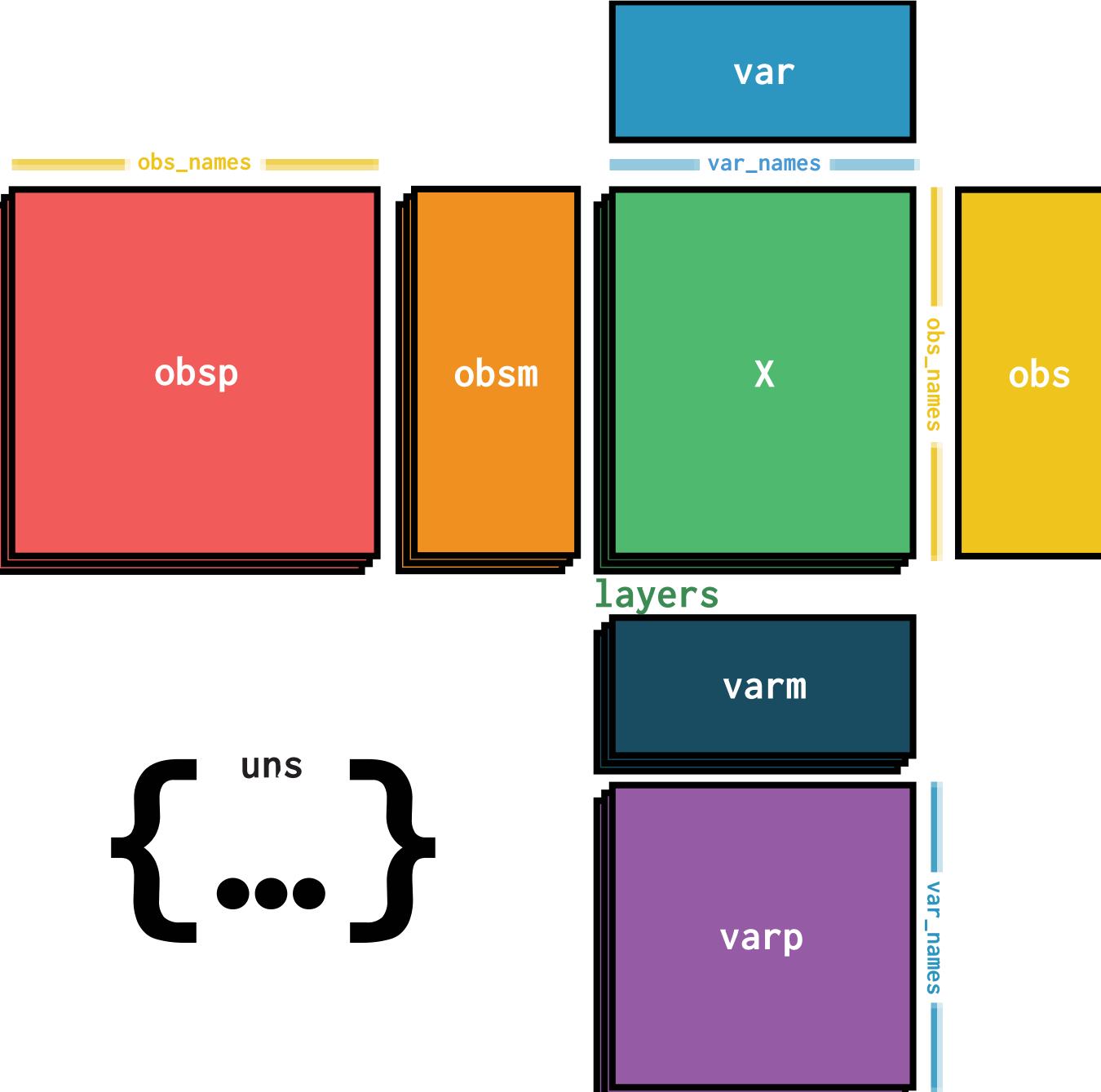
GPU-Accelerated Single-Cell RNA Analysis with RAPIDS-singlecell By Severin Dicks and Corey Nole



CPU	GPU (A100)	GPU (3090)	Speedup
2,460 s (41 min)	110 s	290 s	22x
305 s	28 s	169 s	10x
48 s	1.5 s	13 s	32x
104 s	5.1 s	16 s	20x
8.4 s	1.3 s	5 s	6.4x
86 s	3.7 s	35 s	23x
74 s	17.1 s	1 <mark>8.</mark> 3 s	4.3x
281 s (4.6 min)	6.7 s	7.6 s	60x
786 s (13 min)	10 s	12.9 s	105x
283 s (4.5 min)	4.5 s	5.7 s	62x
282 s (4.5 min)	0.6 s	0.9 s	470x
452 s (7.5 min)	33 s	63 s	13x
30 s	0.75 s	1.3 s	40x
104 s	2.1 s	15.6 s	50x
22 s	0.3 s	ls	73x







https://anndata.readthedocs.io/en/latest/#

RAPIDS-SingleCell The AnnData framework now supports CuPy arrays

AnnData stores a data matrix **X** together with annotations of observations obs (obsm, obsp), variables var (varm, **varp**), and unstructured annotations **uns**.

An AnnData object adata can be sliced like a DataFrame, for instance adata_subset = adata[:, list_of_variable_names] . AnnData 's basic structure is similar to R's ExpressionSet [Huber15]. If setting an .h5ad formatted HDF5 backing file .filename, data remains on the disk but is automatically loaded into memory if needed.

Rapids-singlecell utilizes the scverse AnnData data framework, which supports dense and sparse CuPy arrays



API scanpy-GPU

V

rapids_singlecell.pp.calculate_q c_metrics

rapids_singlecell.pp.filter_cells

rapids_singlecell.pp.filter_gene S

rapids_singlecell.pp.normalize_ total

rapids_singlecell.pp.log1p

rapids_singlecell.pp.highly_vari able_genes

rapids_singlecell.pp.regress_ou

rapids_singlecell.pp.scale

rapids_singlecell.pp.pca

rapids_singlecell.pp.normalize_ pearson_residuals

rapids_singlecell.pp.flag_gene_ family

rapids_singlecell.pp.filter_highl y_variable

RAPIDS-SingleCell API based on ScanPy and SquidPy

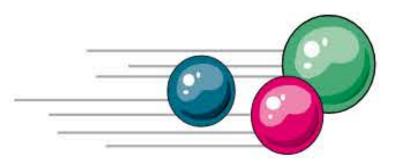
Basic Preprocessing	
<pre>pp.calculate_qc_metrics (adata[, expr_type,])</pre>	Calculates basic
<pre>pp.filter_cells (adata, qc_var[, min_count,])</pre>	Filter cell outliers genes expressed
<pre>pp.filter_genes (adata[, qc_var, min_count,])</pre>	Filter genes base
<pre>pp.normalize_total (adata[, target_sum,])</pre>	Normalizes rows target_sum
pp.log1p (adata[, layer, copy])	Calculated the na sparse matrix.
<pre>pp.highly_variable_genes (adata[, layer,])</pre>	Annotate highly
pp.regress_out (adata, keys[, layer,])	Use linear regres
<pre>pp.scale (adata[, max_value, layer, inplace])</pre>	Scales matrix to
pp.pca (adata[, layer, n_comps, zero_center,])	Performs PCA us function.
<pre>pp.normalize_pearson_residuals (adata[,])</pre>	Applies analytic

https://rapids-singlecell.readthedocs.io/en/latest/index.html



Q 7 CO d
lates basic qc Parameters.
cell outliers based on counts and numbers of expressed.
genes based on number of cells or counts.
alizes rows in matrix so they sum to
lated the natural logarithm of one plus the e matrix.
ate highly variable genes.
near regression to adjust for the effects of need noise and variation.
s matrix to unit variance and clips values
rms PCA using the cuml decomposition on.
es analytic Pearson residual normalization,





RAPIDS-SINGLECELL

Installation

Usage Principles

API

Release notes

References

Notebooks

Demo Workflow & Decoupler

HVG:seurat_v3 & harmony workflow

Pearson Residues Example

1 Million Brain Cells

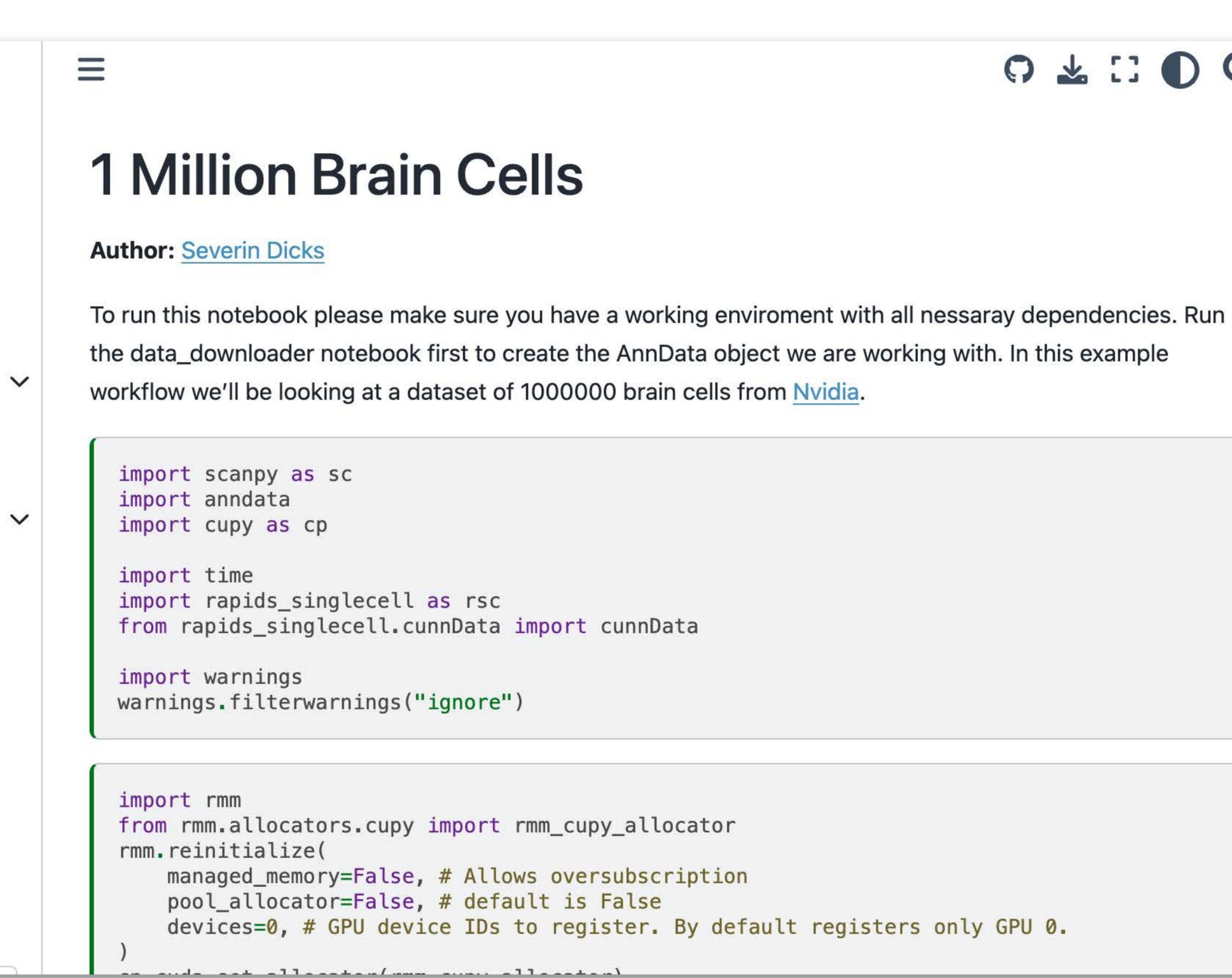
Spatial Autocorrelation

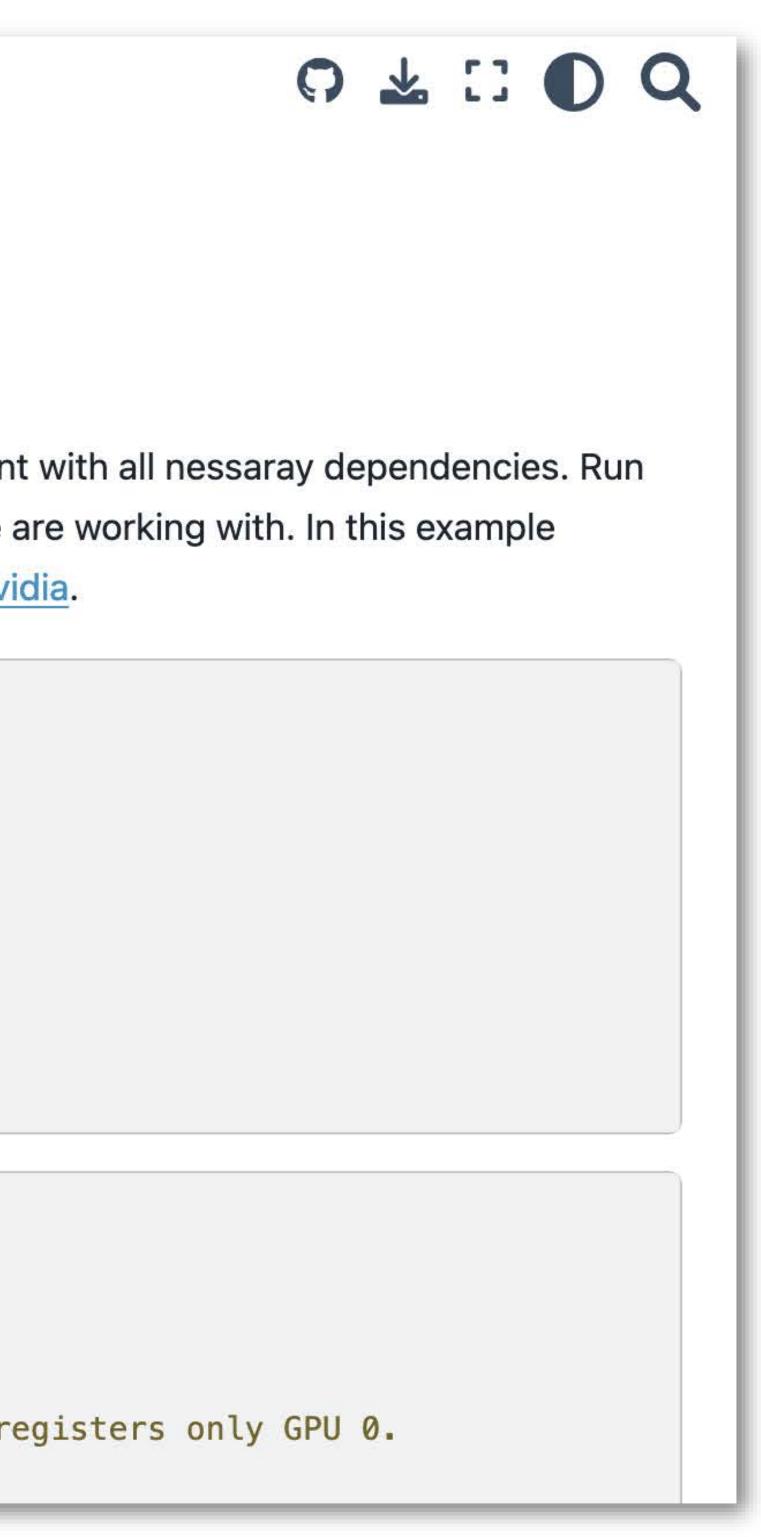
Ligrec Benchmark

Acknowledgements

https://rapids-singlecell.readthedocs.io/en/latest/notebooks/demo_gpu-seuratv3-brain-1M.html

RAPIDS-SingleCell Get Started Now with Example Notebooks







or search for the title on NVIDIA On-Demand

Everything, All at Once: Processing Spatial Transcriptomics Data using Accelerated Computing

Jonny Hancox, Senior Solution Architect, NVIDIA

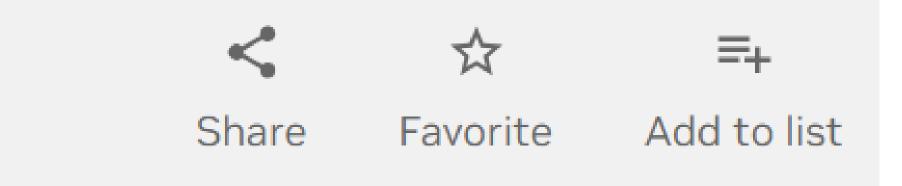
Rate Now

The potential clinical benefits of combining the power of mRNA expression with the rich context of tissue morphology are considerable. Equally impressive is the amount of data preparation and processing needed to perform this analysis. In the absence of well-established pipelines dedicated to this analysis, scientists often have to make do with their own curated set of tools and techniques. Learn how RAPIDS and compatible tools can be used to address the key steps in the process, reducing the time to turn biological mysteries into actionable insights.

Spatial Genomics

GTC DLI Workshop - Everything, All at Once: Processing Spatial Transcriptomics Data using Accelerated Computing - Recording: https://www.nvidia.com/en-us/on-demand/session/gtc24-dlit61337/

You'll learn to use GPU tools in python environment - RAPIDS, CuPy, Numba





1. Medical imaging specifi

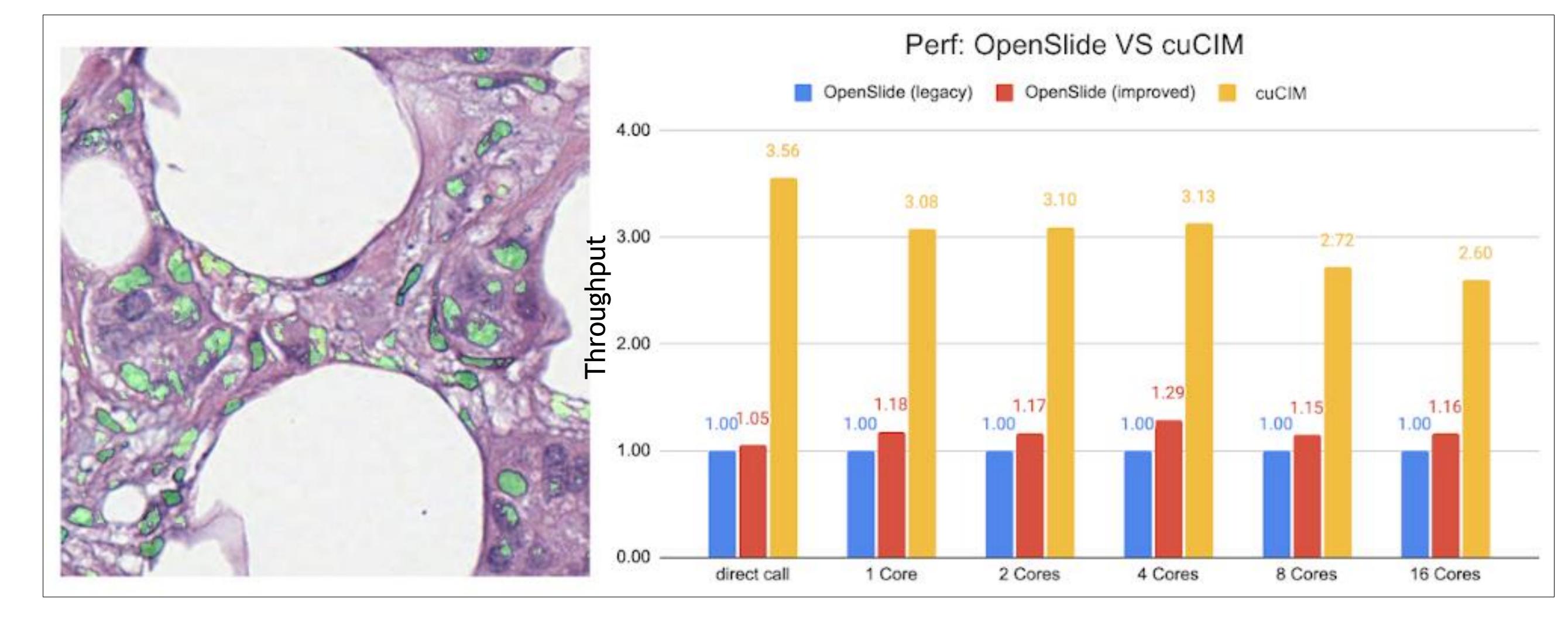
2. Superior performance

3. Friendly community

MONAL Core

Optimize data loading

cuCIM - Whole Slide Imaging (digital pathology)



cuCIM - a library within <u>RAPIDS</u>

2. Superior performance

MONAL Core **Optimize GPU utilization**

cuCIM -> common transforms in digital pathology

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Do transforms on GPU

```
from monai.transforms import (
   Activations,
   AsDiscrete,
   CastToType,
   CastToTyped,
   Compose,
    CuCIM,
   GridSplitd,
   Lambdad,
   Rand<mark>CuCIM</mark>,
    RandFlipd,
   RandRotate90d,
   RandZoomd,
   ScaleIntensityRanged,
   ToCupy,
   ToNumpyd,
   TorchVisiond,
   ToTensor,
   ToTensord,
```

MONAI Core pathology tutorials

Agenda

NVIDIA Parabricks for secondary analysis RAPIDS for tertiary analysis, single-cell RNAseq analysis and spacial genomics



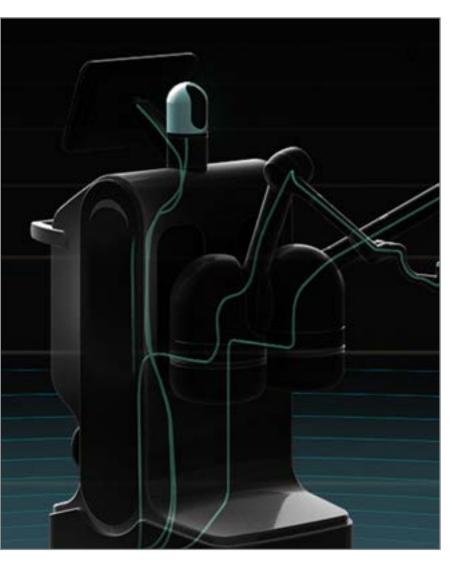
NVIDIA Clara Accelerated Computing Platform for Healthcare & Life Sciences

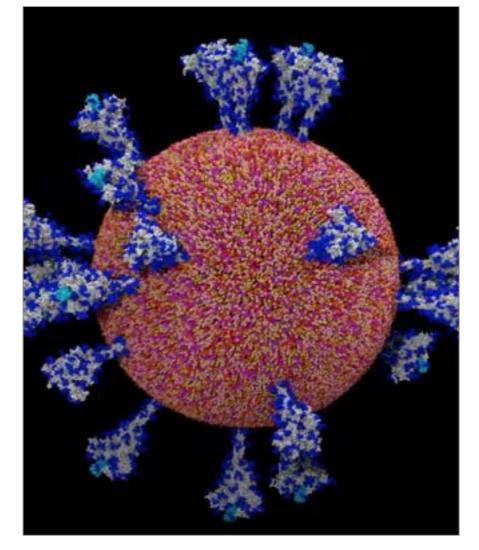




PARABRICKS Genomics

NVIDIA CLARA





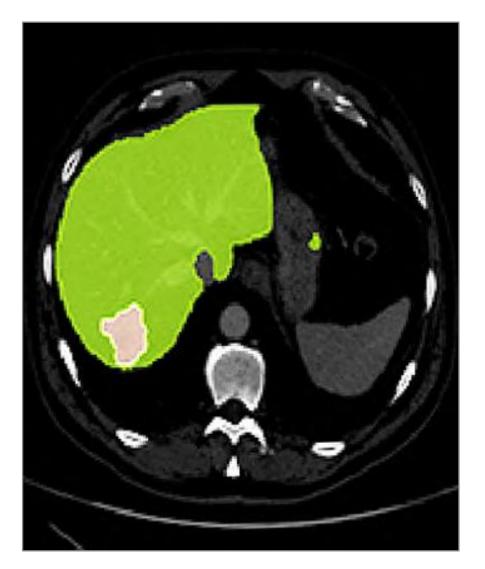
ISAAC Robotics

HOLOSCAN Instruments

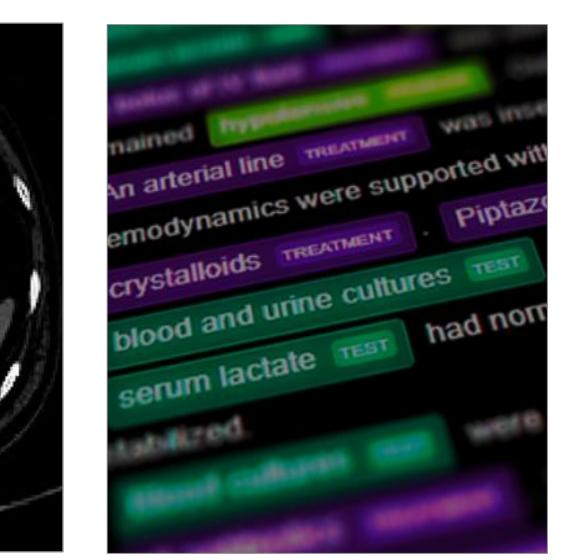
BIONEMO Biomolecules



Federated Learning

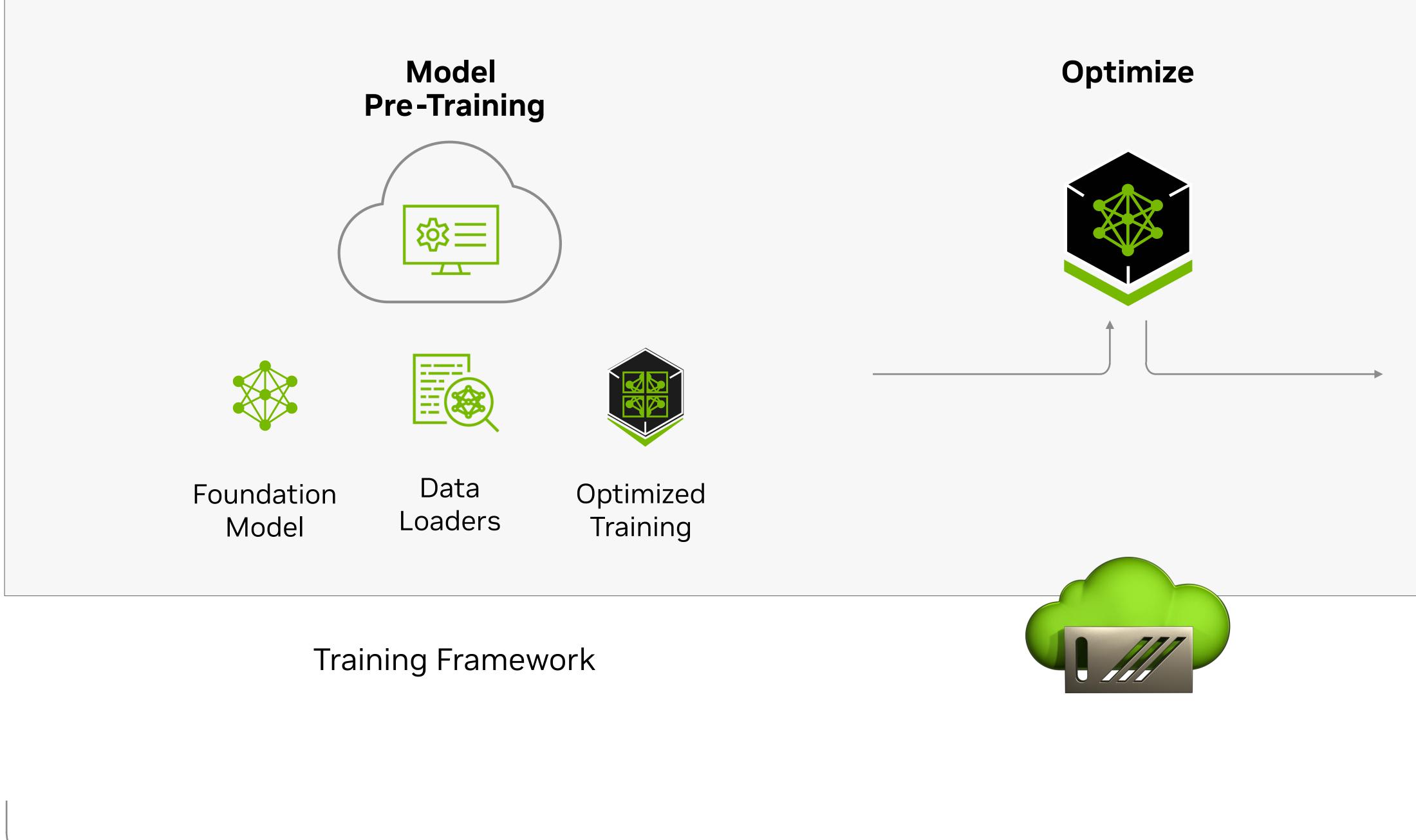


MONAI Imaging



NEMO Natural Language

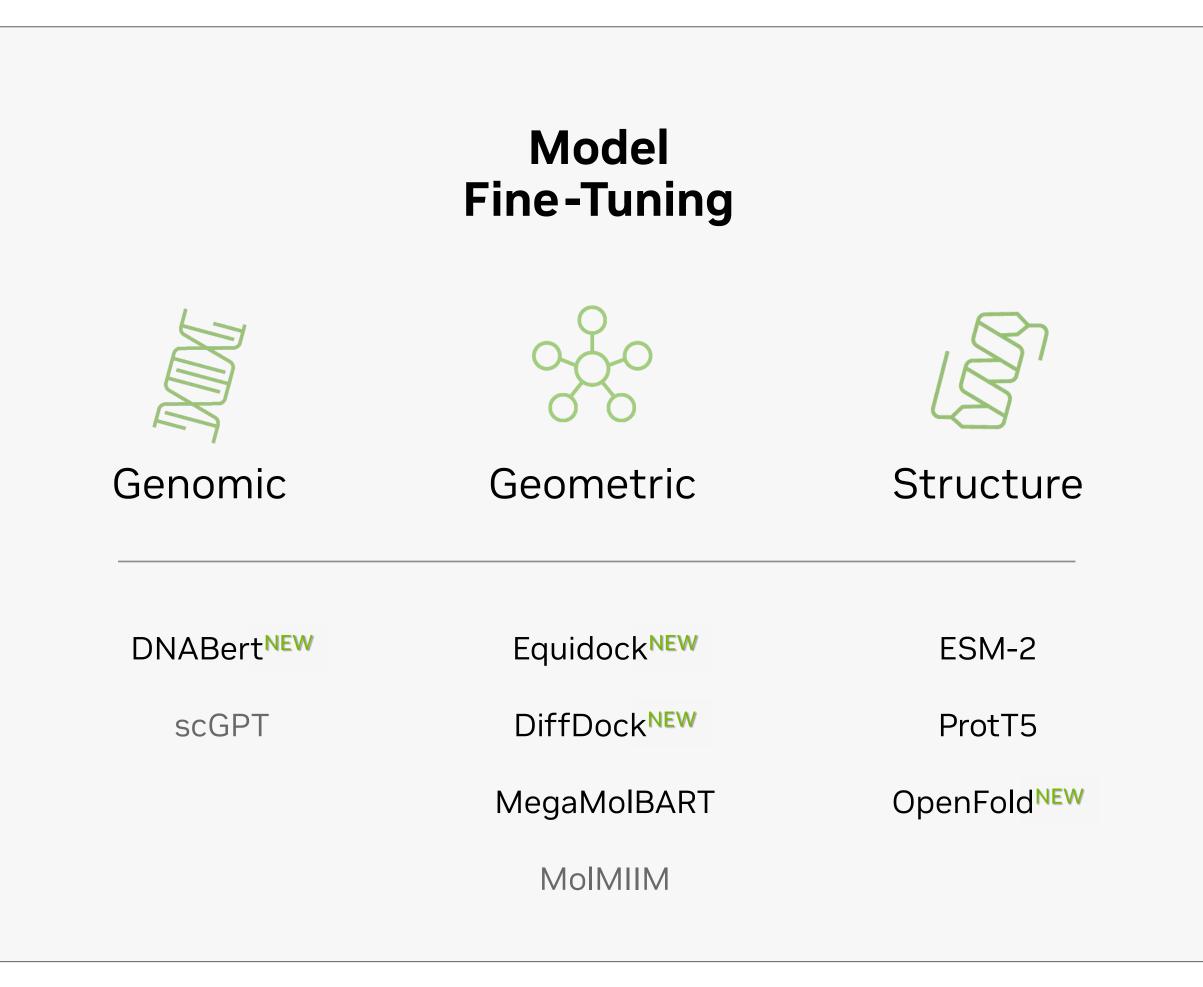




NVIDIA BioNeMo Framework Enables Data Scientists and Researchers Train on DNA, Protein, Chemistry Data

Microsoft Azure

aws Soogle Cloud ORACLE



Pre-Trained Models



search for the title on <u>NVIDIA On-Demand</u>

Genomics Recommended Sessions to Attend

FEATURED TALKS

Kimberly Powell Special Address: Generative AI is Accelerating Healthcare into One of the Largest Technology Industries [S62604] Kimberly Powell | General Manager and VP, Healthcare and Life Sciences Tuesday, Mar 19 | 8:00 AM PDT

The Role of Generative AI in Modern Medicine [S62777] Kimberly Powell | General Manager and VP, Healthcare and Life Sciences Eric Topol | Professor and Executive Vice President Catherine D. Wood | Chief Executive Officer/Chief Investment Officer Peter Lee | Corporate Vice President of Research and Incubations Tuesday, Mar 19 | 11:00 AM - 11:50 AM PDT

How Artificial Intelligence is Powering the Future of Biomedicine [S62283] Priscilla Chan | Co-Founder and co-CEO, Chan Zuckerberg Initiative Mona Flores | Global Head of Medical AI, NVIDIA Tuesday, Mar 19 | 10:00 AM - 10:25 AM PDT

WORKSHOPS & TRAININGS

Training DeepVariant Models using Parabricks [DLIT61813] Thursday, Mar 21 | 2:00 PM - 3:40 PM PDT

First-Ever Whole Transcriptome Imaging of Tissues using CosMx-SMI: Highest-**Density Dataset Ever Collected [S61995]**

Joseph Beechem | Senior Vice President of Research and Development, Nanostring Wednesday, Mar 208:00 AM - 8:25 AM PDT

Nucleotide Transformer: Advancing Genomic Analysis with Large Language Models [S62438]

Karim Beguir | CEO and Co-founder, InstaDeep Tuesday, Mar 19 | 9:00 AM - 9:25 AM PDT

Computer Vision for Rare Disease Genomic Medicine [S62535]

Wolfgang Pernice | Assistant Professor of Neurological Sciences, Columbia University In The City Of New York Thursday, Mar 21 | 9:00 AM - 9:25 AM PDT

Introduction to GPU-Accelerated Genomics with Parabricks [S62322]

Harry Clifford | Genomics Product Lead, NVIDIA Wednesday, Mar 20 | 4:30 PM - 4:55 PM PDT



Thanks for your attention



