Smart EPU

Workshop on Smart Data Collection for CryoEM, 6-7 April 2022

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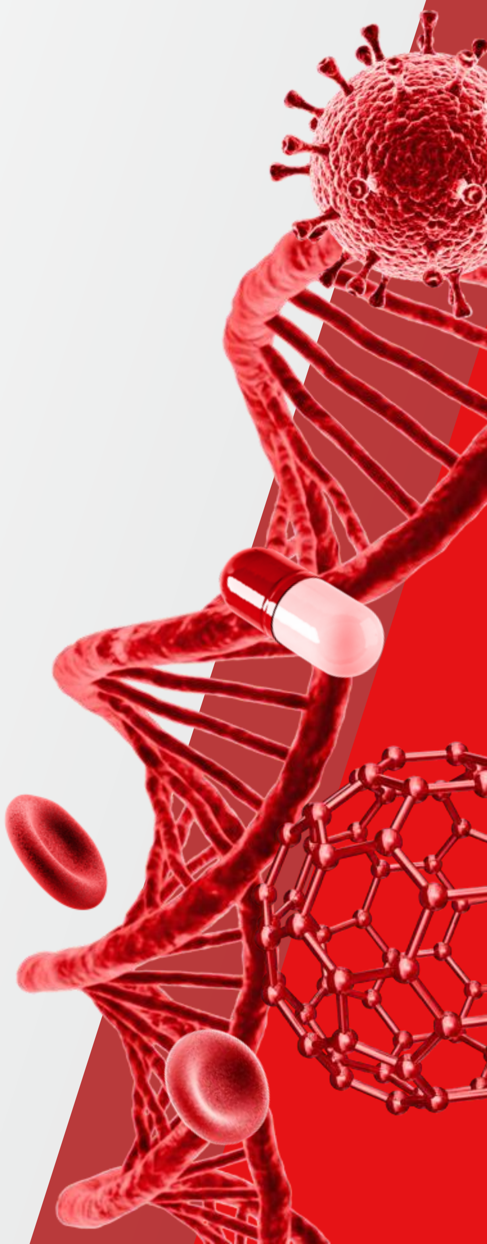
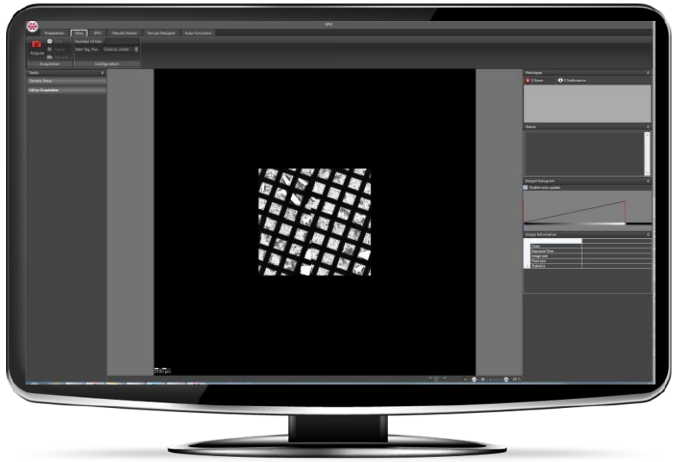
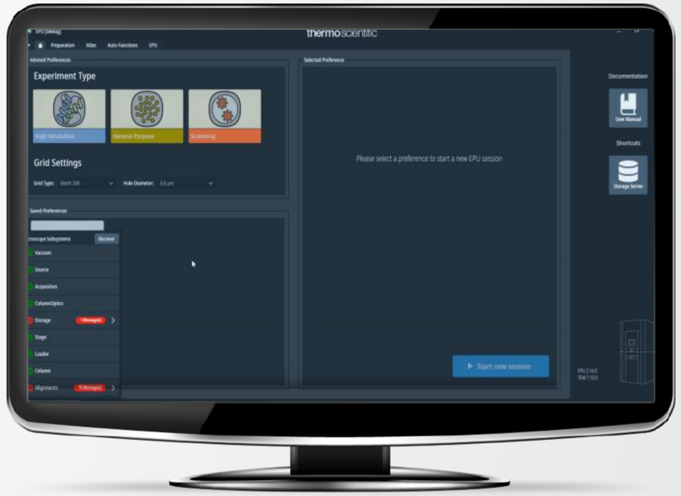


Smart EPU– How did we get here?





EPU 1.0

(2011-2018)

Enabling SPA

EPU 2.0

(2018-2022)

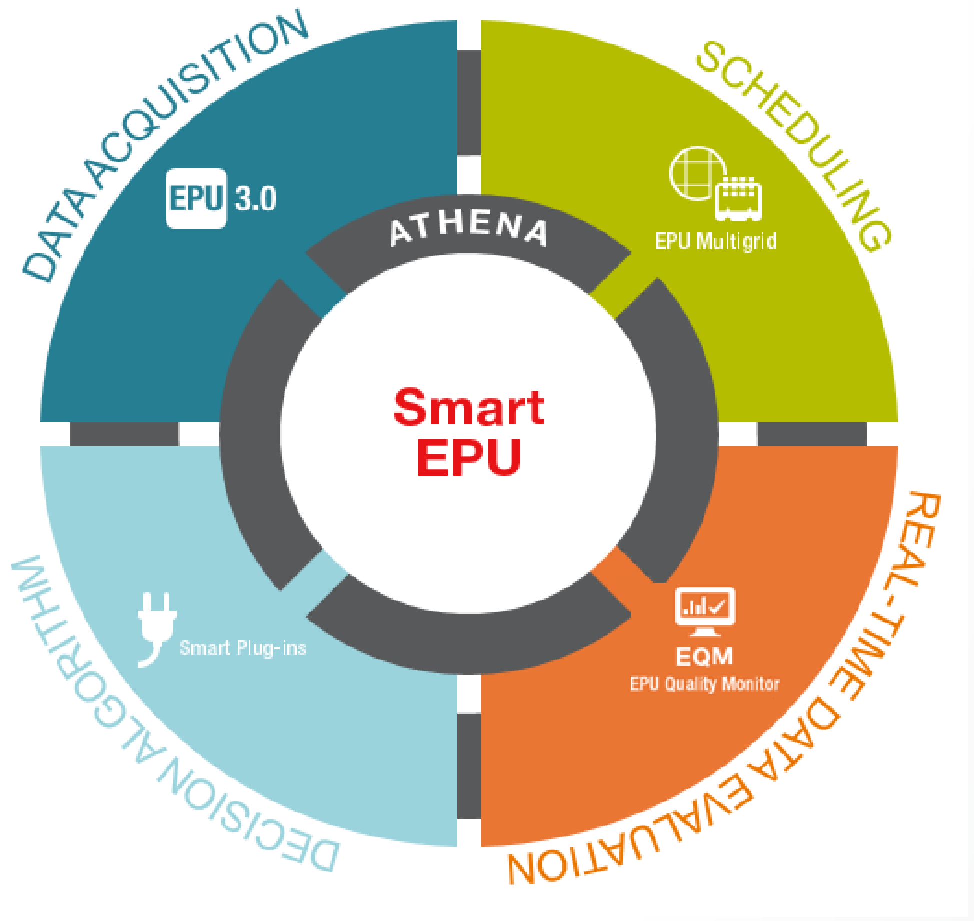
Easier and more efficient SPA

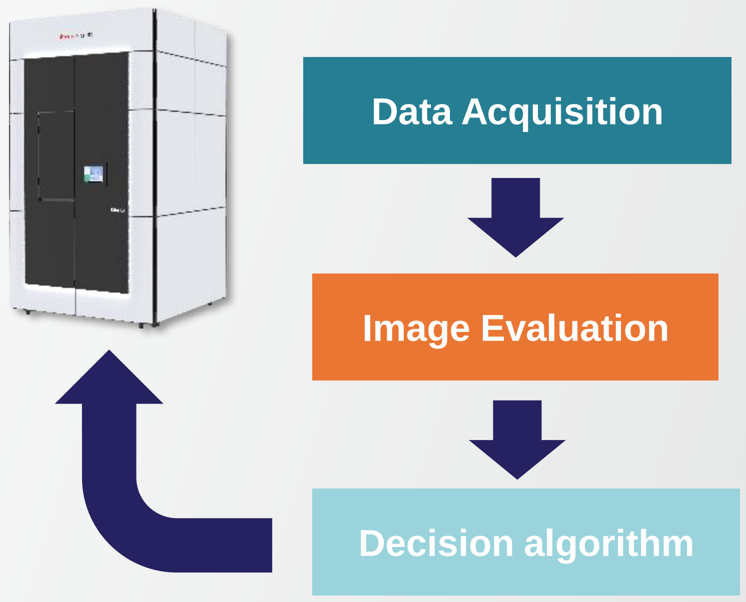
EPU 3.0

Automated SPA

Increasing ease of use and microscope efficiency

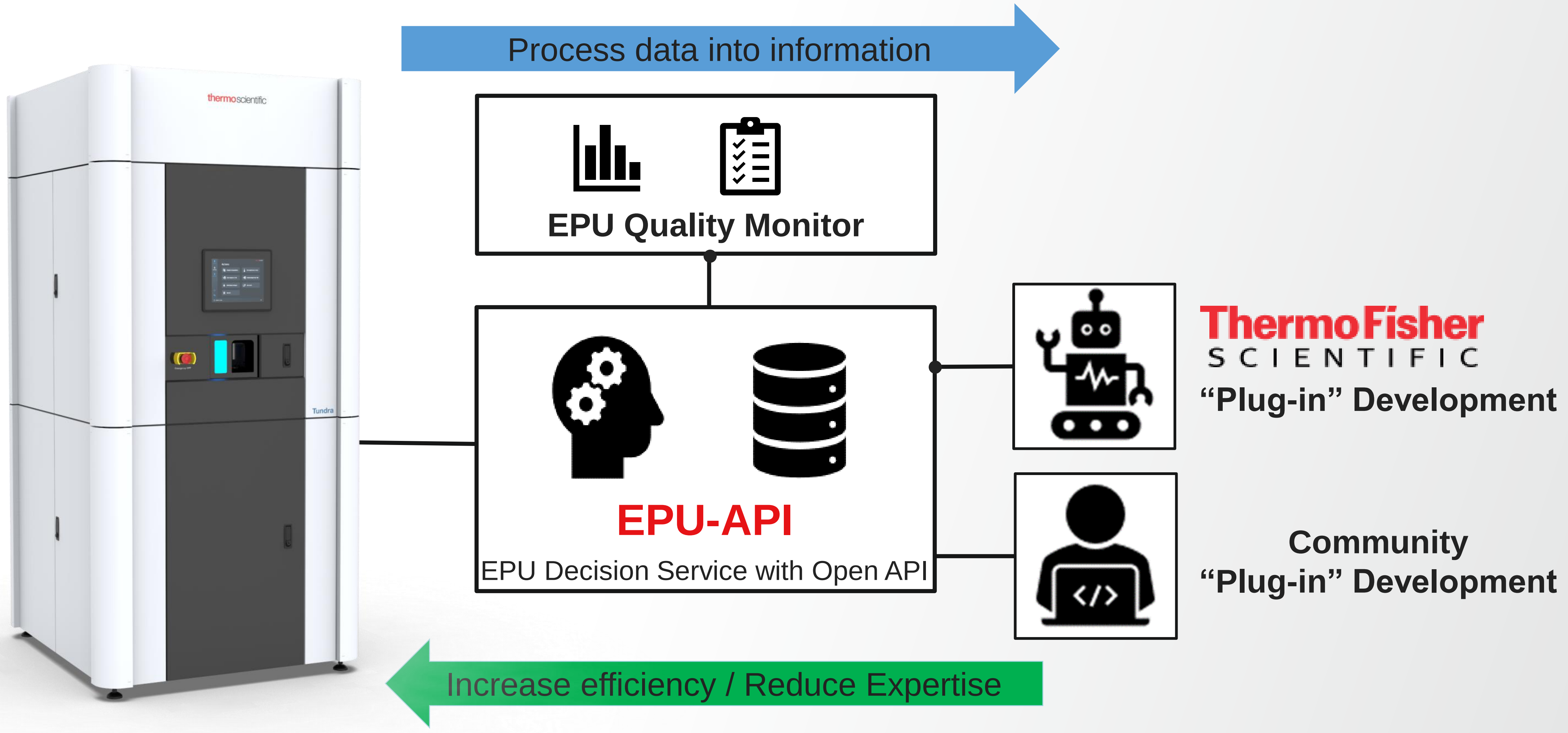
Introducing the Smart EPU ecosystem





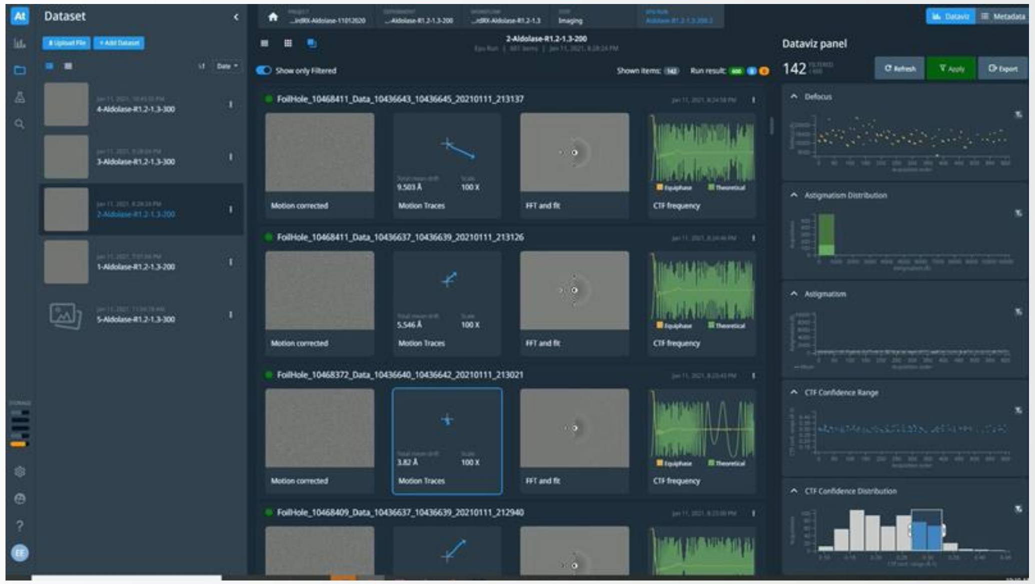
Smart EPU

A platform to enhance efficiency and ease of use for Cryo-EM



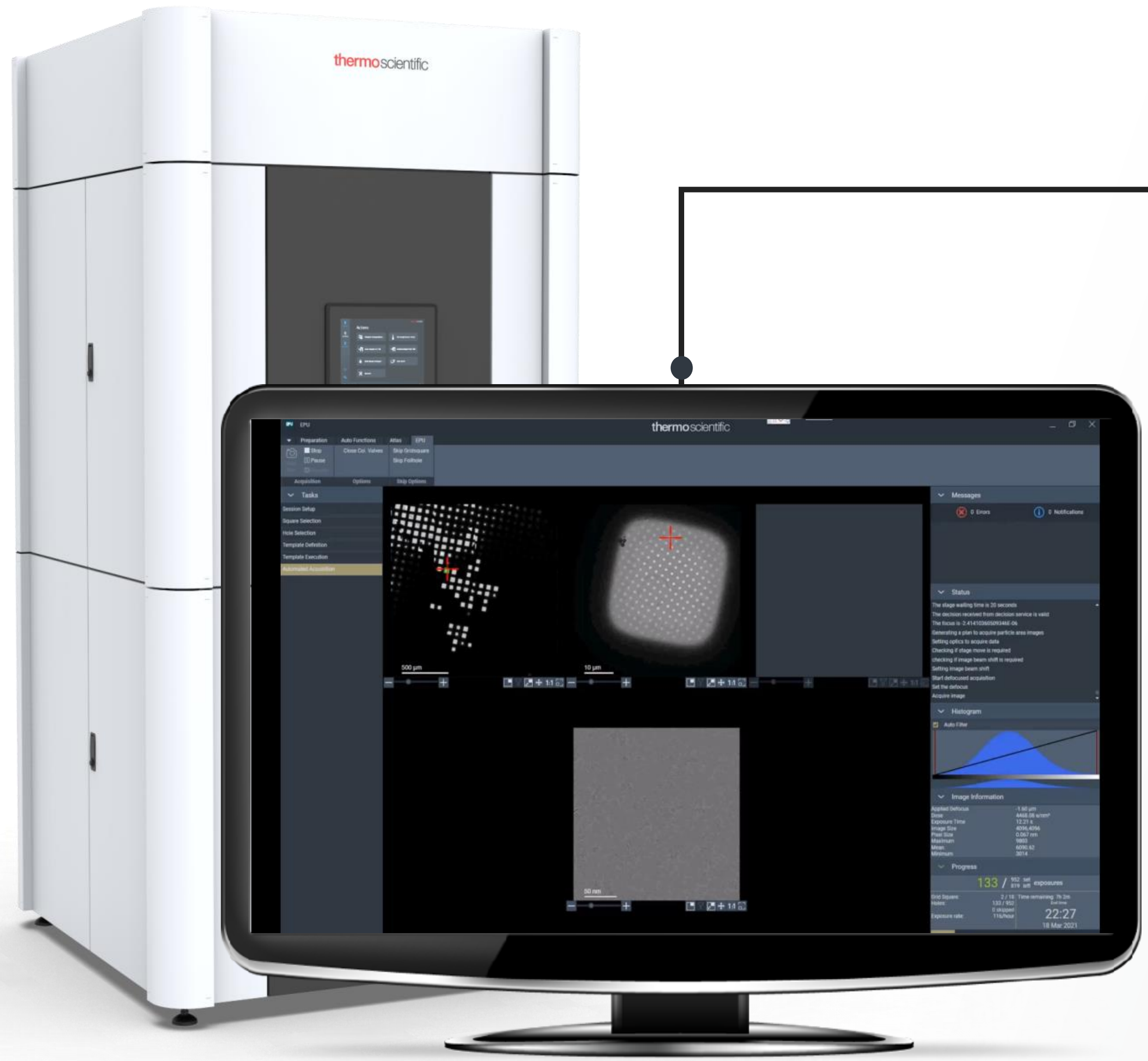
Smart Plug-ins

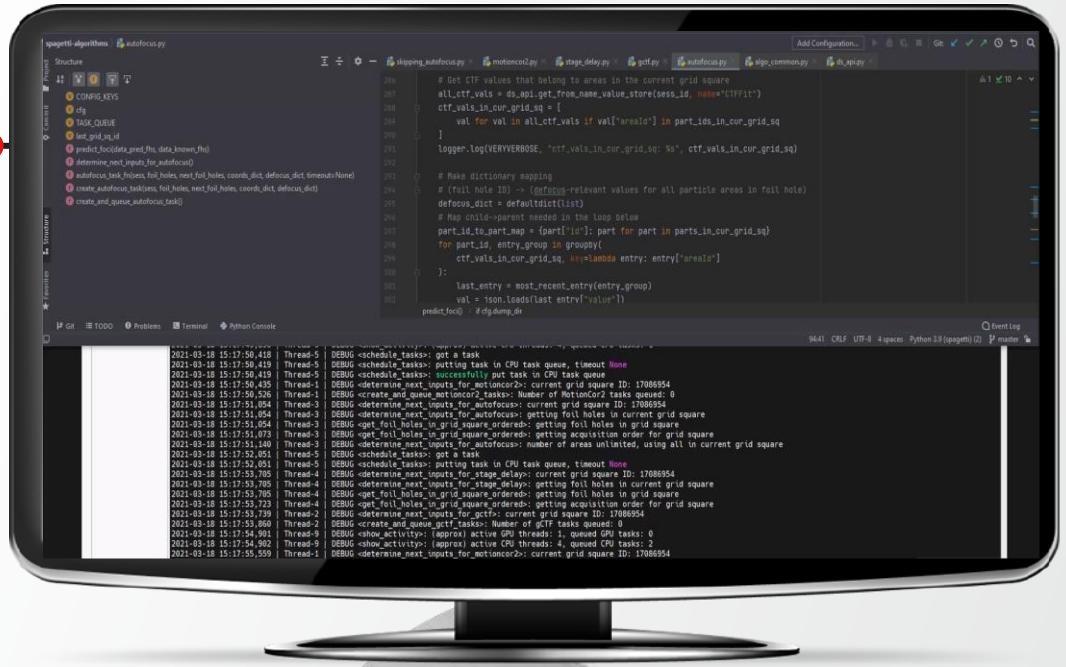
- Focus Stabilization
- Stage Waiting Optimization
- Skip Gridsquare
- Automatic Foil Hole Selection



Smart Plugins use real-time data to make *automated* decisions, making the workflow more efficient and reducing the need for prior expertise.

Smart EPU in action




spagetti-algorithms › autofocus.py

Structure
- CONFIG_KEYS
- cfg
- TASK_QUEUE
- last_grid_sq_id
- predict_foci(data_pred_fhs, data_known_fhs)
- determine_next_inputs_for_autofocus()
- autofocus_task_fn(sess, foil_holes, next_foil_holes, coords_dict, defocus_dict, timeout=None)
- create_autofocus_task(sess, foil_holes, next_foil_holes, coords_dict, defocus_dict)
- create_and_queue_autofocus_task()

skipping_autofocus.py · motioncor2.py · stage_delay.py · gctf.py · autofocus.py · algo_common.py · ds_api.py

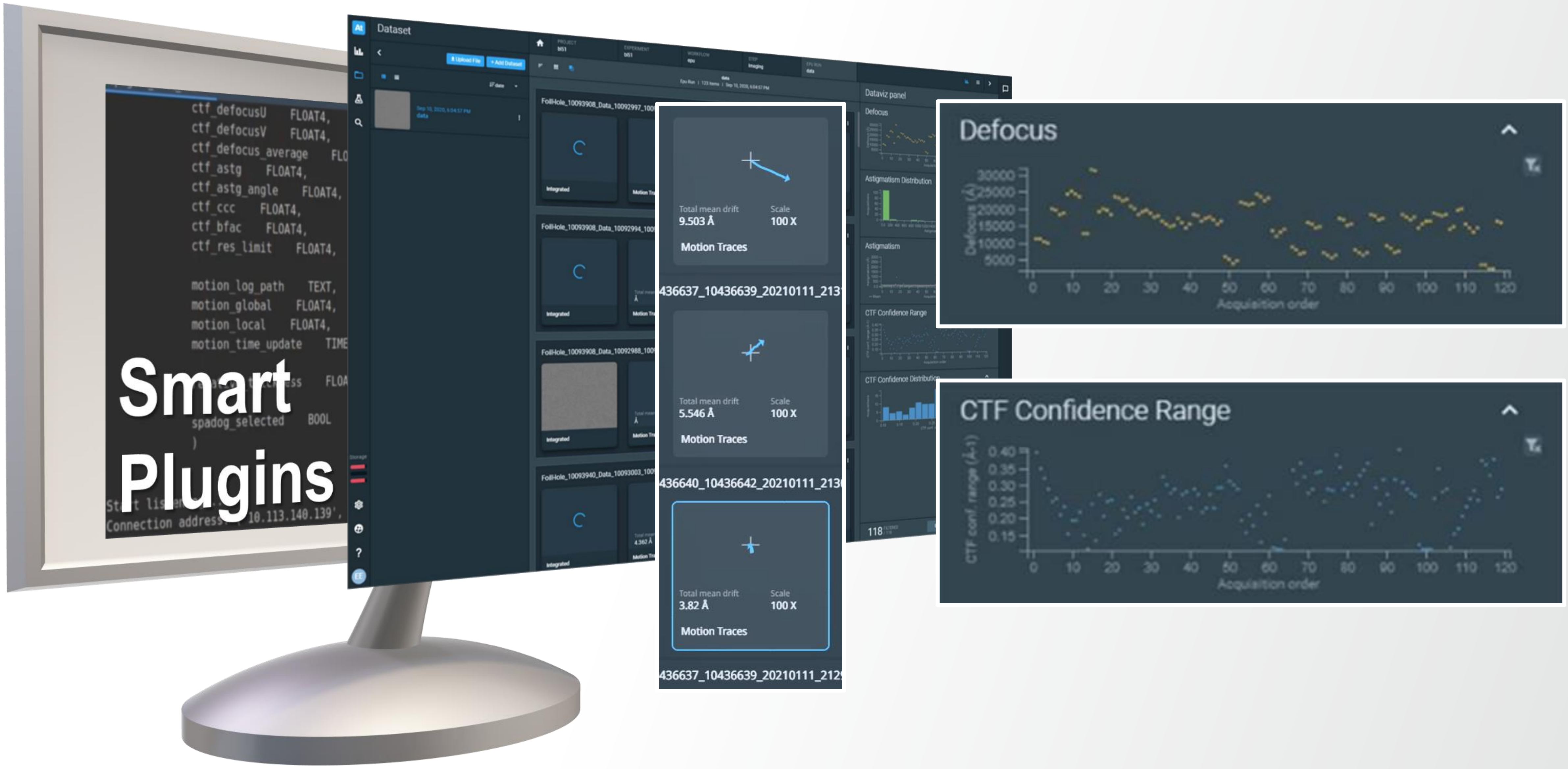
```python
    # Get CTF values that belong to areas in the current grid square
    all_ctf_vals = ds_api.get_from_name_value_store(sess_id, name="CTFFit")
    ctf_vals_in_cur_grid_sq = [
        val for val in all_ctf_vals if val["areaId"] in part_ids_in_cur_grid_sq
    ]
    logger.log(VERYVERBOSE, "ctf_vals_in_cur_grid_sq: %s", ctf_vals_in_cur_grid_sq)

    # Make dictionary mapping
    # (foil hole ID) -> (defocus-relevant values for all particle areas in foil hole)
    defocus_dict = defaultdict(list)
    # Map child->parent needed in the loop below
    part_id_to_part_map = {part["id"]: part for part in parts_in_cur_grid_sq}
    for part_id, entry_group in groupby(
        ctf_vals_in_cur_grid_sq, key=lambda entry: entry["areaId"]
    ):
        last_entry = most_recent_entry(entry_group)
        val = json.loads(last_entry["value"])
```

predict_foci() › if cfg.dump_dir

94:41 CRLF UTF-8 4 spaces Python 3.9 (spagetti) (2) master

```
2021-03-18 15:17:50,418 | Thread-5 | DEBUG <schedule_tasks>: got a task
2021-03-18 15:17:50,419 | Thread-5 | DEBUG <schedule_tasks>: putting task in CPU task queue, timeout None
2021-03-18 15:17:50,419 | Thread-5 | DEBUG <schedule_tasks>: successfully put task in CPU task queue
2021-03-18 15:17:50,435 | Thread-1 | DEBUG <determine_next_inputs_for_motioncor2>: current grid square ID: 17086954
2021-03-18 15:17:50,526 | Thread-1 | DEBUG <create_and_queue_motioncor2_tasks>: Number of MotionCor2 tasks queued: 0
2021-03-18 15:17:51,054 | Thread-3 | DEBUG <determine_next_inputs_for_autofocus>: current grid square ID: 17086954
2021-03-18 15:17:51,054 | Thread-3 | DEBUG <determine_next_inputs_for_autofocus>: getting foil holes in current grid square
2021-03-18 15:17:51,054 | Thread-3 | DEBUG <get_foil_holes_in_grid_square_ordered>: getting foil holes in grid square
2021-03-18 15:17:51,073 | Thread-3 | DEBUG <get_foil_holes_in_grid_square_ordered>: getting acquisition order for grid square
2021-03-18 15:17:51,140 | Thread-3 | DEBUG <determine_next_inputs_for_autofocus>: number of areas unlimited, using all in current grid square
2021-03-18 15:17:52,051 | Thread-5 | DEBUG <schedule_tasks>: got a task
2021-03-18 15:17:52,051 | Thread-5 | DEBUG <schedule_tasks>: putting task in CPU task queue, timeout None
2021-03-18 15:17:53,705 | Thread-4 | DEBUG <determine_next_inputs_for_stage_delay>: current grid square ID: 17086954
2021-03-18 15:17:53,705 | Thread-4 | DEBUG <determine_next_inputs_for_stage_delay>: getting foil holes in current grid square
2021-03-18 15:17:53,705 | Thread-4 | DEBUG <get_foil_holes_in_grid_square_ordered>: getting foil holes in grid square
2021-03-18 15:17:53,723 | Thread-4 | DEBUG <get_foil_holes_in_grid_square_ordered>: getting acquisition order for grid square
2021-03-18 15:17:53,739 | Thread-2 | DEBUG <determine_next_inputs_for_gctf>: current grid square ID: 17086954
2021-03-18 15:17:53,860 | Thread-2 | DEBUG <create_and_queue_gctf_tasks>: Number of gCTF tasks queued: 0
2021-03-18 15:17:54,901 | Thread-9 | DEBUG <show_activity>: (approx) active GPU threads: 1, queued GPU tasks: 0
2021-03-18 15:17:54,902 | Thread-9 | DEBUG <show_activity>: (approx) active CPU threads: 4, queued CPU tasks: 2
2021-03-18 15:17:55,559 | Thread-1 | DEBUG <determine_next_inputs_for_motioncor2>: current grid square ID: 17086954
```

Smart EPU: monitoring key parameters



```
ctf_defocusU        FLOAT4,
ctf_defocusV        FLOAT4,
ctf_defocus_average    FLO
ctf_astg         FLOAT4,
ctf_astg_angle       FLOAT4,
ctf_ccc         FLOAT4,
ctf_bfac         FLOAT4,
ctf_res_limit       FLOAT4,

motion_log_path      TEXT,
motion_global       FLOAT4,
motion_local       FLOAT4,
motion_time_update     TIME
                    ss    FLOA
spadog_selected      BOOL
)
St  t lis
Connection address    10.113.140.139',
```

Smart Plugins

Dataset

FoilHole_10093908_Data_10092997_100

FoilHole_10093908_Data_10092994_100

FoilHole_10093908_Data_10092988_100

FoilHole_10093940_Data_10093003_100

Total mean drift 9.503 Å — Scale 100 X — Motion Traces

436637_10436639_20210111_213

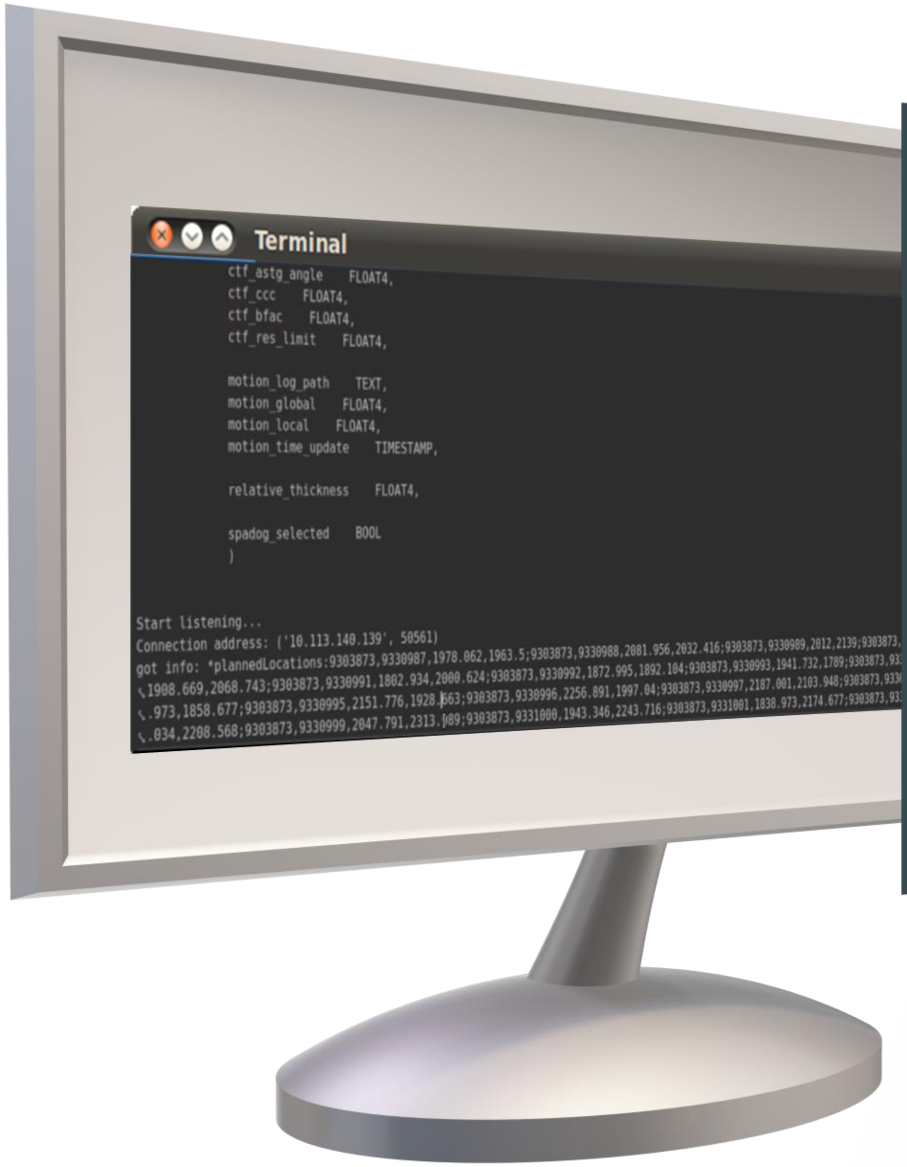
Total mean drift 5.546 Å — Scale 100 X — Motion Traces

436640_10436642_20210111_213

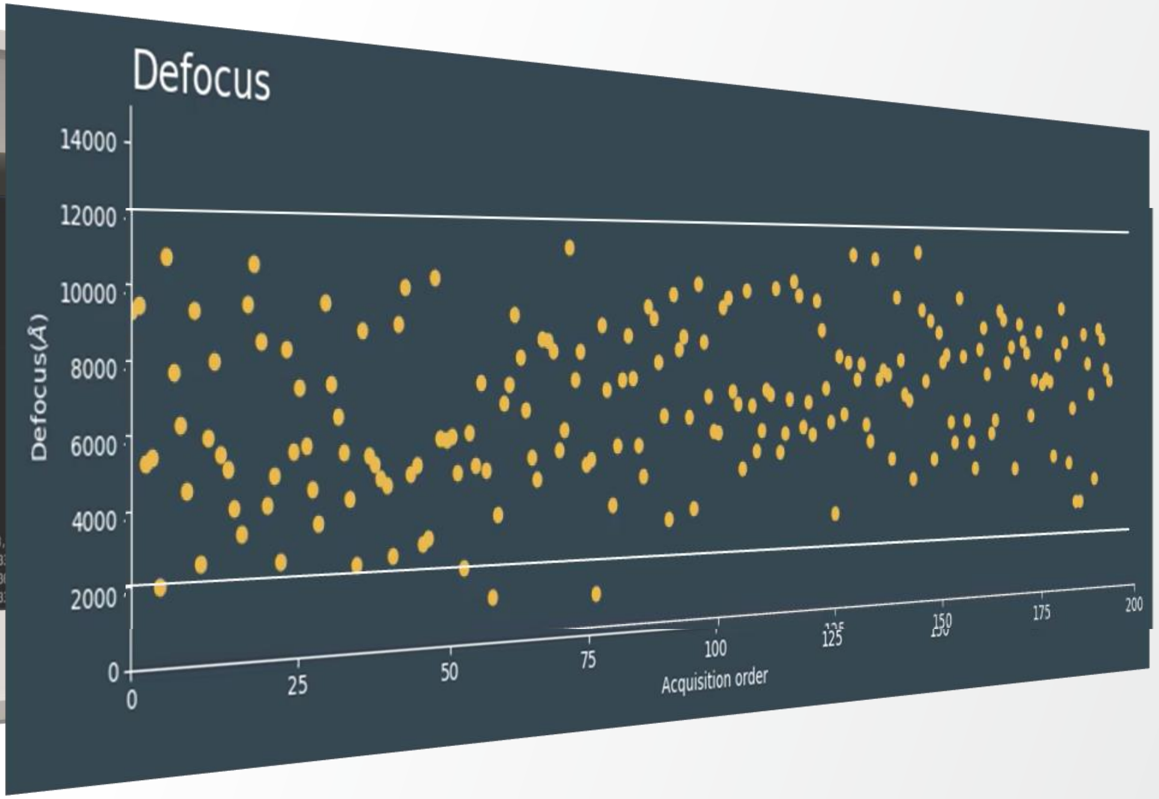
Total mean drift 3.82 Å — Scale 100 X — Motion Traces

436637_10436639_20210111_212

Smart plugin #1: automatically adjust focus

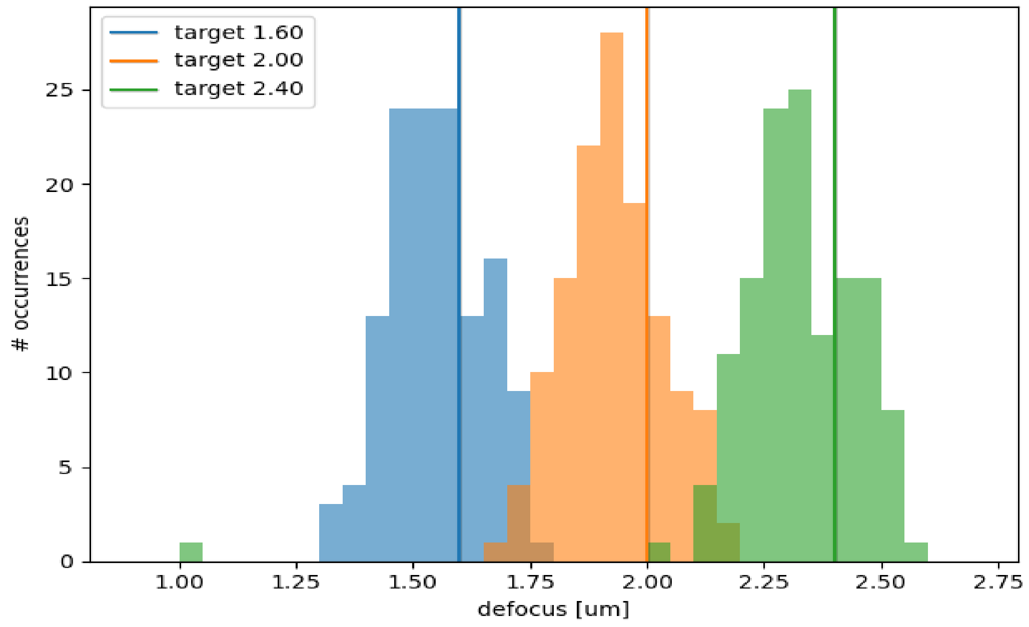


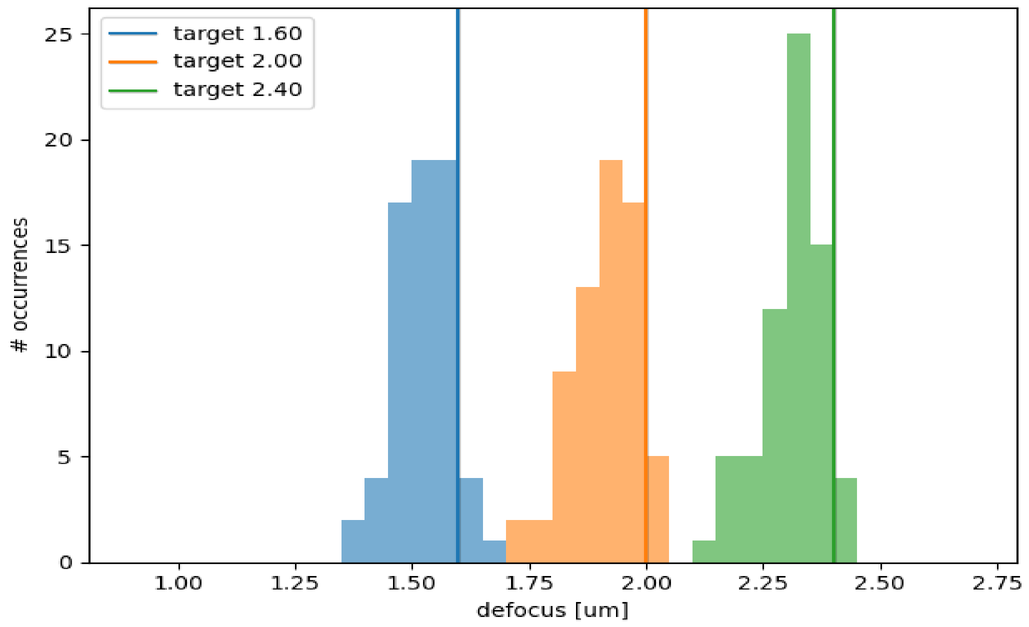
```
        ctf_astg_angle    FLOAT4,
        ctf_ccc    FLOAT4,
        ctf_bfac    FLOAT4,
        ctf_res_limit    FLOAT4,

        motion_log_path    TEXT,
        motion_global    FLOAT4,
        motion_local    FLOAT4,
        motion_time_update    TIMESTAMP,

        relative_thickness    FLOAT4,

        spadog_selected    BOOL
        )

Start listening...
Connection address: ('10.113.140.139', 50561)
got info: *plannedLocations:9303873,9330987,1978.062,1963.5;9303873,9330988,2081.956,2032.416;9303873,9330989,2012,2139;9303873,
↳1908.669,2068.743;9303873,9330991,1802.934,2000.624;9303873,9330992,1872.995,1892.104;9303873,9330993,1941.732,1789;9303873,93
↳.973,1858.677;9303873,9330995,2151.776,1928.663;9303873,9330996,2256.891,1997.04;9303873,9330997,2187.001,2103.948;9303873,933
↳.034,2208.568;9303873,9330999,2047.791,2313.989;9303873,9331000,1943.346,2243.716;9303873,9331001,1838.973,2174.677;9303873,93
```



Smart Focus results

Faster and more consistent focus values measured





- EPU Auto-focus
- Smart Focus

*600 acquired images

Benefits

Data Quality

Focusing becomes more accurate as it is based on CTF fits from acquired images.

Efficiency

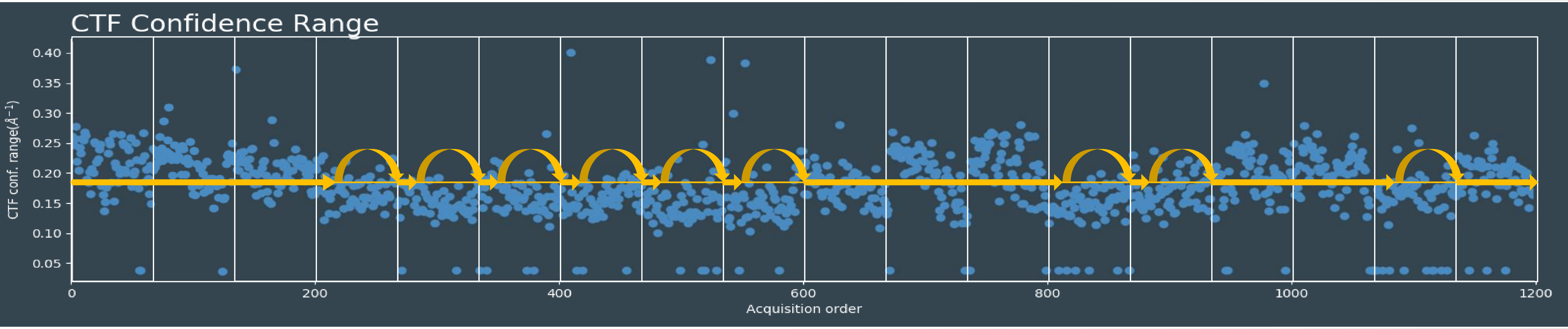
Minimization of beam-tilt-based autofocus executions improves throughput

Ease of Use

Smart Focus routine intervenes and re-adjusts user settings on its own

Smart plugin #2: automatically skip bad areas

Skip grid squares with CTF resolution estimation above 6 Å



Benefits

Data Quality

Areas that lead to suboptimal data are automatically excluded

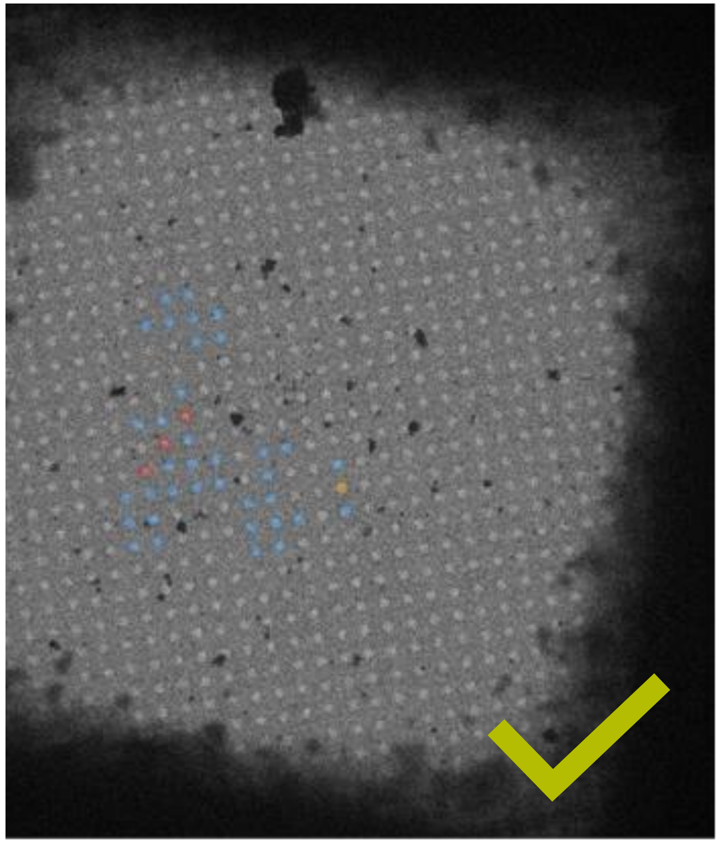
Efficiency

The fraction of useable data is increased, so fewer images are needed.

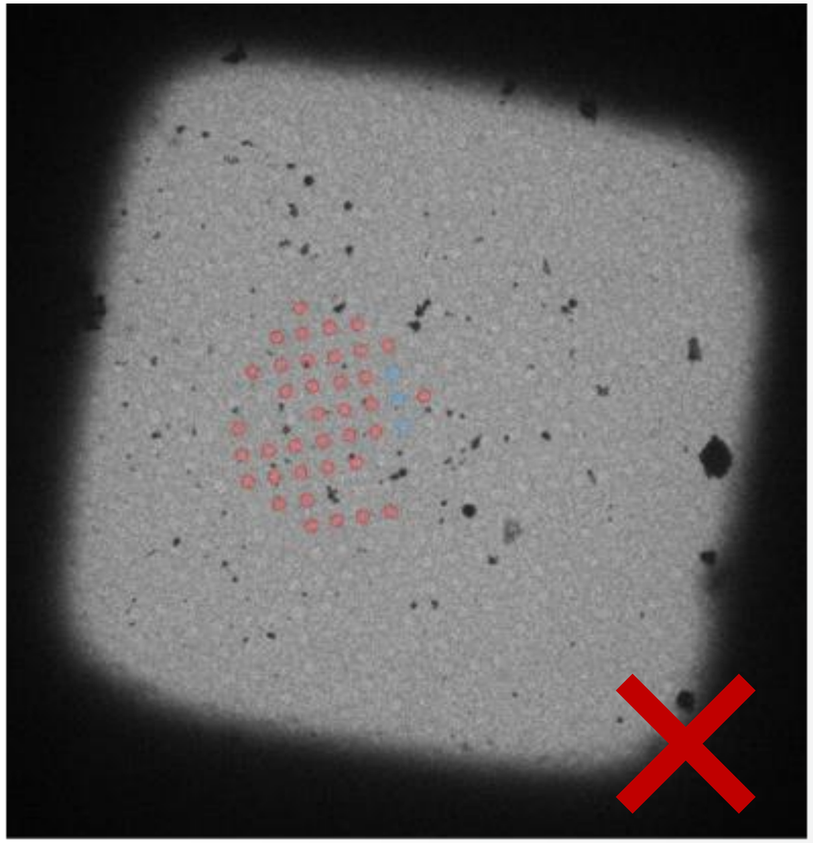
Ease of Use

No need to pre-select grid squares carefully as the selection will be optimized on the fly.

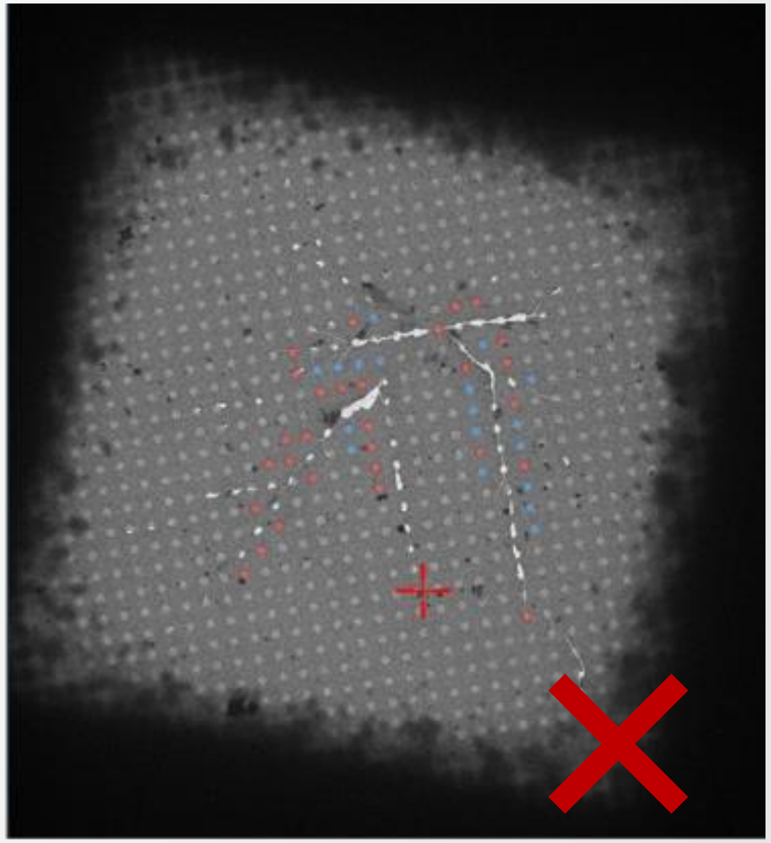
Skip Gridsquare in Action



Square1

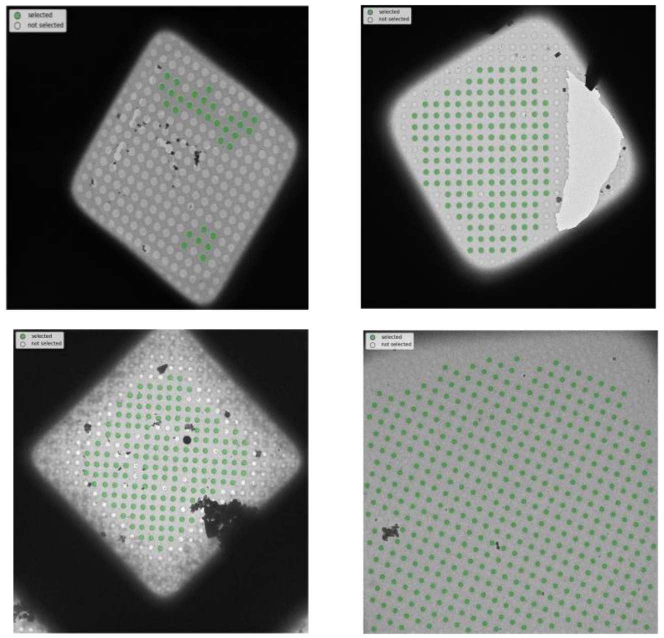


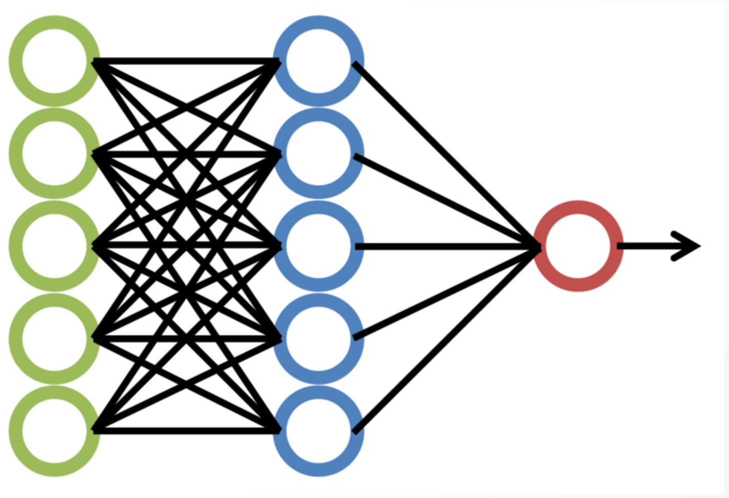
Square2

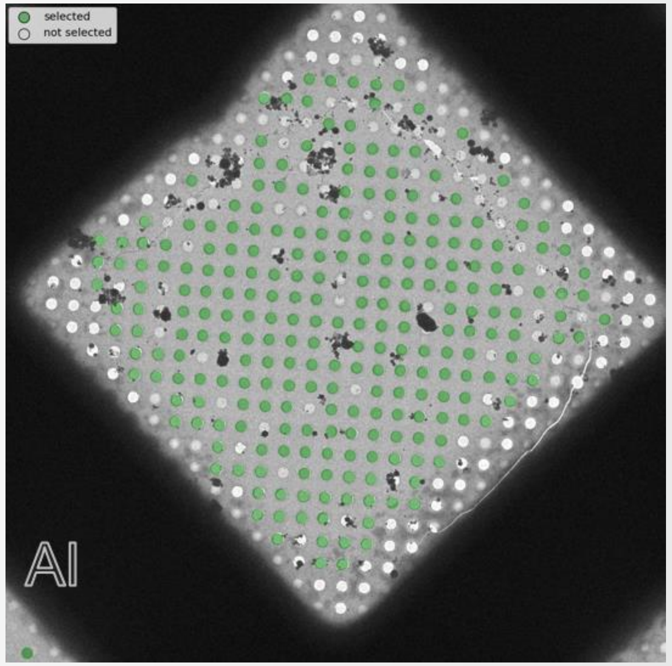


Square3

AI Foil Hole Selection







Training
Grid square images are used to train a Neural Network to identify good/bad foil holes

Inference
The network can be used by EPU to determine the selection of holes to be acquired

Benefits

Data Quality

Areas that are predicted to give sub-optimal data are automatically excluded

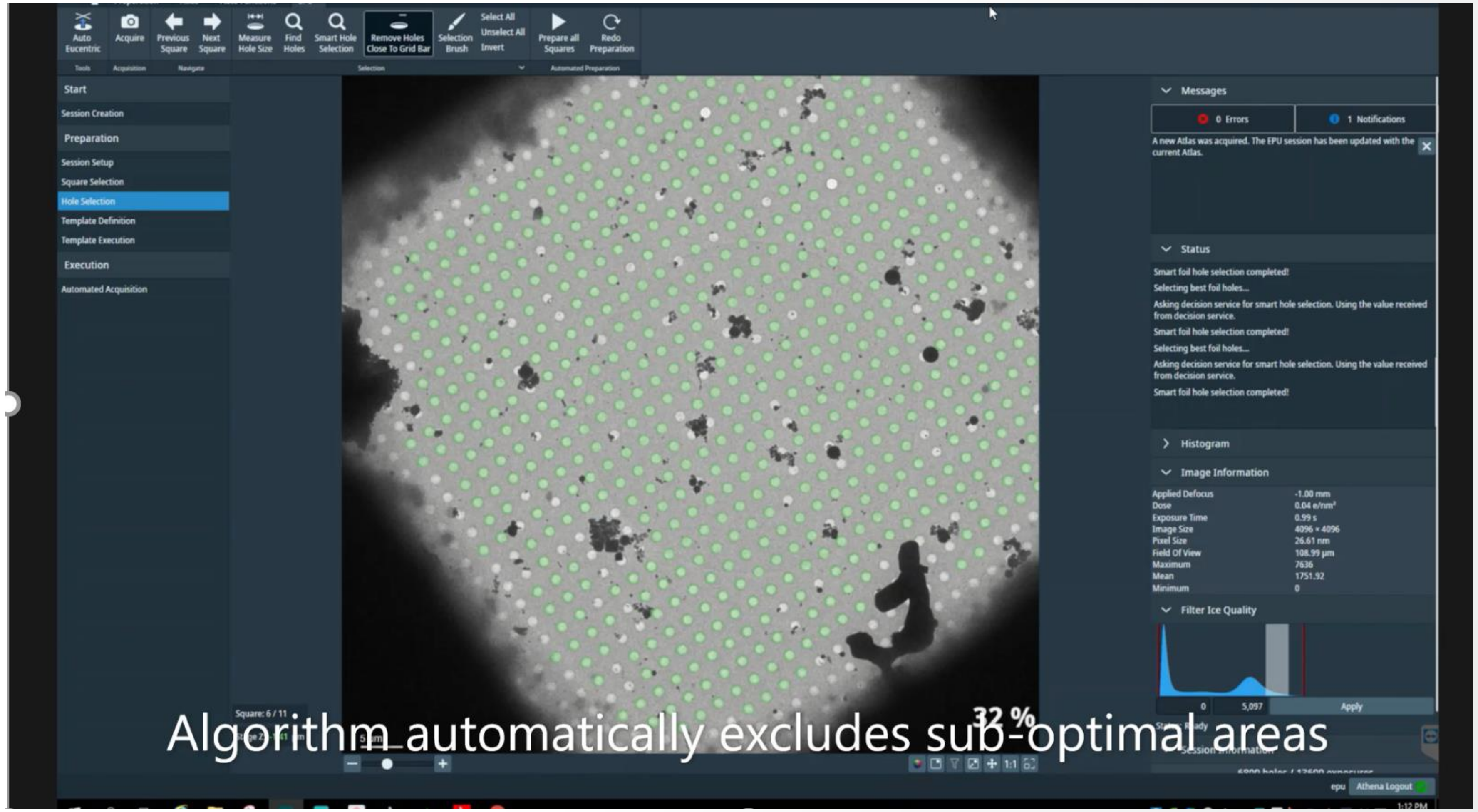
Efficiency

Less time is need to exclude bad foil holes by hand. Smart EPU automatically creates an efficient set-up

Ease of Use

No expertise needed to identify bad foil holes.

Set up using Smart Algorithms Video



Messages

0 Errors 1 Notifications

A new Atlas was acquired. The EPU session has been updated with the current Atlas.

Status

Smart foil hole selection completed!
Selecting best foil holes...
Asking decision service for smart hole selection. Using the value received from decision service.
Smart foil hole selection completed!
Selecting best foil holes...
Asking decision service for smart hole selection. Using the value received from decision service.
Smart foil hole selection completed!

Histogram

Image Information

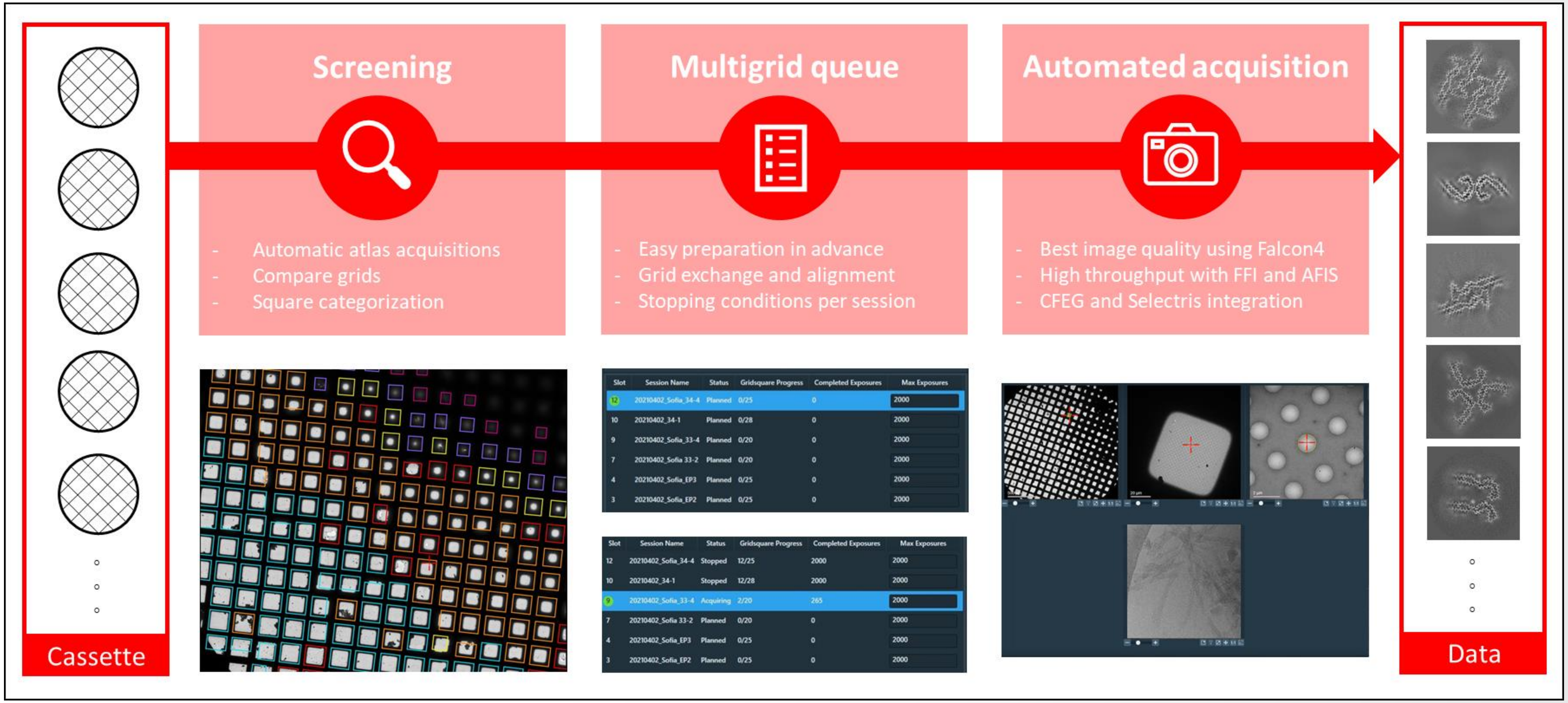
Applied Defocus	-1.00 mm
Dose	0.04 e/nm²
Exposure Time	0.99 s
Image Size	4096 × 4096
Pixel Size	26.61 nm
Field Of View	108.99 µm
Maximum	7636
Mean	1751.92
Minimum	0

Filter Ice Quality

Algorithm automatically excludes sub-optimal areas

EPU Multigrid

Combine easy set-up with EPU Multigrid



Screening

- Automatic atlas acquisitions
- Compare grids
- Square categorization

Multigrid queue

- Easy preparation in advance
- Grid exchange and alignment
- Stopping conditions per session

Automated acquisition

- Best image quality using Falcon4
- High throughput with FFI and AFIS
- CFEG and Selectris integration

Slot	Session Name	Status	Gridsquare Progress	Completed Exposures	Max Exposures
12	20210402_Sofia_34-4	Planned	0/25	0	2000
10	20210402_34-1	Planned	0/28	0	2000
9	20210402_Sofia_33-4	Planned	0/20	0	2000
7	20210402_Sofia 33-2	Planned	0/20	0	2000
4	20210402_Sofia_EP3	Planned	0/25	0	2000
3	20210402_Sofia_EP2	Planned	0/25	0	2000

Slot	Session Name	Status	Gridsquare Progress	Completed Exposures	Max Exposures
12	20210402_Sofia_34-4	Stopped	12/25	2000	2000
10	20210402_34-1	Stopped	12/28	2000	2000
9	20210402_Sofia_33-4	Acquiring	2/20	265	2000
7	20210402_Sofia 33-2	Planned	0/20	0	2000
4	20210402_Sofia_EP3	Planned	0/25	0	2000
3	20210402_Sofia_EP2	Planned	0/25	0	2000

Assembly of recombinant tau filaments identical to those of Alzheimer's disease and chronic traumatic encephalopathy, Lövestam, et.al., eLife 2022;11:e76494 DOI: 10.7554/eLife.76494)

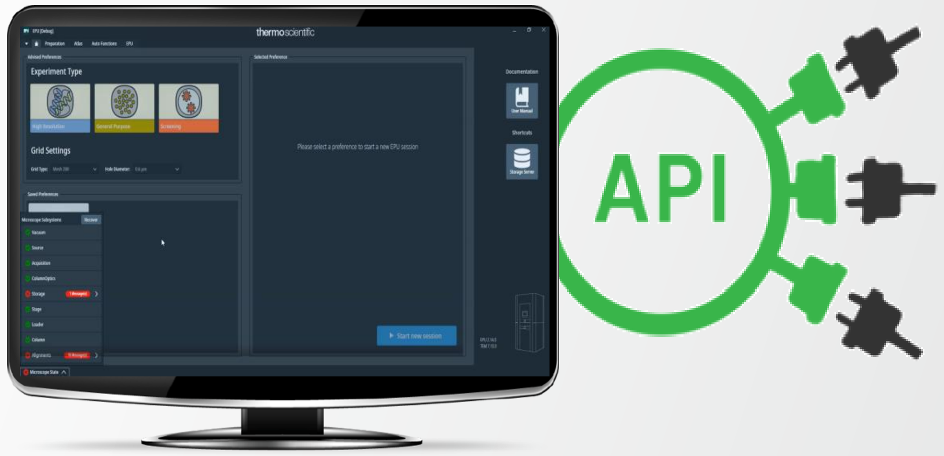
Community Plugins / Open API

Method development

Enables users to develop specific plugins for their needs

Expedite plugin development

Enables faster innovation of new automation

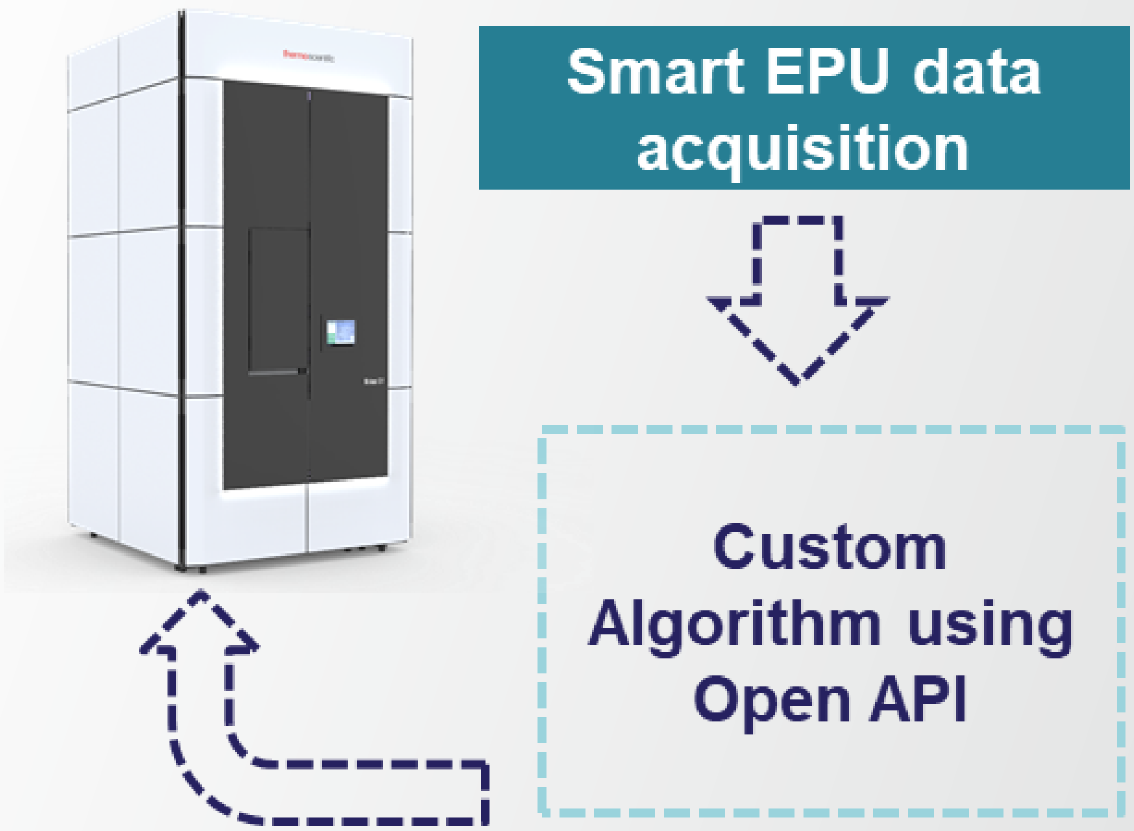


Our robust API enables the community to be part of the ecosystem.

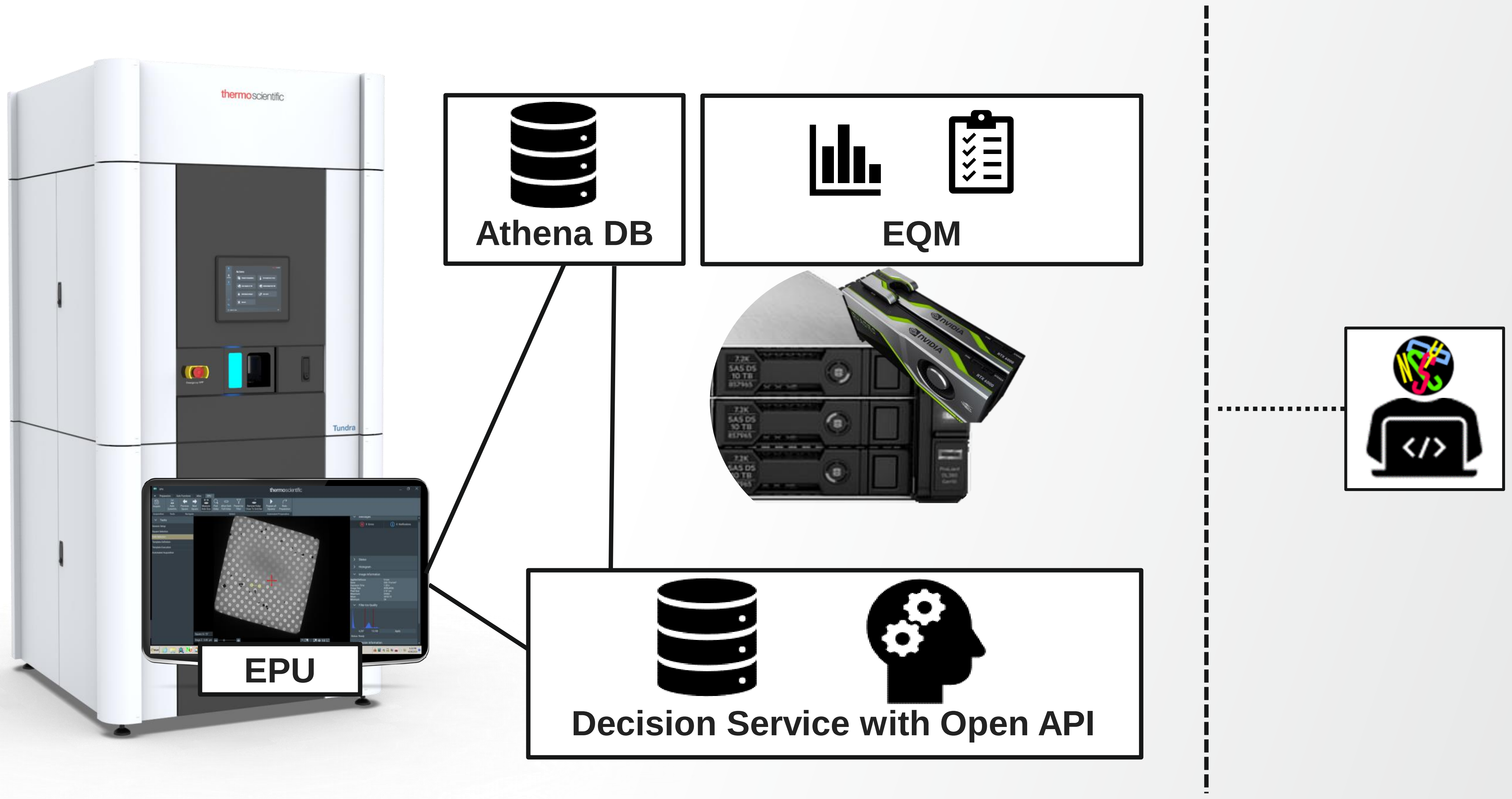
Open API

An API to retrieve data and drive EPU

```
# 1. Get area currently processed by EPU
app_state = requests.get(
    "http://decision-service:5000/CurrentApplicationState"
).json()
current_area_id = app_state["areaId"]  # we assume here that it’s a foil hole

# 2. Retrieve relevant motion correction results to calculate new stage waiting
time
grid_square_id = requests.get(
    f"http://decision-service:5000/Area/{current_area_id}"
).json()["parentId"]
motion_correction_results = requests.get(
    "http://decision-service:5000/AlgorithmResults",
    params={"parentAreaId": grid_square_id, "name": "motioncorrection"},
).json()

# 3. Compute new stage waiting time based on motion correction results
new_stage_waiting_time = ...

# 4. Register a new stage settling decision for future areas (“...”)
requests.post(
    "http://decision-service:5000/Decision",
    json={"areaId": ..., "decisionType": "stageWaitingTime",
          "decisionValue": new_stage_waiting_time, "decidedBy": "smart
algorithm"}
)
```

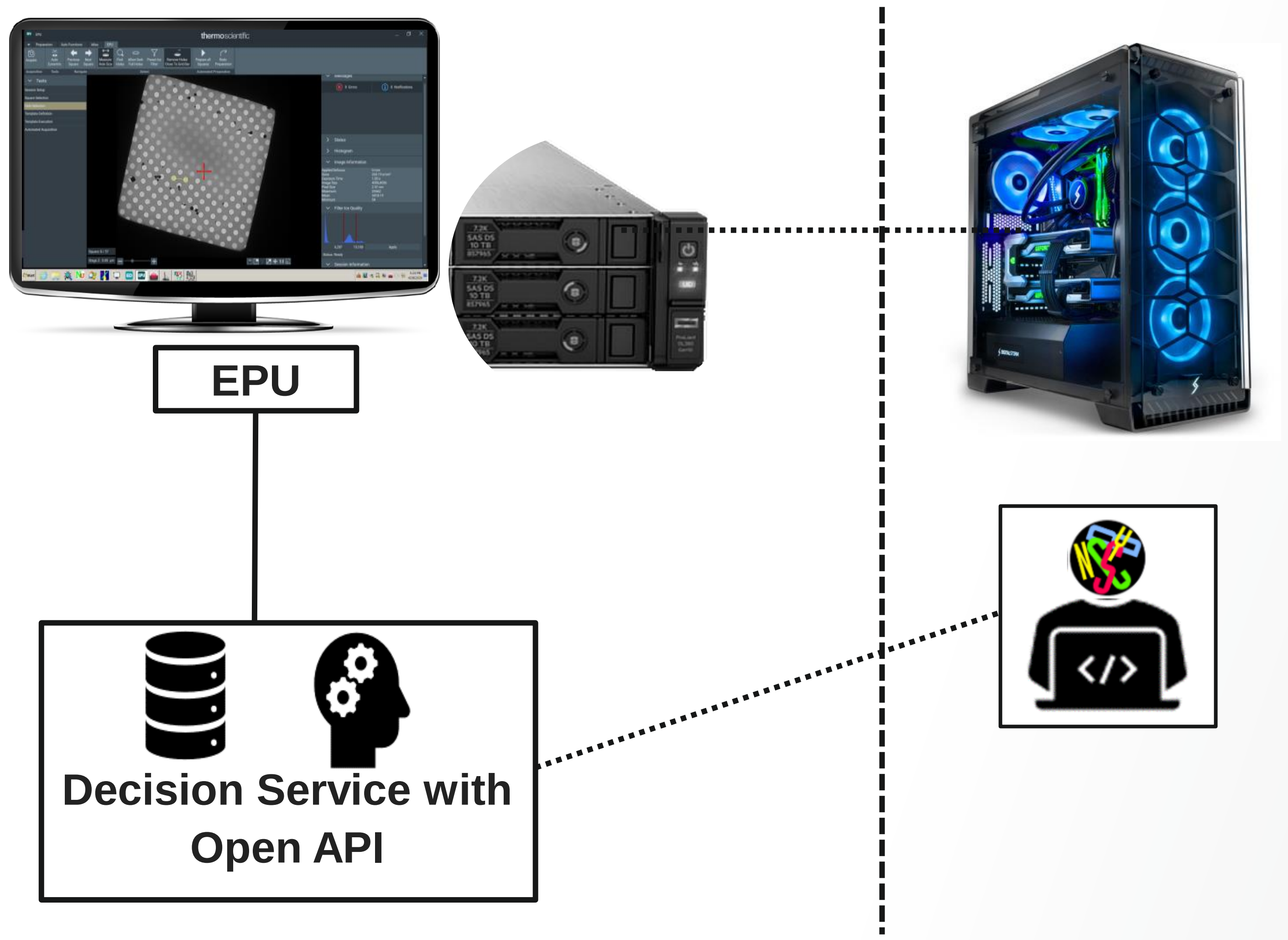


Community Algorithms: 2 Options



Complete DIY

Build your own Algorithms



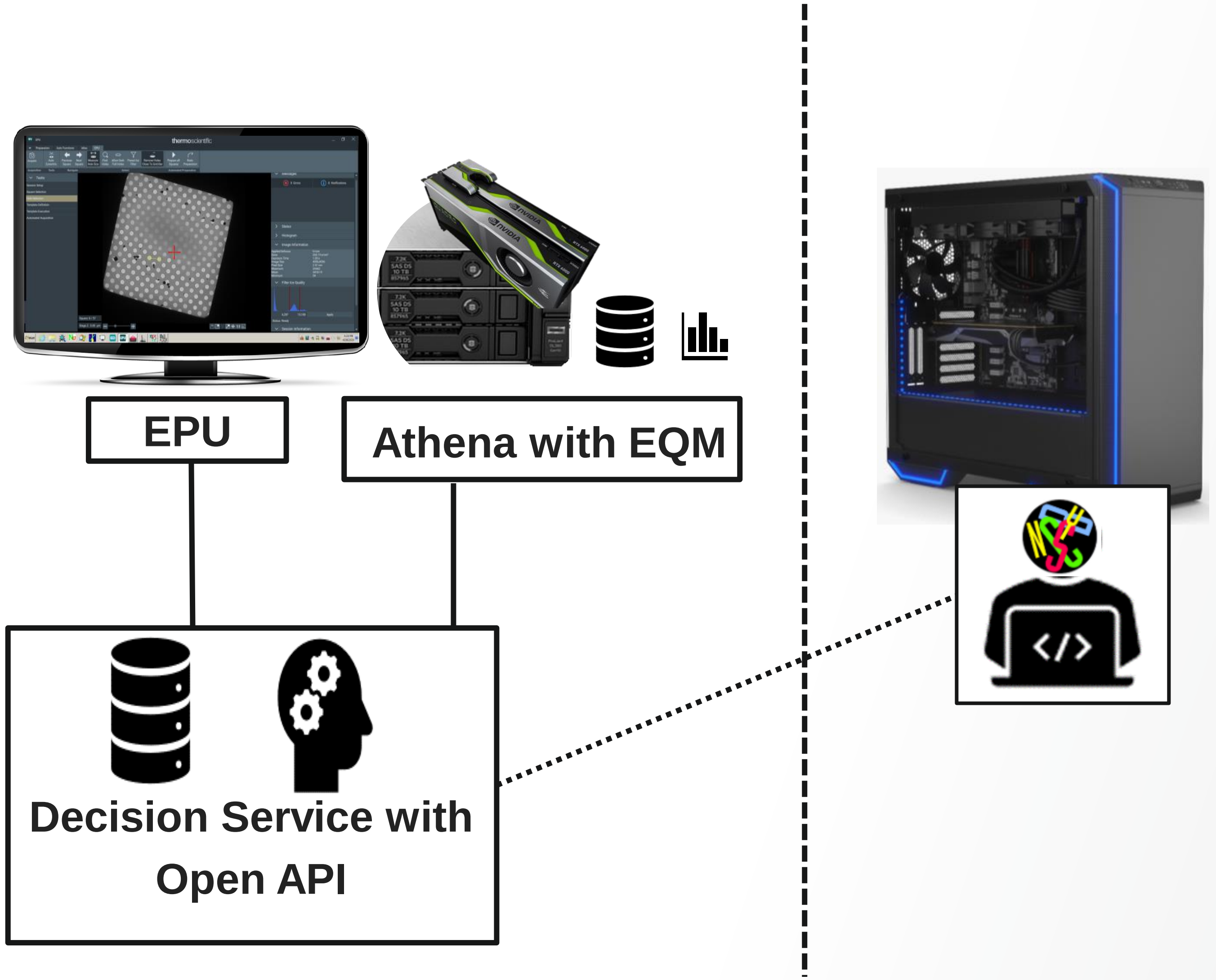
Use own solution for processing/managing data

- Copy data from our domain with own means
- Run all processing on your own infastructure

Communicate with decision service **API to feedback optimizations to EPU**

Plugin DIY

Leverage Athena and EQM as well



Use Athena/EQM for processing/managing data

- Retrieve pre-processed data and results through API

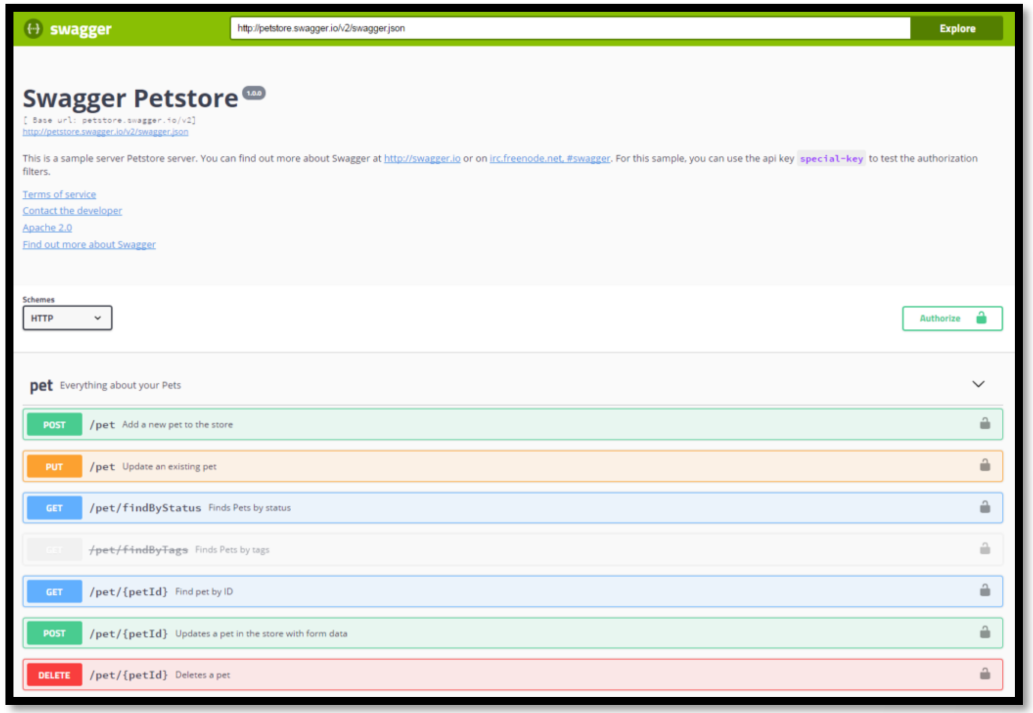
Deploy **plugins on your own infrastructure**

Communicate with decision service **API to feedback optimizations to EPU**

Community Algorithms: What shall we Provide?

Enable the Community to build their own Algorithms

Documentation and Support on API



swagger   http://petstore.swagger.io/v2/swagger.json   Explore

Swagger Petstore 1.0.0

[Base url: petstore.swagger.io/v2]
http://petstore.swagger.io/v2/swagger.json

This is a sample server Petstore server. You can find out more about Swagger at http://swagger.io or on irc.freenode.net, #swagger. For this sample, you can use the api key `special-key` to test the authorization filters.

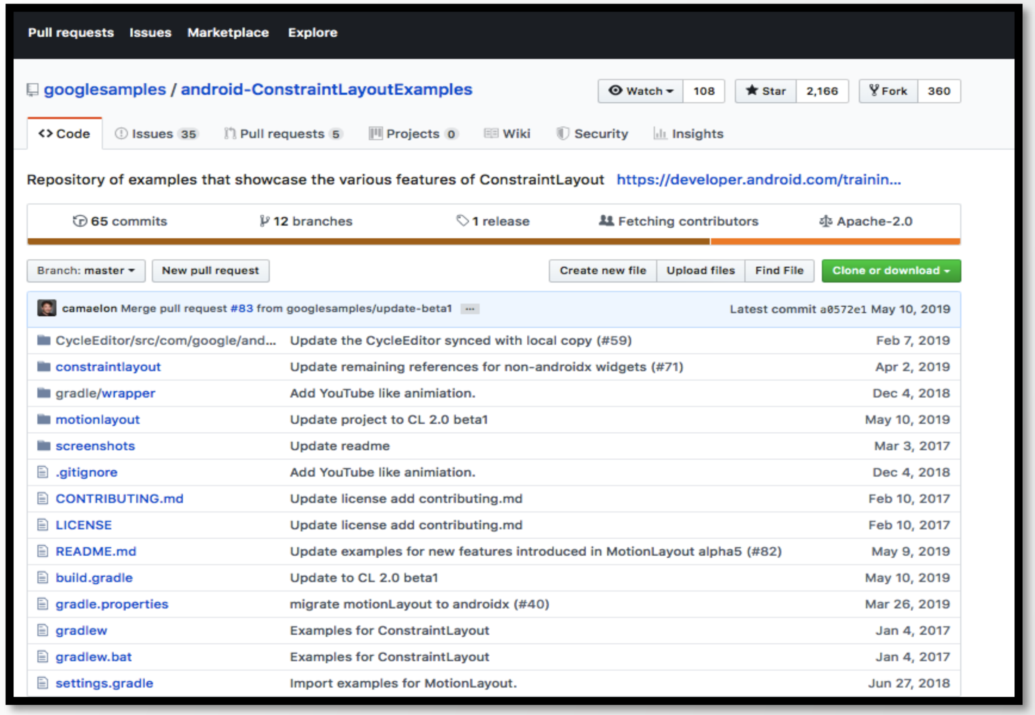
Terms of service
Contact the developer
Apache 2.0
Find out more about Swagger

Schemes: HTTP   Authorize

pet Everything about your Pets

POST	/pet	Add a new pet to the store
PUT	/pet	Update an existing pet
GET	/pet/findByStatus	Finds Pets by status
GET	~~/pet/findByTags~~	Finds Pets by tags
GET	/pet/{petId}	Find pet by ID
POST	/pet/{petId}	Updates a pet in the store with form data
DELETE	/pet/{petId}	Deletes a pet

Example algorithms



Pull requests   Issues   Marketplace   Explore

googlesamples / android-ConstraintLayoutExamples   Watch 108   Star 2,166   Fork 360

Code   Issues 35   Pull requests 5   Projects 0   Wiki   Security   Insights

Repository of examples that showcase the various features of ConstraintLayout https://developer.android.com/trainin...

65 commits   12 branches   1 release   Fetching contributors   Apache-2.0

Branch: master   New pull request   Create new file   Upload files   Find File   Clone or download

camaelon Merge pull request #83 from googlesamples/update-beta1 ...   Latest commit a0572e1 May 10, 2019

CycleEditor/src/com/google/and...	Update the CycleEditor synced with local copy (#59)	Feb 7, 2019
constraintlayout	Update remaining references for non-androidx widgets (#71)	Apr 2, 2019
gradle/wrapper	Add YouTube like animiation.	Dec 4, 2018
motionlayout	Update project to CL 2.0 beta1	May 10, 2019
screenshots	Update readme	Mar 3, 2017
.gitignore	Add YouTube like animiation.	Dec 4, 2018
CONTRIBUTING.md	Update license add contributing.md	Feb 10, 2017
LICENSE	Update license add contributing.md	Feb 10, 2017
README.md	Update examples for new features introduced in MotionLayout alpha5 (#82)	May 9, 2019
build.gradle	Update to CL 2.0 beta1	May 10, 2019
gradle.properties	migrate motionLayout to androidx (#40)	Mar 26, 2019
gradlew	Examples for ConstraintLayout	Jan 4, 2017
gradlew.bat	Examples for ConstraintLayout	Jan 4, 2017
settings.gradle	Import examples for MotionLayout.	Jun 27, 2018

What else would you need ?

Do we need a standard API?

Questions

EPU@Thermofisher.com