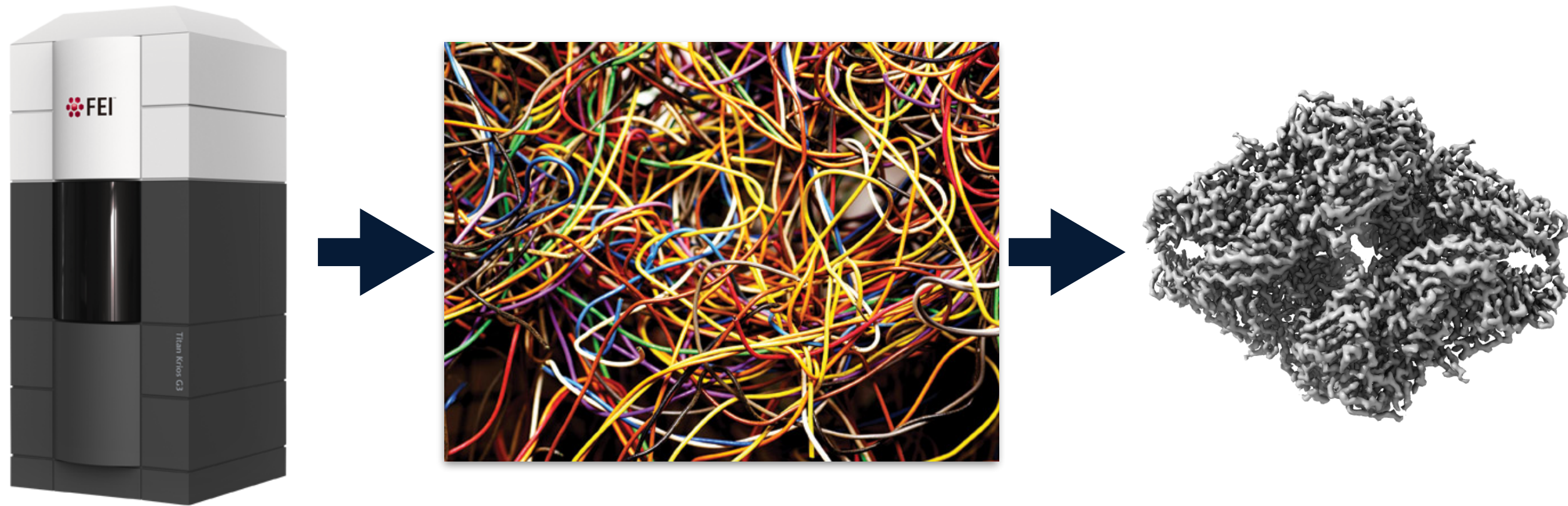


Software tools to deploy and manage cryo-EM jobs in the cloud

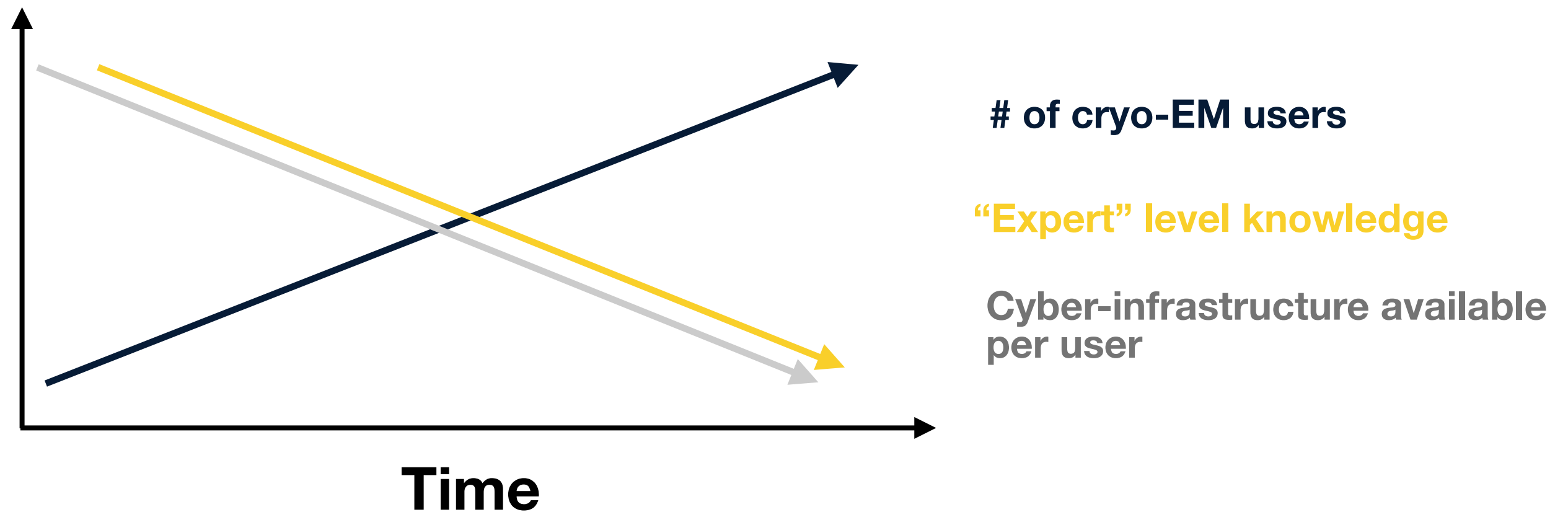
Michael Cianfrocco
Life Sciences Institute
Department of Biological Chemistry
University of Michigan

‘State of the art’ computing for cryo-EM

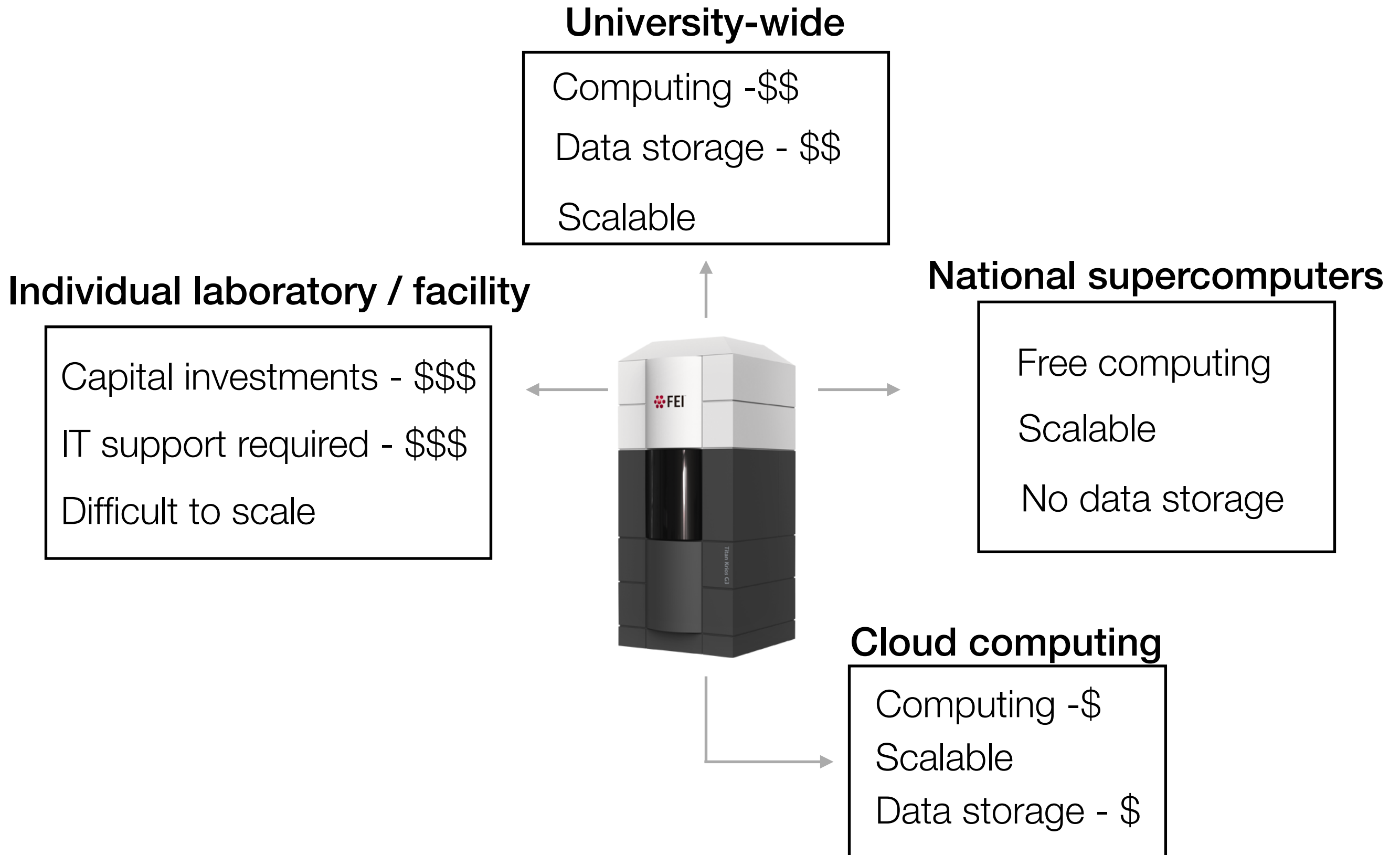


- ▶ Data processing occurring at a different site than data collection
- ▶ Data copying & moving; living at multiple locations
- ▶ New users left on their own to navigate the complex world of computing & storage

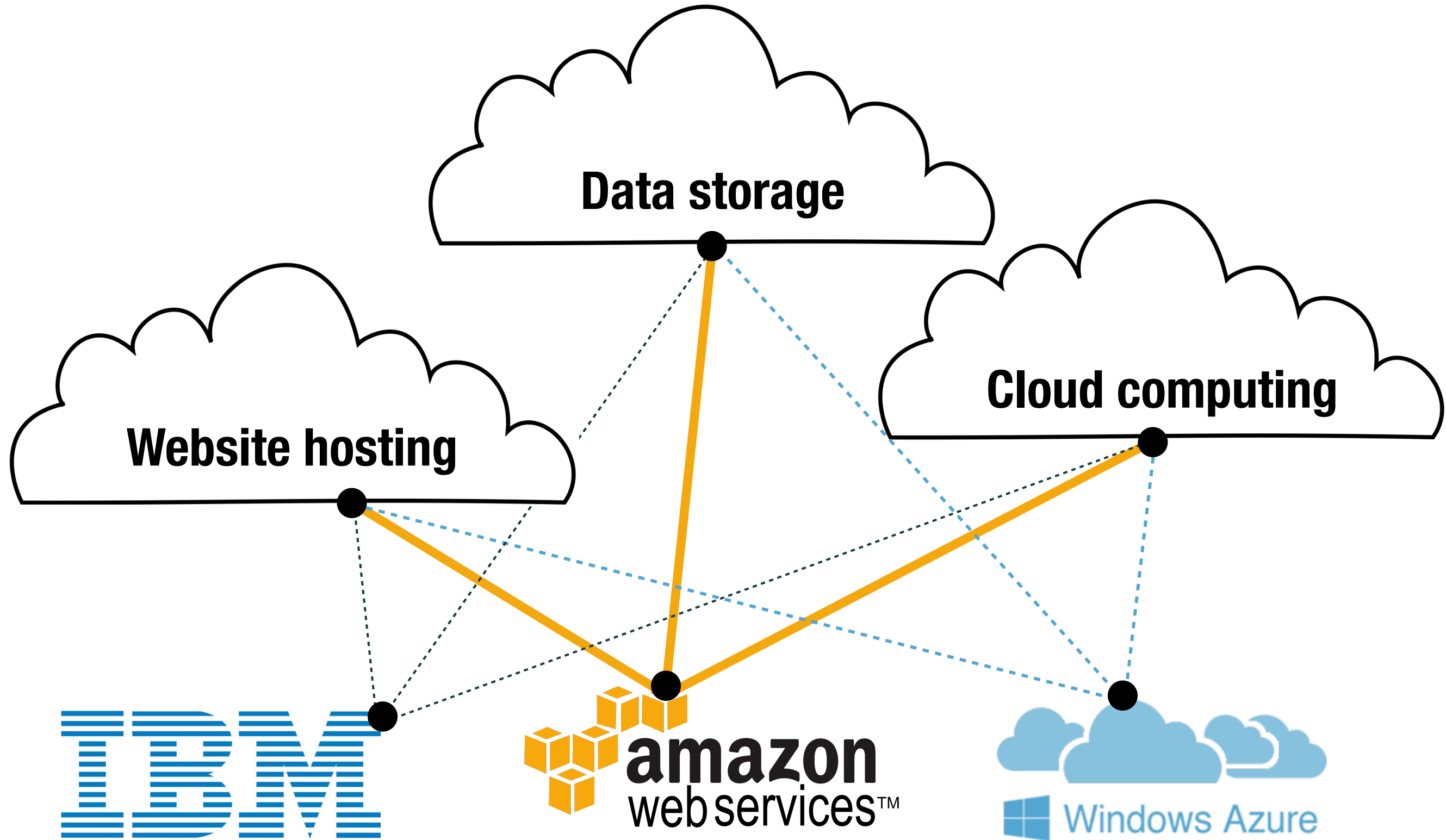
Current state of computing in cryo-EM



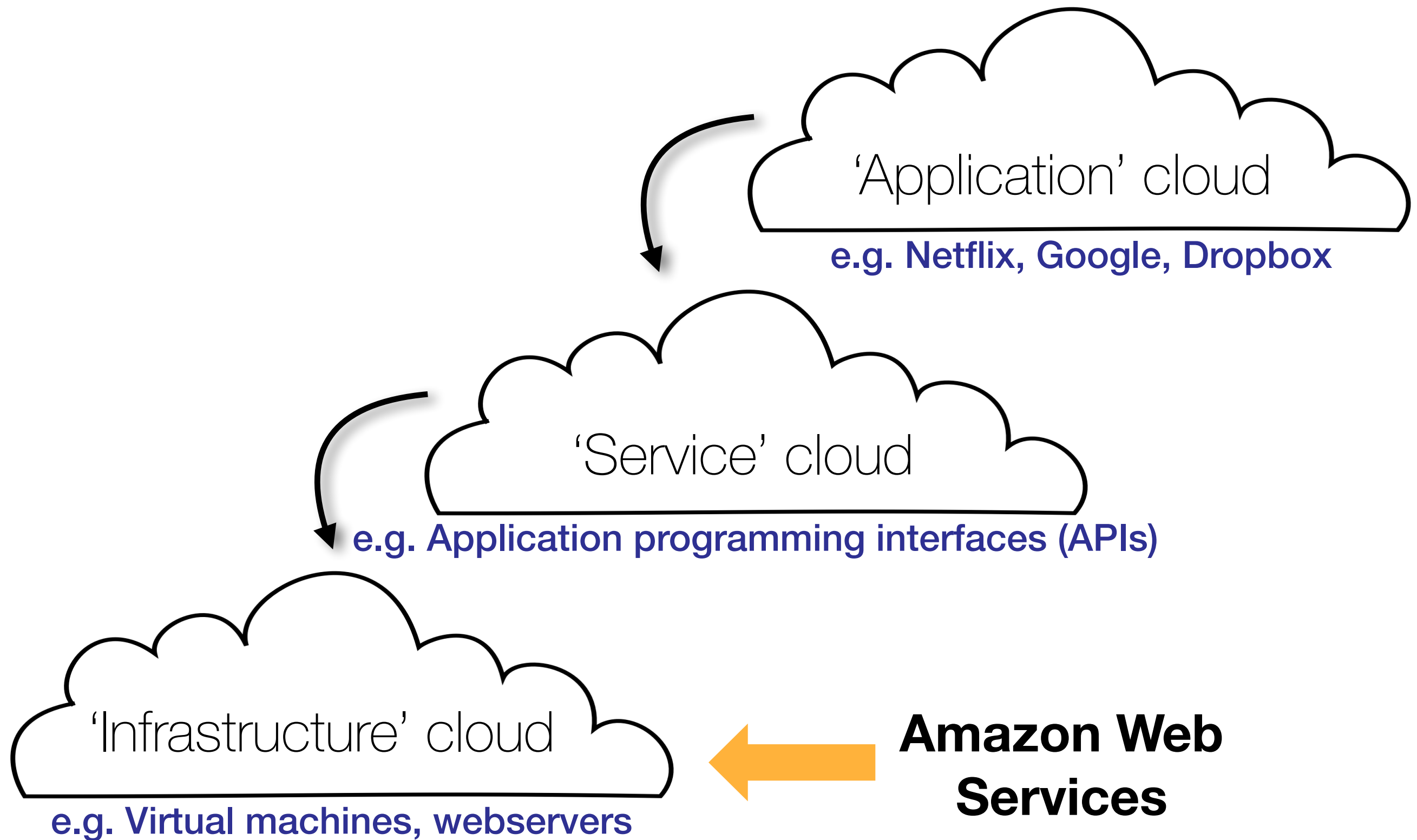
How do we scale computing and storage for cryo-EM?



The cloud is a ubiquitous feature of our daily lives



The cloud is a ubiquitous feature of our daily lives



Key principles of cloud computing

1. Cost effective

- Economies of scale
- Someone else takes care of IT hardware support
- *Pay as you go (pro-rated to the minute)*

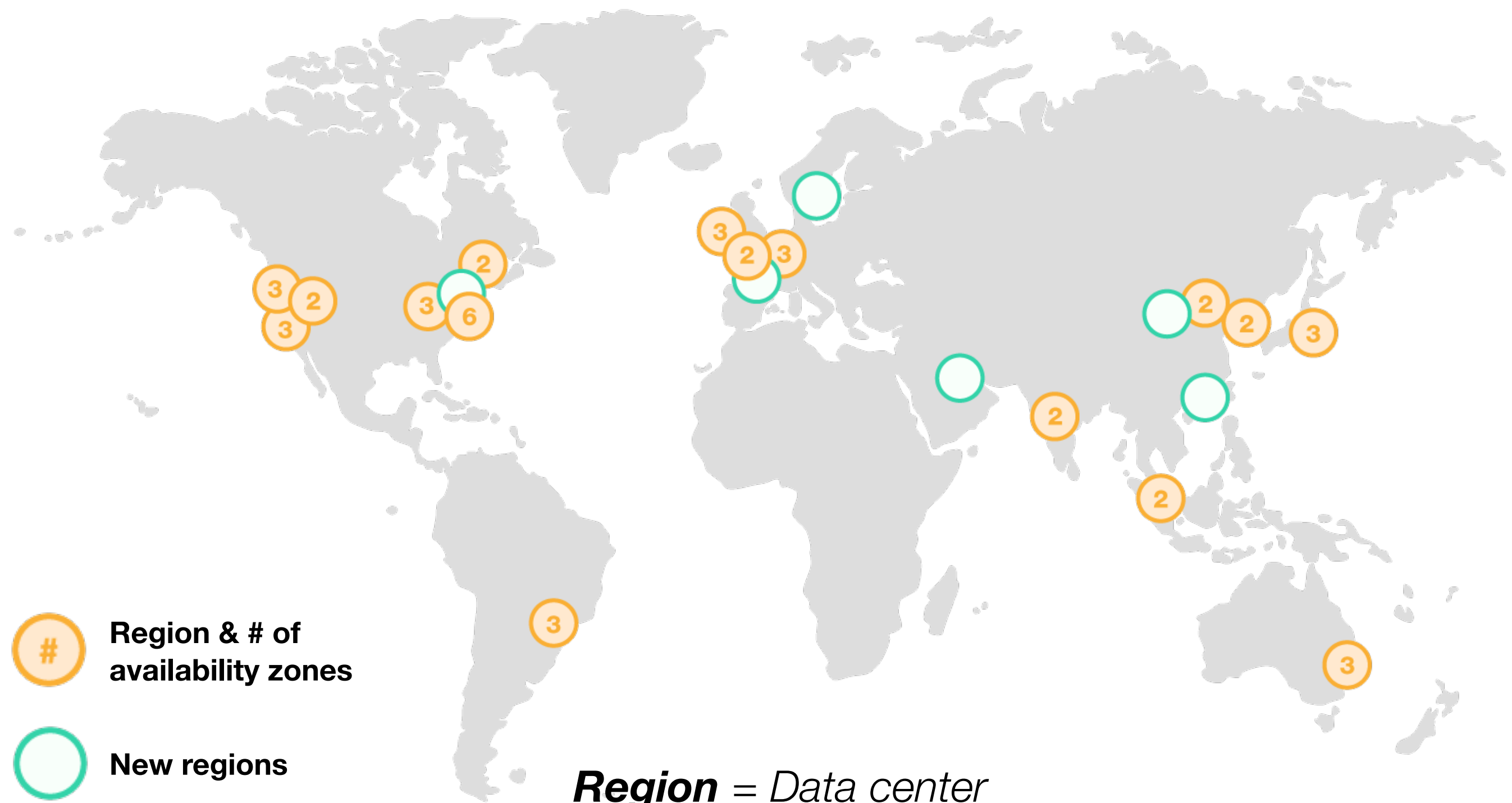
2. Reliable data storage

- Backed up offsite, multiple locations

3. Flexibility

- Global footprint
- As more computing power is needed, easy to add more
- No need to 'choose' between CPU vs GPU resources
- Instant access to hundreds of CPUs

Amazon Web Services (AWS) is the world's largest cloud provider



Region = Data center
Availability Zone = Building within data center

Computing options on AWS

Instance = virtual machine on AWS

vCPU = hyper thread on CPU core

Memory (GB RAM)

t2.nano

1 vCPU
0.5 GB RAM

c4.8xlarge

36 vCPU
60 GB RAM

g3.4xlarge

1 GPU / 16 vCPU
122 GB RAM

p2.xlarge

1 GPU / 4 vCPU
61 GB RAM

m4.16xlarge

64 vCPU
256 GB RAM

r4.16xlarge

64 vCPU
488 GB RAM

g3.8xlarge

2 GPU / 32 vCPU
244 GB RAM

p2.8xlarge

8 GPU / 32 vCPU
488 GB RAM

g3.16xlarge

4 GPU / 64 vCPU
488 GB RAM

p2.16xlarge

16 GPU / 64 vCPU
732 GB RAM

x1.32xlarge

128 vCPU
1952 GB RAM

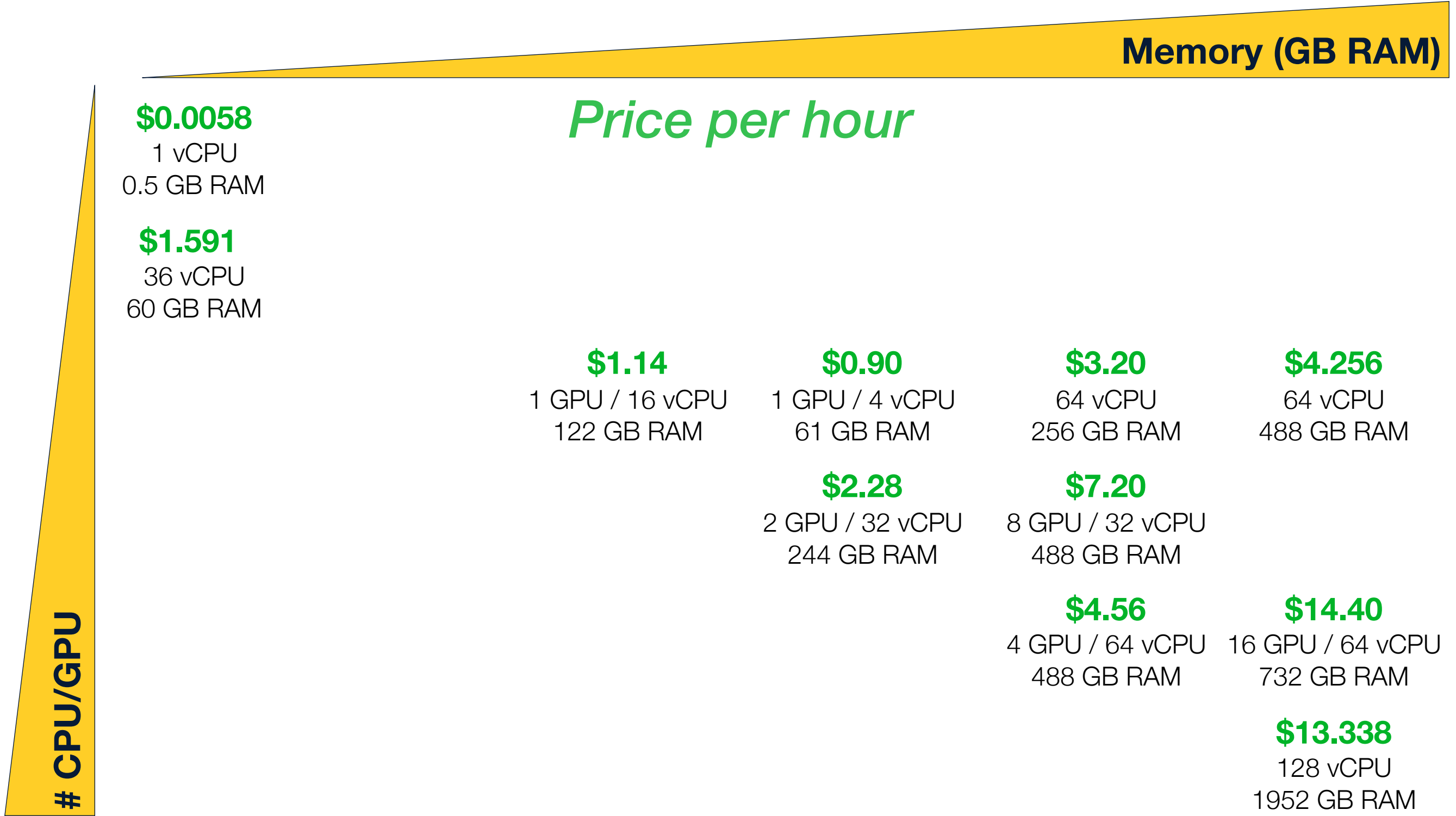
...59 total instances (48 more than shown here)

CPU/GPU



Computing options on AWS

Instance = virtual machine on AWS **vCPU** = hyper thread on CPU core



Reserving instances on AWS

Pay-per-hour

On-demand

Pay 'standard' price
Instance is 100% yours

Cheaper

Reserved

Pay 1-3 yr upfront to reserve instance
Instance is 100% yours

Cheaper

Spot

Bid on marketplace
Instance is yours until somehow outbids you

Data storage on AWS

Local SSDs

Directly attached to instance

No cost

Elastic block storage (EBS)

SSDs that can be attached/detached *\$0.10/GB/mo.*

Object storage: Scalable storage (active & cold)

Simple storage service (S3)

\$0.023/GB/mo.

Glacier

\$0.004/GB/mo.



Previously...

Problems:

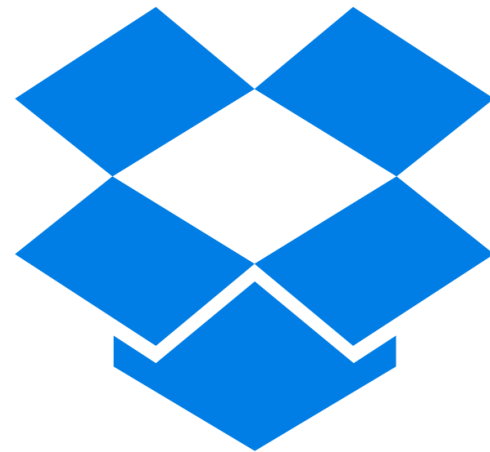
- ▶ **Manual** deployment & management of AWS resources
- ▶ **Cumbersome** data movement
- ▶ Medium/expert-level **linux experience required** to interface



Pay < \$10/hr for 150+ CPUs with spot pricing

What is the best way to use the cloud?

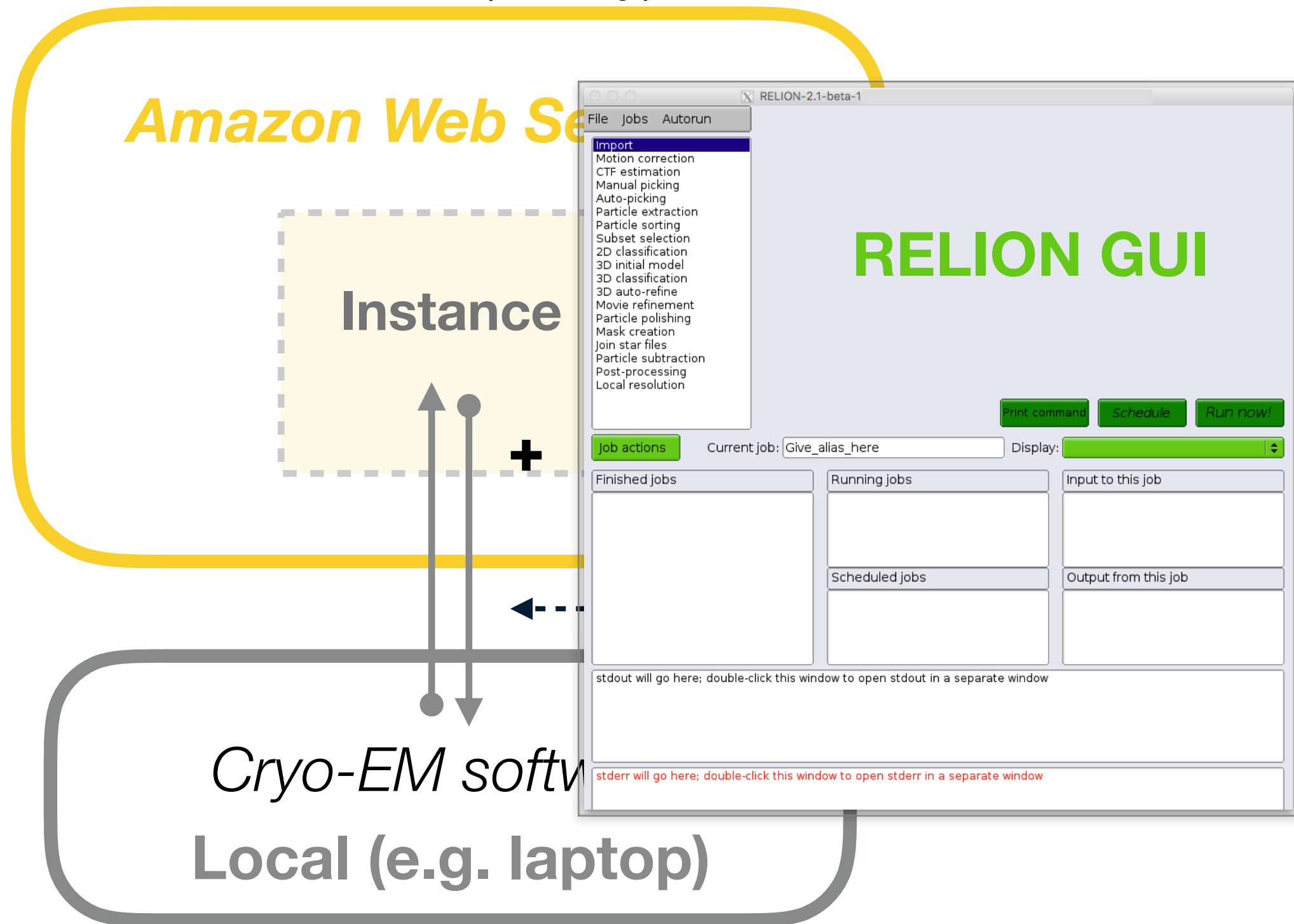
“Hybrid cloud architecture is the integration of on-premises resources with cloud resources.”



e.g. **Dropbox**

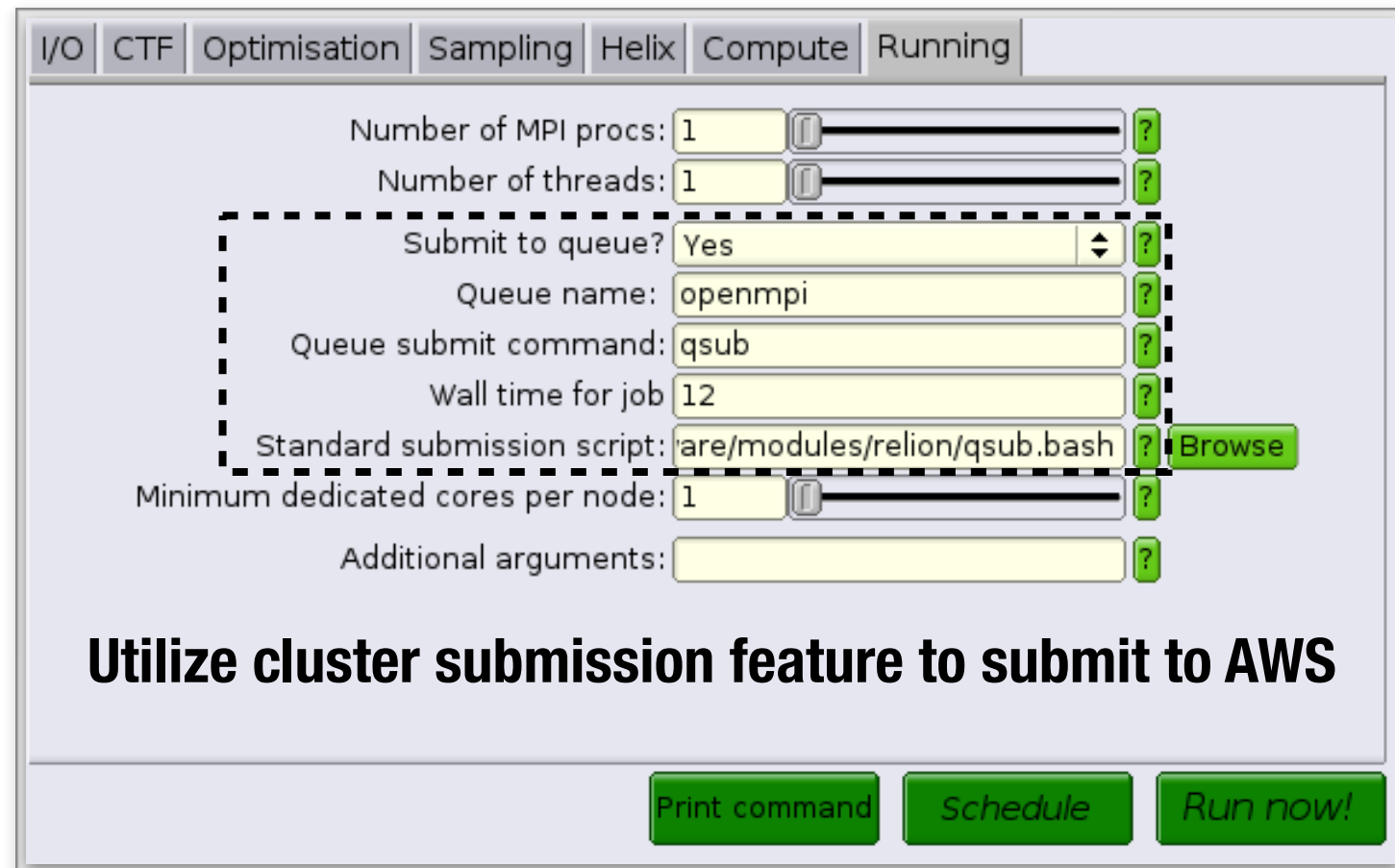
Building a hybrid cloud infrastructure for cryo-EM

RELION as a prototype



Building a hybrid cloud infrastructure for cryo-EM

RELION as a prototype



The image shows a configuration window for the RELION GUI. It features a tabbed interface with tabs for I/O, CTF, Optimisation, Sampling, Helix, Compute, and Running. The Compute tab is active, displaying various configuration options for job submission. A dashed box highlights the submission-related fields: 'Submit to queue?' (Yes), 'Queue name' (openmpi), 'Queue submit command' (qsub), 'Wall time for job' (12), 'Standard submission script' (are/modules/relion/qsub.bash), and 'Minimum dedicated cores per node' (1). Each field has a green question mark icon to its right. A 'Browse' button is next to the submission script field. At the bottom, there are three green buttons: 'Print command', 'Schedule', and 'Run now!'. Below the buttons, the text 'Utilize cluster submission feature to submit to AWS' is displayed.

Number of MPI procs: 1
Number of threads: 1
Submit to queue? Yes
Queue name: openmpi
Queue submit command: qsub
Wall time for job: 12
Standard submission script: are/modules/relion/qsub.bash
Minimum dedicated cores per node: 1
Additional arguments:

Utilize cluster submission feature to submit to AWS

Print command Schedule Run now!



The image shows the main window of the RELION GUI. The title bar indicates the version is RELION-2.1-beta-1. The menu bar includes File, Jobs, and Autorun. A list of job actions is visible on the left, including Import, Motion correction, CTF estimation, Manual picking, Auto-picking, Particle extraction, Particle sorting, Subset selection, 2D classification, 3D initial model, 3D classification, 3D auto-refine, Movie refinement, Particle polishing, Mask creation, Join star files, Particle subtraction, Post-processing, and Local resolution. The main area displays 'RELION GUI' in large green letters. Below this, there are buttons for 'Print command', 'Schedule', and 'Run now!'. A 'Job actions' button is also present. The 'Current job' field is set to 'Give_alias_here', and the 'Display' dropdown is set to 'stdout'. The window is divided into several panes: 'Finished jobs', 'Running jobs', 'Input to this job', 'Scheduled jobs', and 'Output from this job'. The 'stdout' pane shows the text 'stdout will go here; double-click this window to open stdout in a separate window'. The 'stderr' pane shows the text 'stderr will go here; double-click this window to open stderr in a separate window'.

RELION GUI

Print command Schedule Run now!

Job actions Current job: Give_alias_here Display: stdout

Finished jobs Running jobs Input to this job

Scheduled jobs Output from this job

stdout will go here; double-click this window to open stdout in a separate window

stderr will go here; double-click this window to open stderr in a separate window

Building a hybrid cloud infrastructure for cryo-EM

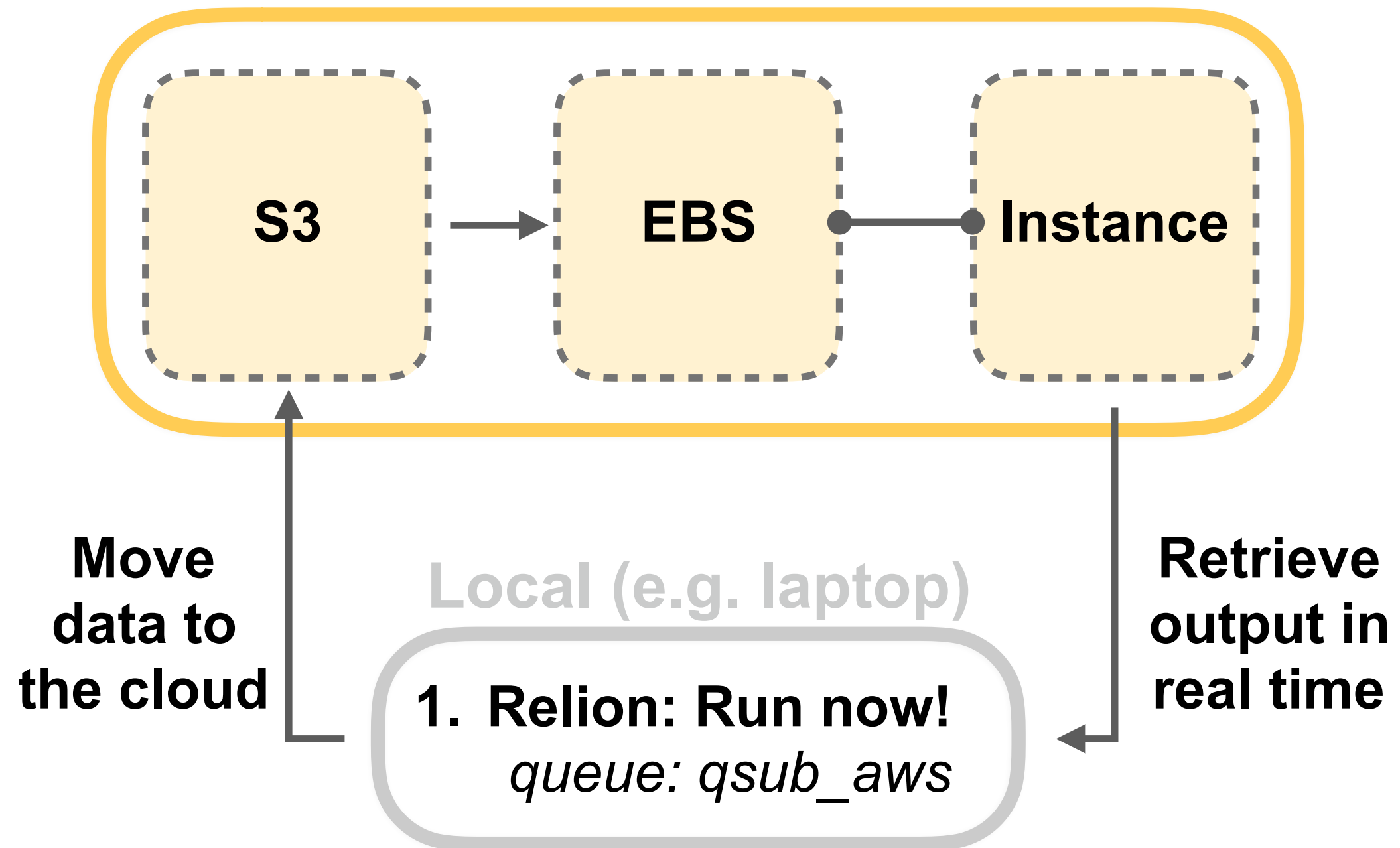
RELION as a prototype

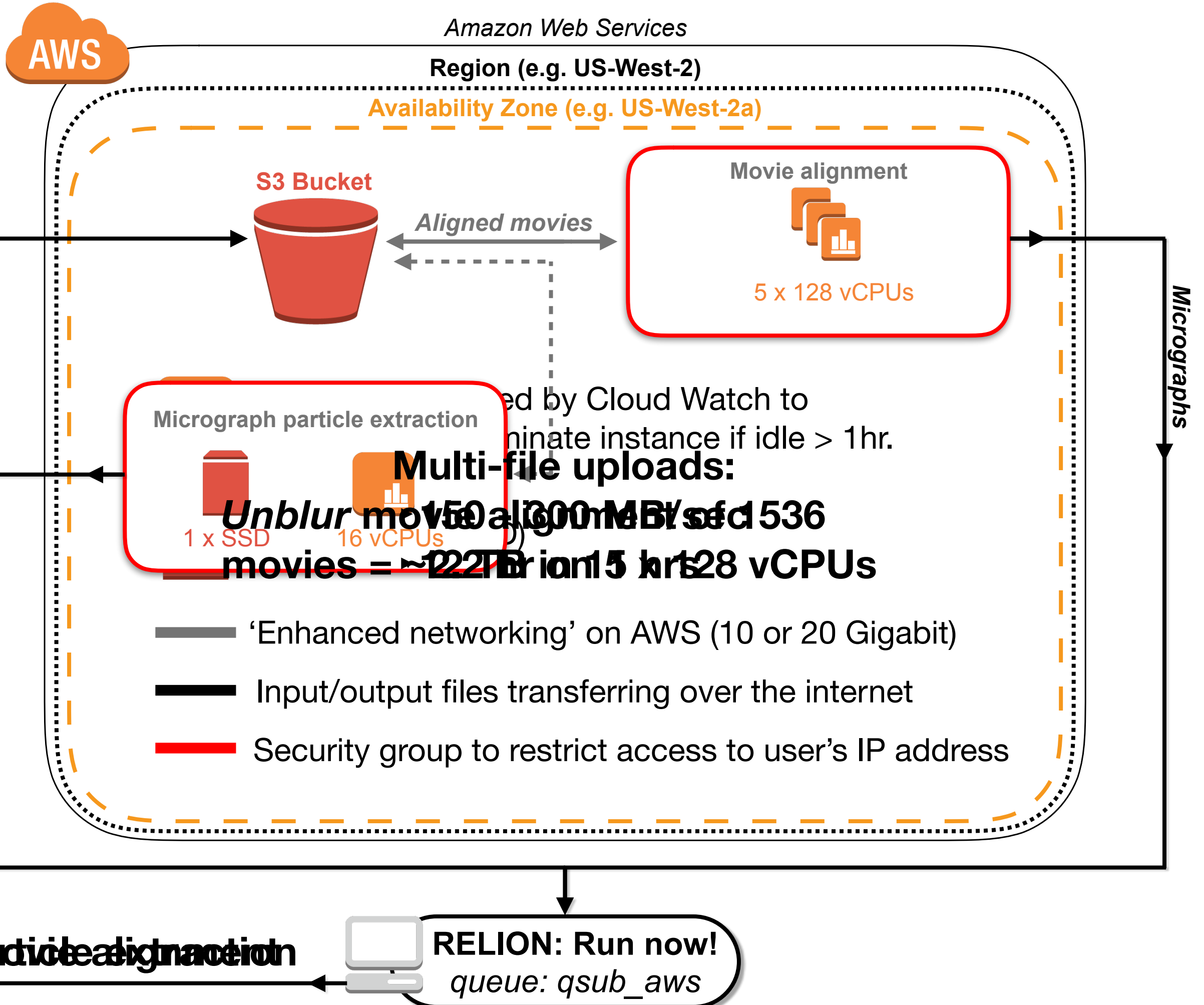


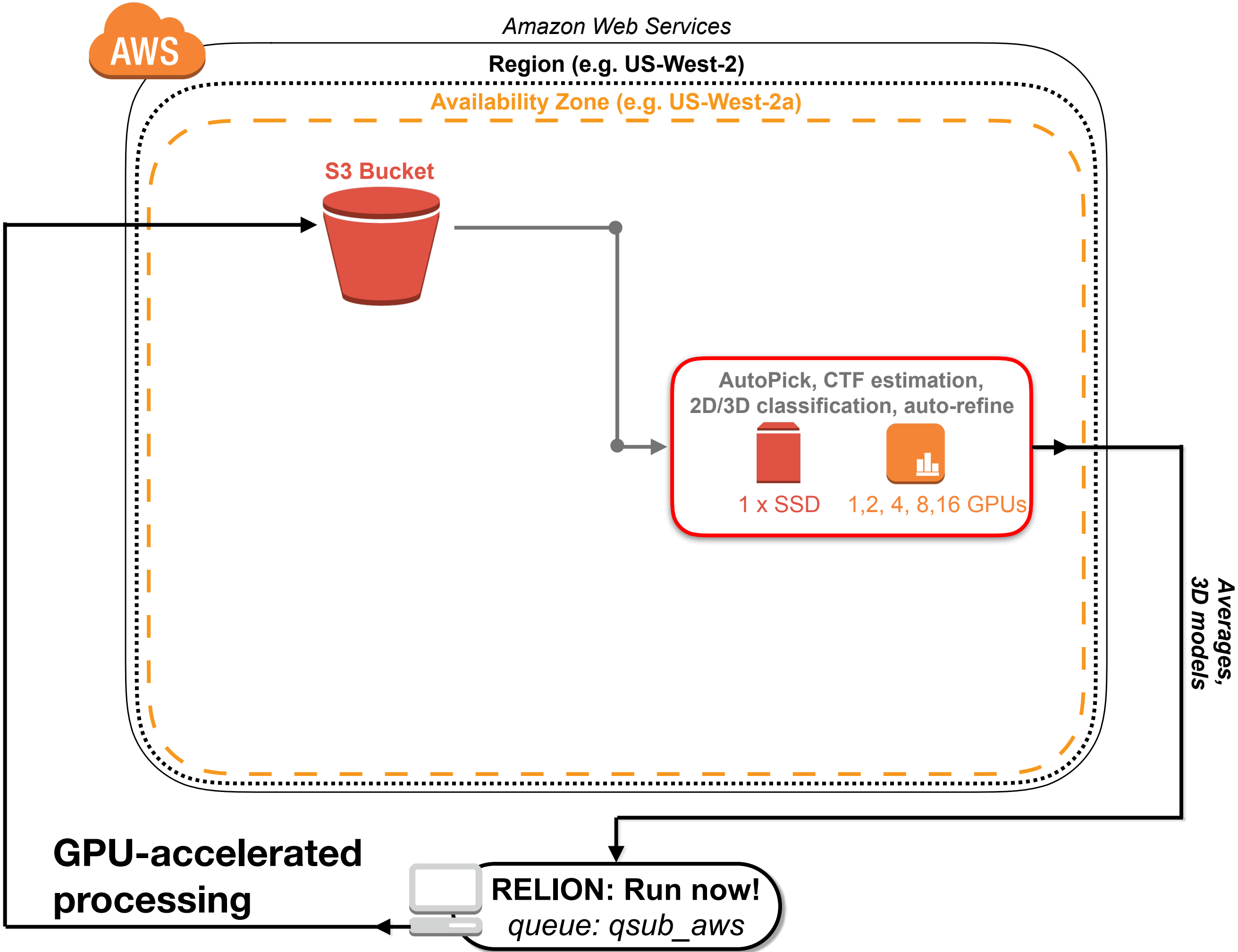
Implement for all jobtypes

cryoem-cloud-tools: software to run cryo-EM on the cloud

Amazon Web Services









Amazon Web Services

Region (e.g. US-West-2)

Availability Zone (e.g. US-West-2a)

S3 Bucket



Movie particle
extraction



8 x 36 vCPUs
42 TB / instance

Movie
refinement



1 x 128 vCPUs

Particle polishing



1 x 128 vCPUs

Particles

Movie processing



RELION: Run now!

queue: qsub_aws



Amazon Web Services

Region (e.g. US-West-2)

Availability Zone (e.g. US-West-2a)

S3 Bucket



Movie alignment



5 x 128 vCPUs

Micrograph particle extraction



1 x gp2 SSD



16 vCPUs

AutoPick, CTF estimation,
2D/3D classification, auto-refine



1 x gp2 SSD



1,8,16 GPUs

Movie particle
extraction



8 x 36 vCPUs
42 TB / instance

Movie
refinement



1 x 128 vCPUs

Particle polishing



1 x 128 vCPUs

Particles

Micrographs

Averages,
3D models

Particles



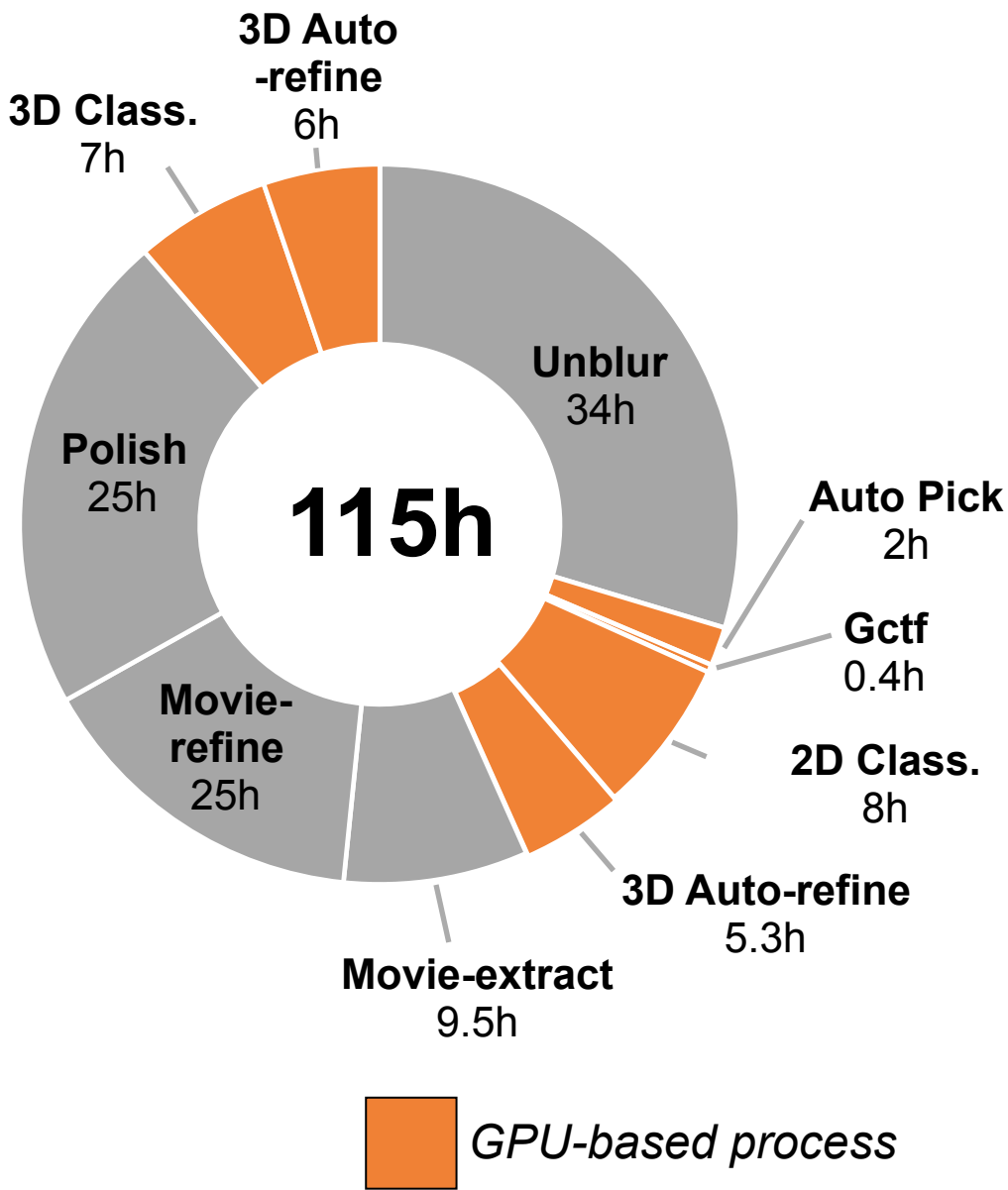
RELION: Run now!

queue: qsub_aws

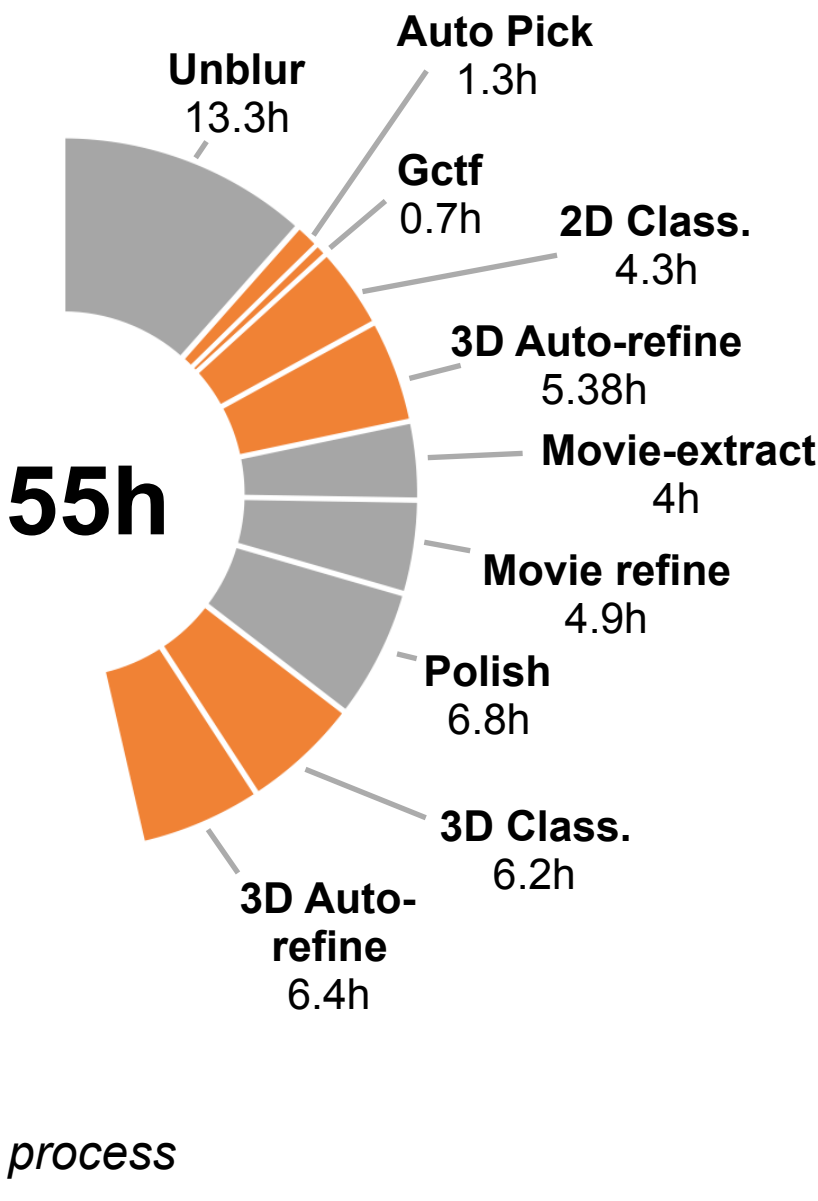
Comparison of AWS vs. local GPU workstation for RELION2

Comparing 2.2 Å beta-galactosidase dataset (EMPIAR 10061)

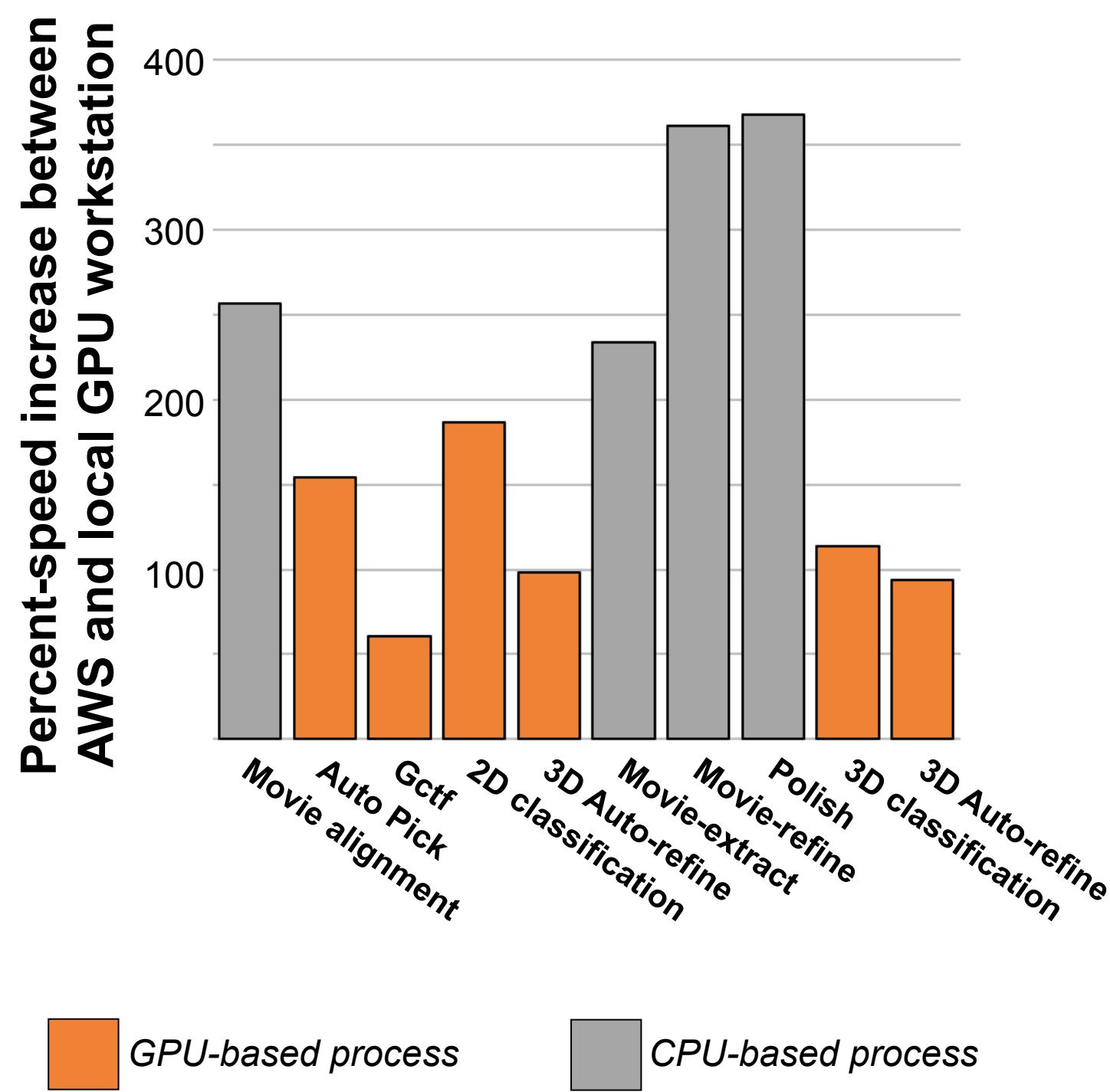
GPU workstation (Kimanius et al.)



AWS

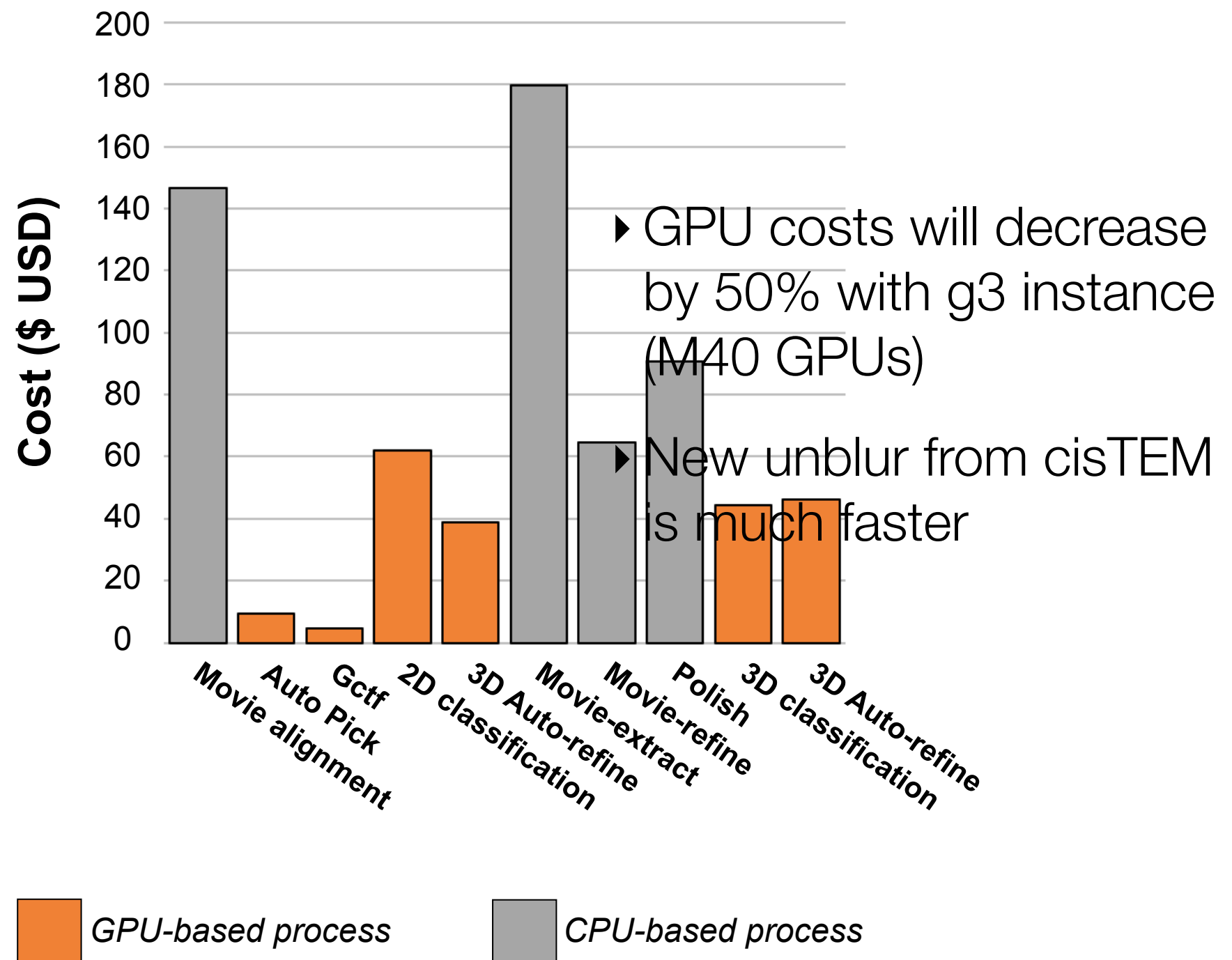


Comparison of AWS vs. local GPU workstation for RELION2



Cost breakdown of AWS

Total computing cost: \$688.15

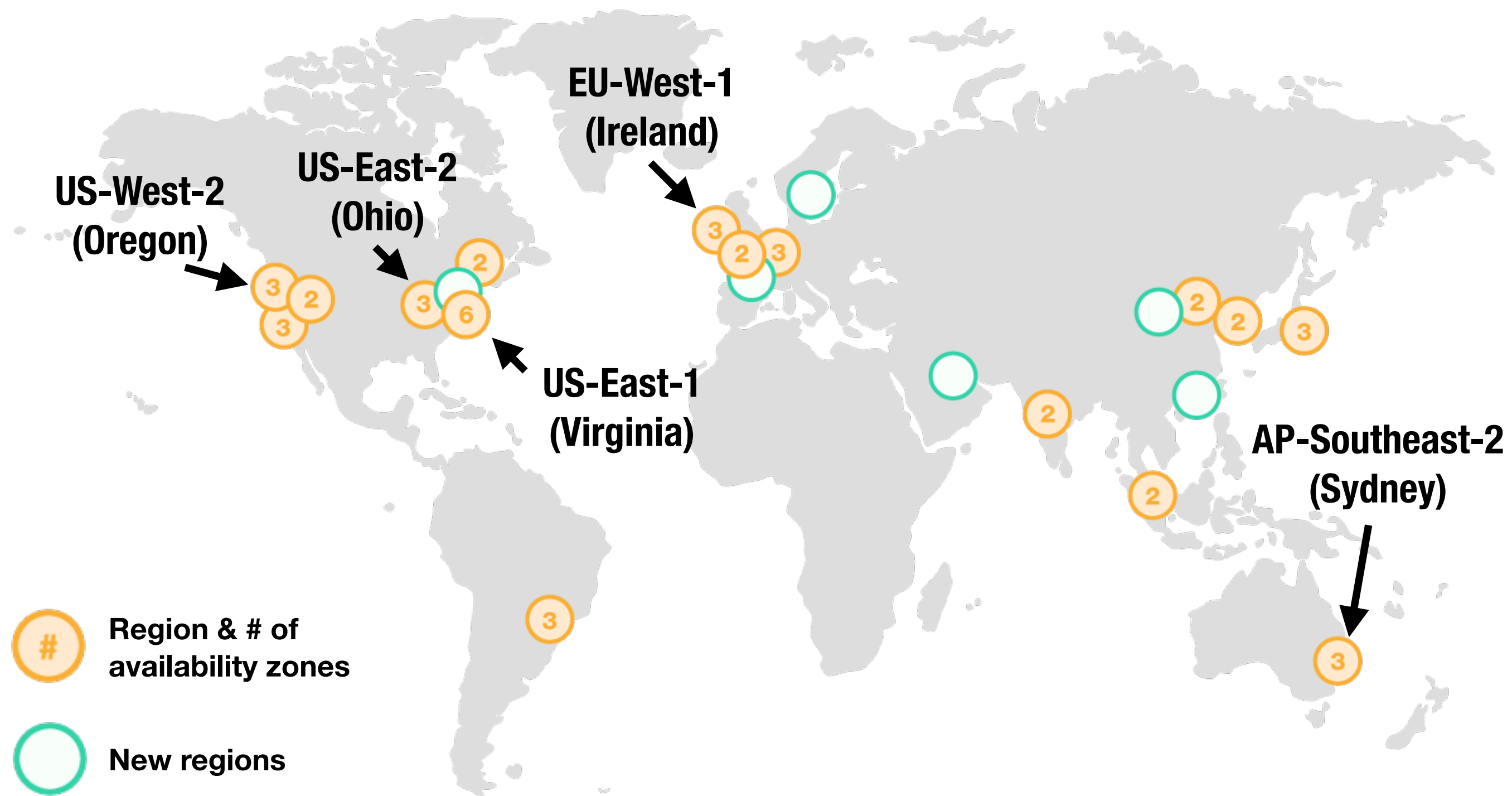


Cost comparison between AWS and local GPU workstation

	AWS	Local GPU workstation
Computing costs*	\$688.17	\$72.45
Processing time (h)	55	115
Number of working days	5	10

**For local GPU workstation, \$10,000 workstation cost = \$0.63/hr (60% utilization).*

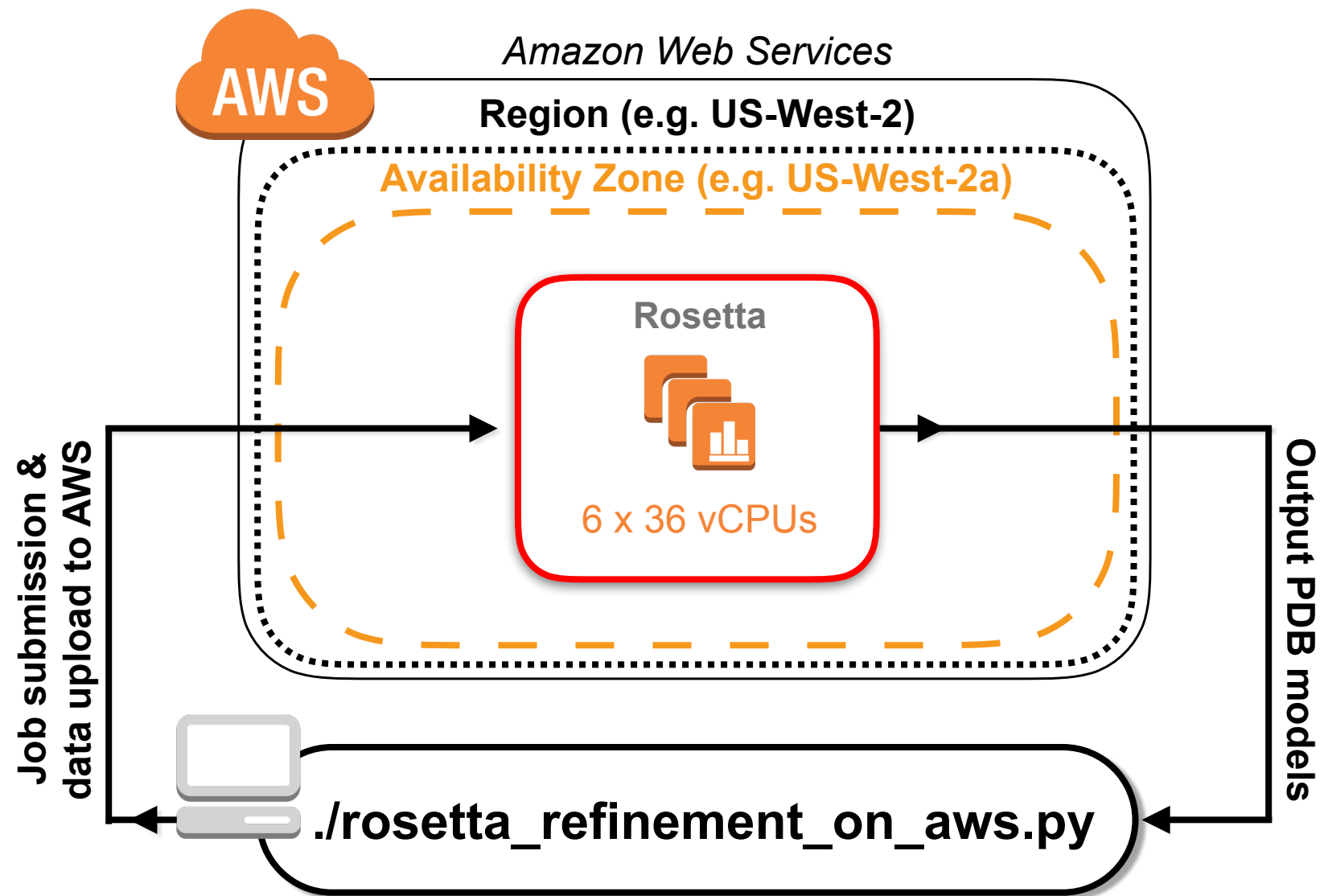
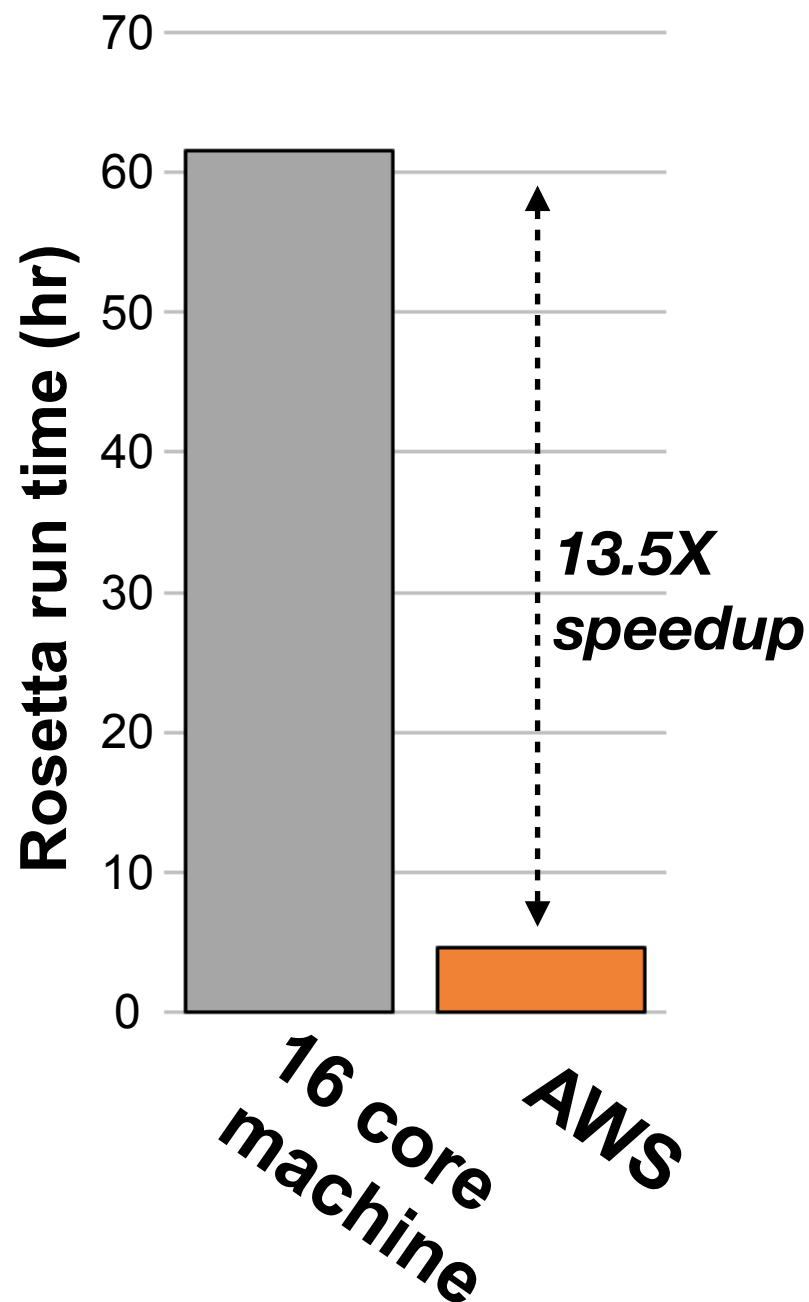
Global footprint of *cryoem-cloud-tools*



Tracking with expanding GPU availability on AWS

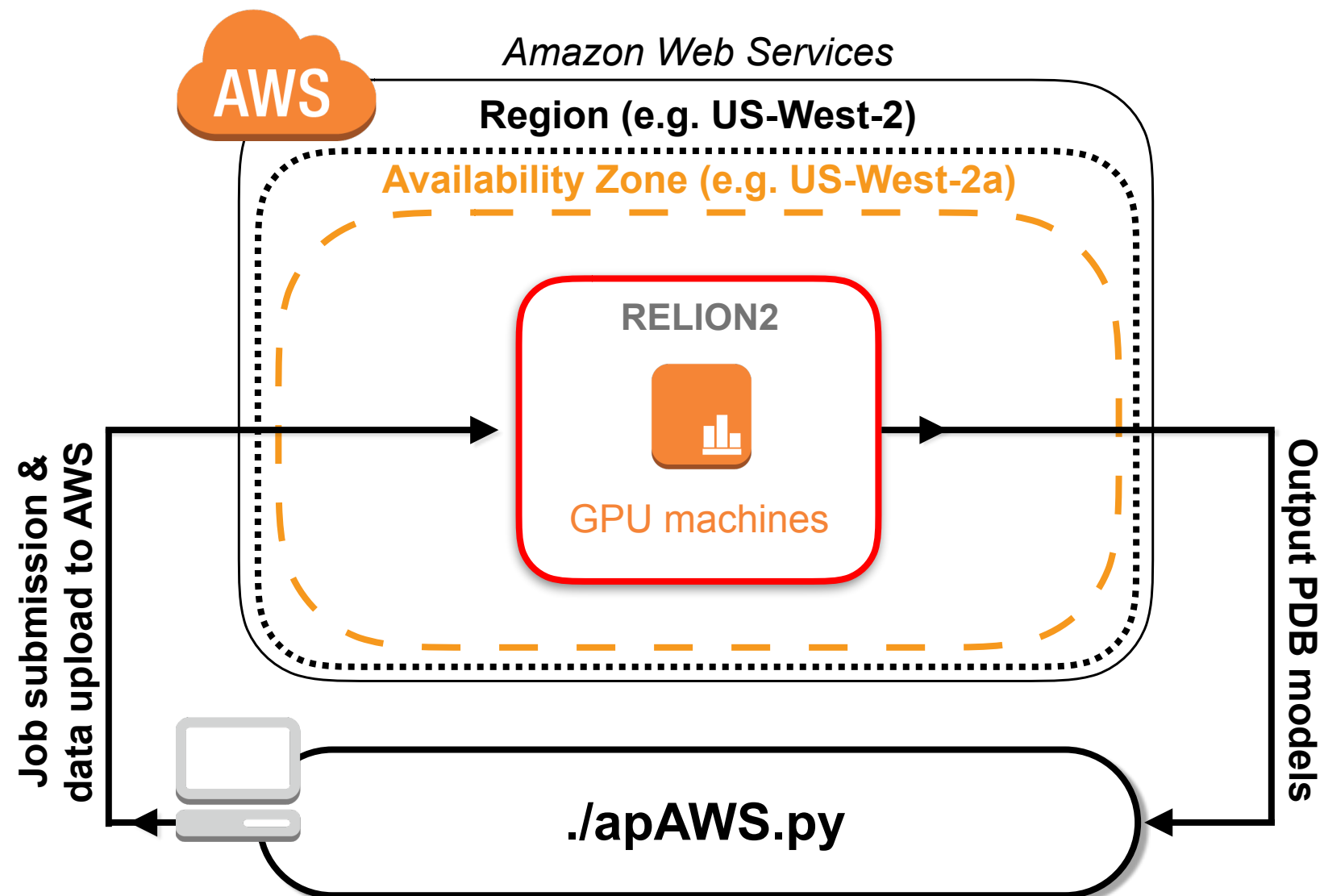
Extending *cryoem-cloud-tools*: Rosetta on AWS

216 structures for each CM & Relax into 2.2 Å beta-galactosidase



Total AWS Cost: \$43.60

Extending *cryoem-cloud-tools*: Appion on AWS



Extending *cryoem-cloud-tools*: Appion on AWS



Relion 2D Maximum Likelihood Alignment in AWS

Project: SEMC - Aldolase (381)
Session: 17sep21j - aldolase 1.2/1.3 ultraAufoil (130K image shift, krios2 k2)
Image Path: /gpfs/legion/lkim/17sep21j/rawdata

Hide | Expand | Contract

- ▼ **Object Selection : 3**
 - Select Particle Picker...
3 complete
 - Repeat an image loop run
- ▼ **CTF Estimation**
 - Estimate the CTF...
3 complete
1 running
 - Transfer results to another preset
 - Repeat an image loop run
- ▼ **Stacks : 18**
 - Stack Creation...
23 complete
- ▼ **Particle Alignment**
 - Select Particle Alignment...
11 complete
 - Run Feature Analysis...
 - Run Particle Clustering...
 - Run MaskItOn
 - Template Stacks
- ▼ **Ab Initio Reconstruction**
 - EMAN Common Lines
 - SIMPLE Common Lines
 - ▼ Refine Reconstruction

Run name

Output directory

Description

Stack Selection

Select a stack of particles to use

qstack10 ID: 98 (57,644 particles, 1.70 Å/pix, 96x96) (Relion Stack) ▾

Select AWS Instance type

Amazon GPU Instance type

✓ Select instance type

- p2.xlarge (1 GPU, \$0.90/hour)
- p2.8xlarge (8 GPU's, \$7.20/hour)
- p2.16xlarge (16 GPU's, \$14.40/hour)
- g3.8xlarge (2 GPU's, \$2.28/hour)
- g3.16xlarge (4 GPU's, \$4.56/hour)
- p3.2xlarge (1 GPU, \$3.06/hour)
- p3.8xlarge (4 GPU, \$12.24/hour)
- p3.16xlarge (8 GPU, \$24.48/hour)

96 Unbinned Clip Diameter (pixels)

1 Particle Binning

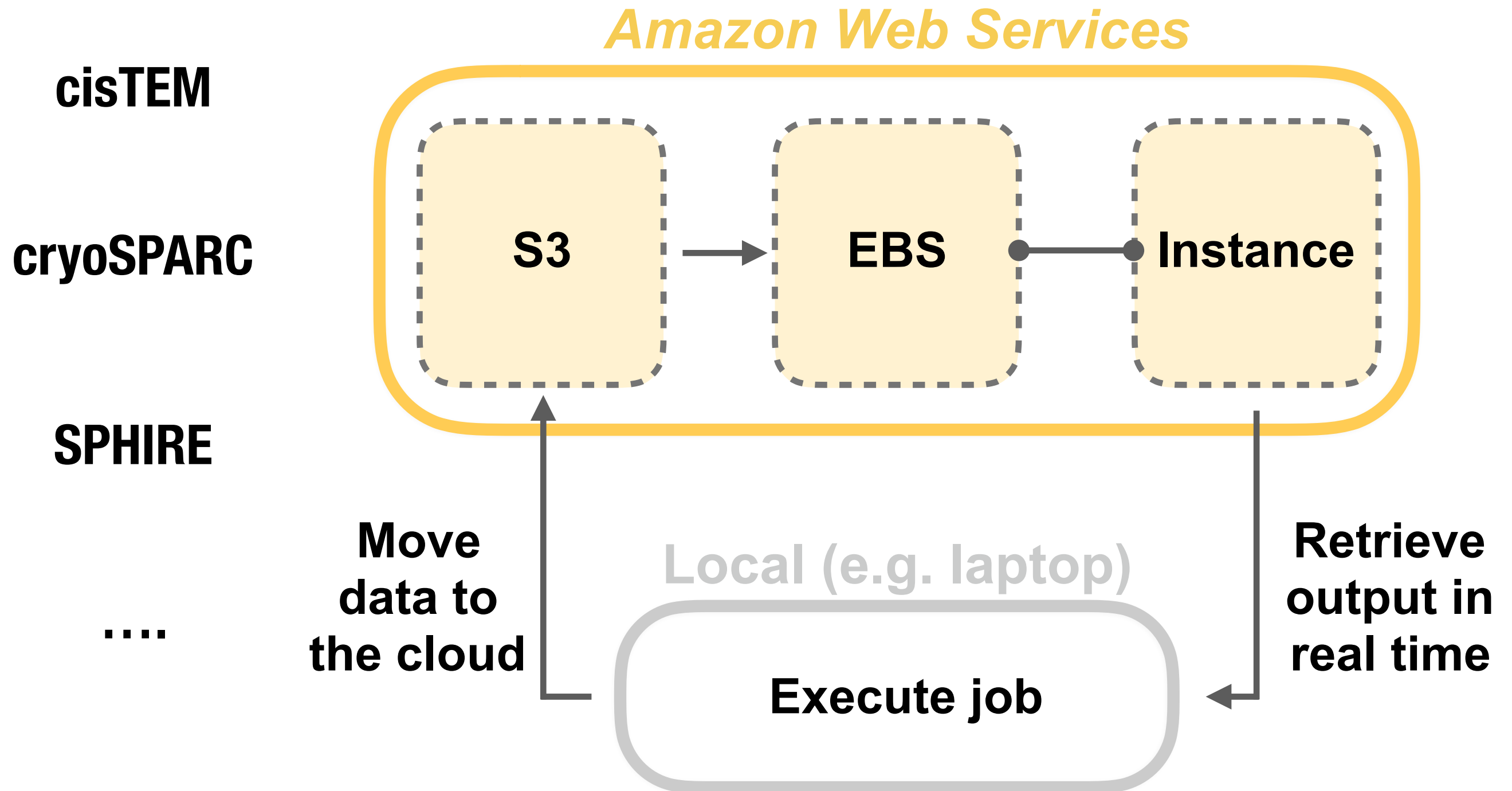
5764 Number of Particles

Filters

(Ignore these parameters when using a Relion Stack)



Extending *cryoem-cloud-tools*: Future directions



Take-home points

Is the cloud useful for cryo-EM?

Yes - the cloud offers the following features:

- 1) Outsourcing of IT administration
- 2) Large choice of computing configurations
- 3) Active & cold data storage options

What types of resources are at the disposal of users?

Small to large CPU/GPU systems.

What are the appropriate workflows and benchmark comparisons?

Benchmarking can be found online at cryoem-tools.cloud under the RELION2 section of AWS

Punchline: There are many types of GPU machines to satisfy all types of RELION2 computing tasks

Take-home points

How does the cost compare to local infrastructure?

Per hour - these machines are more expensive than simply buying a standalone workstation. But, standalone workstations don't come with back up storage.

Example storage quote:

\$200/TB/year -> \$0.0167/GB/mo. (S3: \$0.023/GB/mo.) WITHOUT IT support

When should someone use the cloud?

- 1) Whenever someone is waiting for computing time. For RELION, 4xGPU machines cost \$4.56/hr to run, which is much less than the hour wage of individuals working in the lab
- 2) Large facilities - the cloud lets users launch jobs from a single point of contact and can expand (seemingly) indefinitely
- 3) Need to solve successive structures under time limit



Questions?

cryoem-tools.cloud

***Demo of cryoem-cloud-tools @
Thursday breakout session***

Take-home points

Cloud for software dissemination

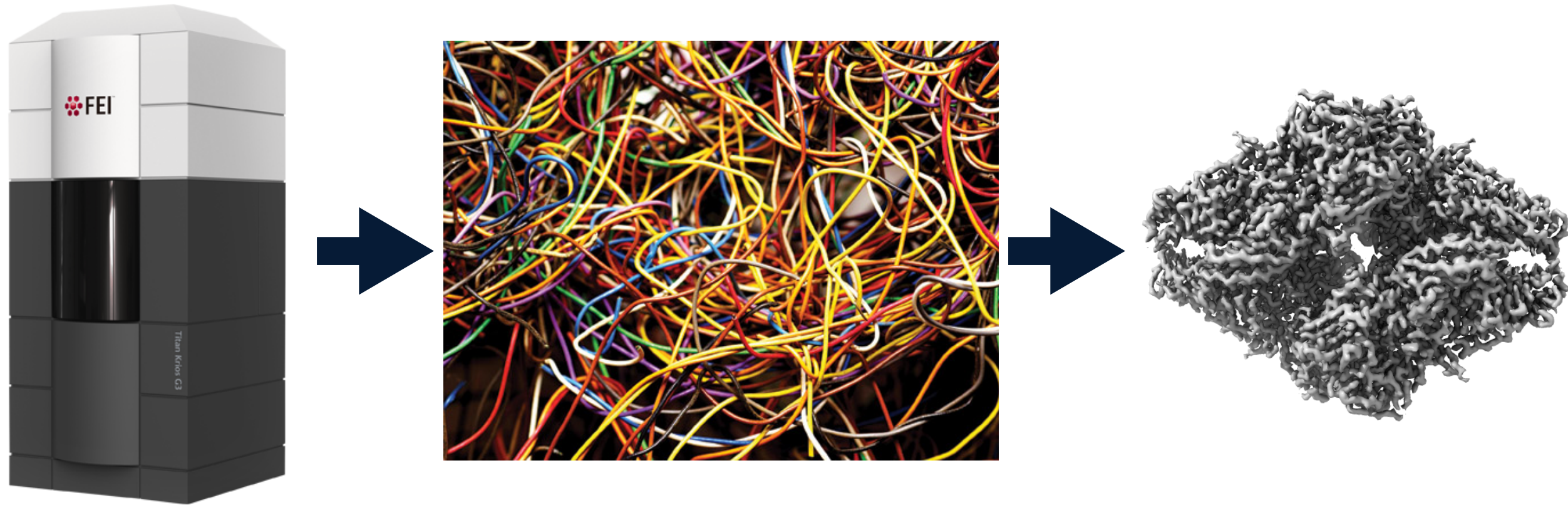
No need to be pigeon-holed into a single setup

‘Hybrid’ architectures will have the biggest impact on the field - end users don't need to see the backend of AWS

Platform for plugging in new analysis (e.g. ML)

Underlying data movement tools > agnostic to cloud; could be adapted for anywhere

What do we need?

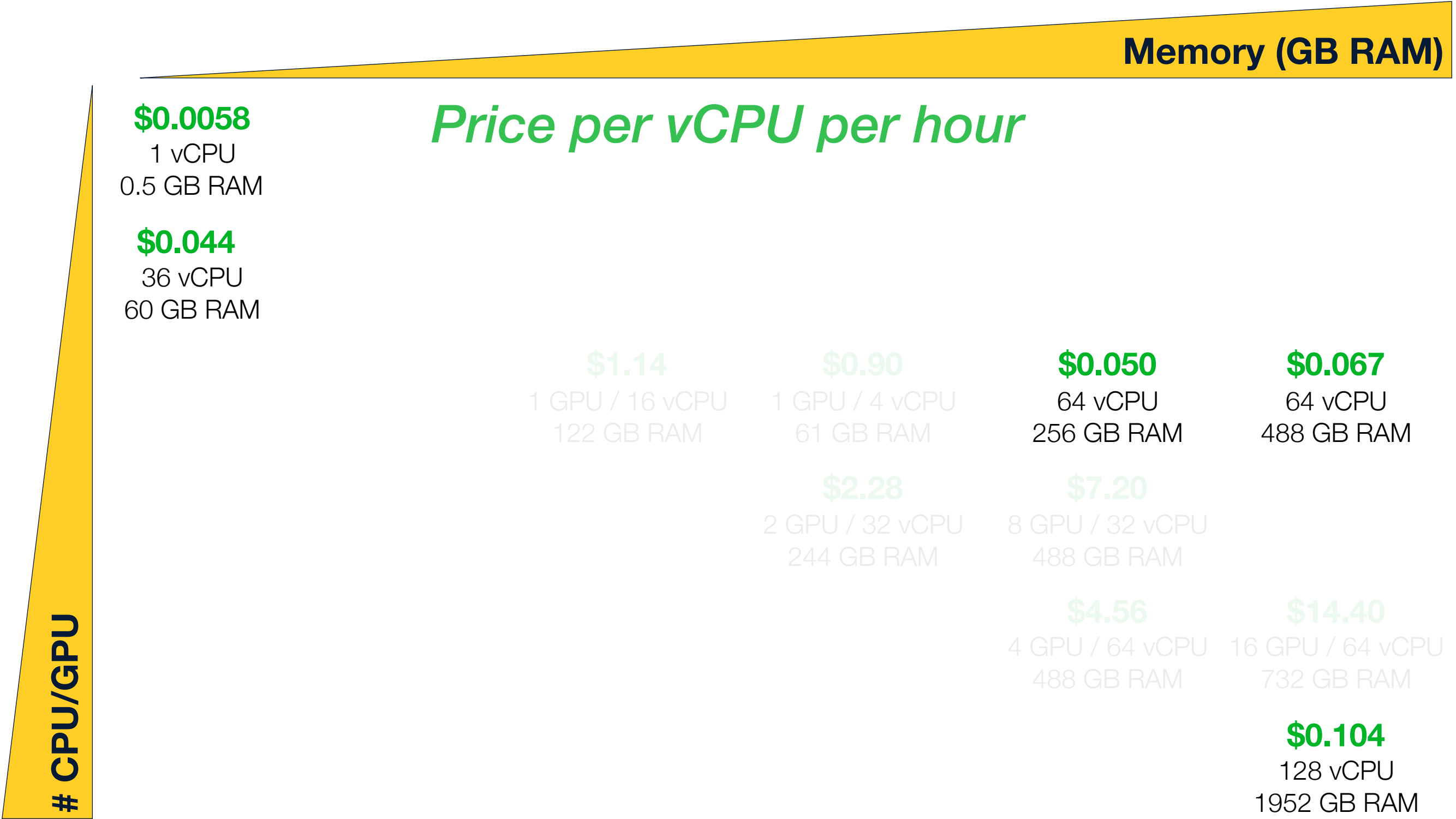


On-the-fly data movement, analysis, and storage as movies are collected

✓ For *all* users who use facility

Computing options on AWS

Instance = virtual machine on AWS **vCPU** = hyper thread on CPU core



Computing options on AWS

Instance = virtual machine on AWS

vCPU = hyper thread on CPU core

Memory (GB RAM)

Price per GPU per hour

\$0.0058

1 vCPU
0.5 GB RAM

\$1.591

36 vCPU
60 GB RAM

\$1.14

1 GPU / 16 vCPU
122 GB RAM

\$0.90

1 GPU / 4 vCPU
61 GB RAM

\$3.20

64 vCPU
256 GB RAM

\$4.256

64 vCPU
488 GB RAM

\$1.14

2 GPU / 32 vCPU
244 GB RAM

\$0.90

8 GPU / 32 vCPU
488 GB RAM

\$1.14

4 GPU / 64 vCPU
488 GB RAM

\$0.90

16 GPU / 64 vCPU
732 GB RAM

x1.32xlarge

128 vCPU
1952 GB RAM

CPU/GPU



	GPU Workstation					Amazon Web Services							
	Total processing time (hr)	Estimated elapsed time (working days)^	Number of GPUs	Number of CPU cores	Amount of RAM (GB)	Total processing time (hr)	Estimated elapsed time (working days)^	Data moving time (hr)	Job running time (hr)	EC2 Cost (USD)*	Number of VMs	VM type	VM cost per hour (USD)
Movie alignment	34.0	1	4	8	64	13.26	1	11.06	2.20	\$146.72	5	x1.32xlarge	\$13.34
Autopick	2.0	3	4	8	64	1.30	2	1.10	0.20	\$9.36	1	p2.8xlarge	\$7.20
CTF Estimation	0.4	3	4	8	64	0.66	2	0.55	0.11	\$4.75	1	p2.8xlarge	\$7.20
Extract	-	3	4	8	64	1.30	2	0.68	0.62	\$1.04	1	m4.4xlarge	\$0.80
2D classification	8.0	3	4	8	64	4.30	2	0.17	4.13	\$61.92	1	p2.16xlarge	\$14.40
3D autorefine	5.3	4	4	8	64	5.38	2	0.08	5.30	\$38.74	1	p2.8xlarge	\$7.20
Movie extract	9.5	4	4	8	64	4.07	3	3.35	0.72	\$179.73	8	d2.8xlarge	\$5.52
Movie-refine	17.5	5	4	8	64	4.85	3	0.75	4.10	\$64.69	1	x1.32xlarge	\$13.34
Polish	25.0	7	4	8	64	6.80	3	1.40	5.40	\$90.70	1	x1.32xlarge	\$13.34
3D classification	7.0	8	4	8	64	6.17	4	0.17	6.00	\$44.42	1	p2.8xlarge	\$7.20
3D autorefine	6.0	8	4	8	64	6.40	4	0.10	6.30	\$46.08	1	p2.8xlarge	\$7.20
Rosetta	N/A	9	4	8	64		5				6	c4.8xlarge	\$1.59
S3 storage cost#	-	-	-	-	-	-	-	-	-	\$690.00	-	-	-
Totals	114.7	10	-	-	-	54.5	5	19.4	35.1	\$1,378.15	-	-	-

