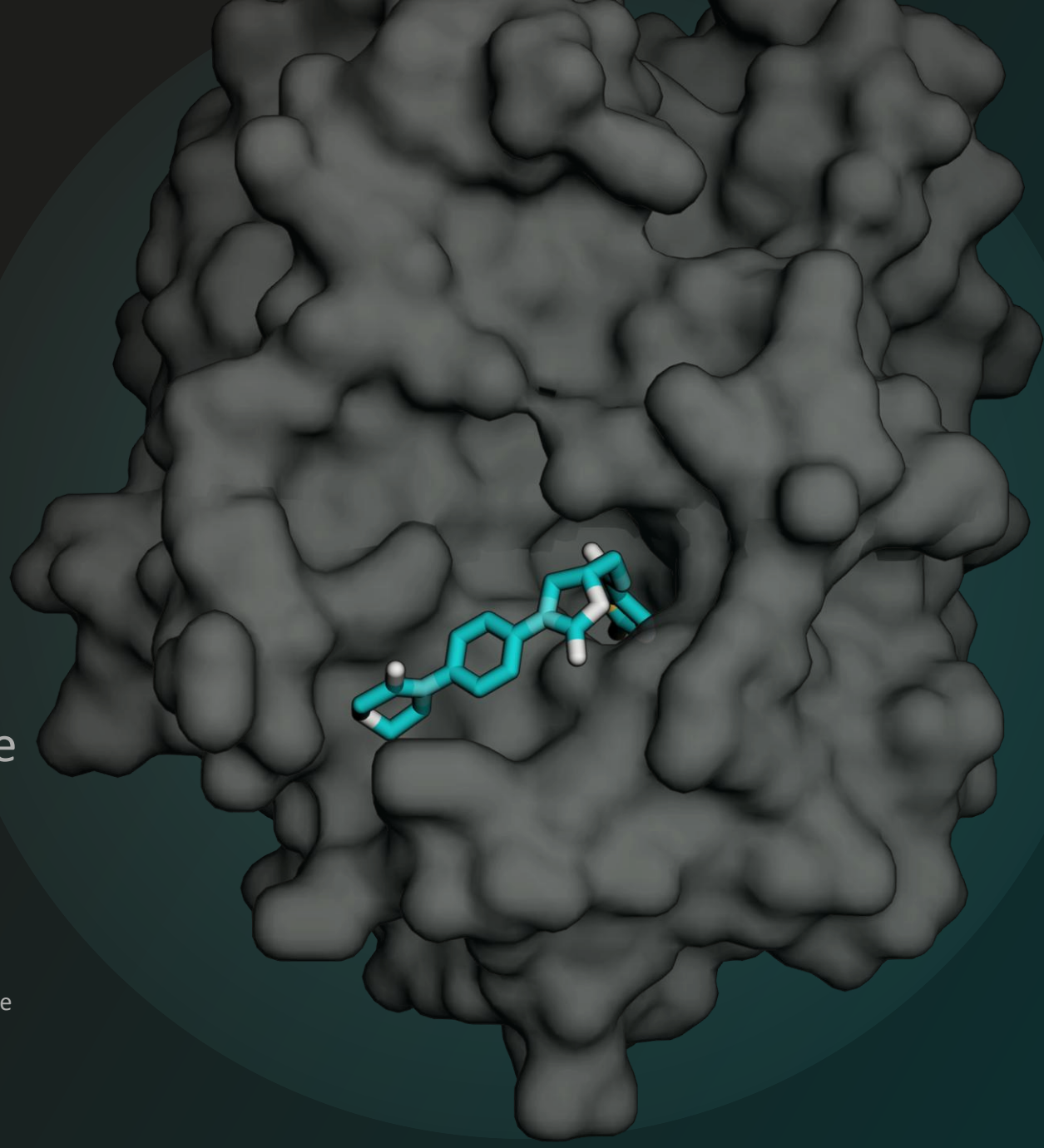
Sigmatic Sciences × OpenEye cadence MOLECULAR SCIENCES

AIDDD 2026 · DISCOVERY CHEMISTRY · 28 OCTOBER

From Hit to Lead Series

What changes when an AI scientist designs the next DMTA cycle



Marcos Camara
Director of AI Solutions, Sigmatic Sciences

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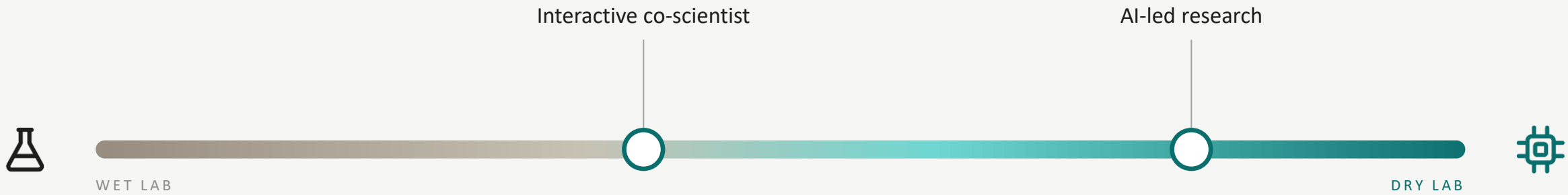
Principal Application Scientist, OpenEye

WHERE THE FIELD IS GOING

Two emerging approaches to AI scientists

Both shift discovery work from the wet lab to the dry lab. Scout runs both.



INTERACTIVE CO-SCIENTIST

The team directs, Scout executes

- Every result checked before the next step
- A force multiplier for scarce computational expertise

AI-LED RESEARCH

Scout runs the work, to an objective

- Most of the work done in silico
- Lab and scientist brought in where warranted

Same connectors, permissions and approval point under both modes.

WHAT IT TAKES

Not an AI agents problem.

Not a data problem.

Not an algorithms problem.

It is a multi-agent orchestration problem.



DATA FLOW

In silico orchestration

- Capture and harmonised model
- In silico design and analysis
- Analytics and ML feedback



WORKFLOW

Lab orchestration

- Scientist and automation-led runs
- AI-designed protocols
- Instrument integration



PROCESS FLOW

Business orchestration

- Project management
- Governance and approvals
- Informatics integration

The hard work is connecting all three in one workflow.

WHAT WE BUILT

Scout, our AI Research Scientist, and SigmaticOS

Works across the systems you already run. Nothing migrated, nothing replaced.

YOUR SYSTEMS, AS THEY ARE

- **ELN and LIMS** — any vendor, several at once
- **Assay and screening data** — results with their source record
- **Registration and inventory** — compound identity and batches
- **In silico tools** — open source and licensed partners
- **Lab automation** — requests out, measurements back
- **Your code and models** — wrapped as agents

SigmaticOS

Orchestrated by Scout, our AI Research Scientist

CONNECTORS
Configured to your systems; records keep their source ID.

PIPELINES
Fixed, auditable sequences, called by Scout or scheduled.

AGENTS
Open-source, partner, Sigmatic and your own methods.

RUN LOG
Inputs, versions and outputs kept for every run.

WHAT SCIENTISTS GET

- **Answers in conversation** — with every source linked
- **Ranked designs** — and a drafted next experiment
- **Reports a scientist can audit** — the working shown, step by step

The scientist decides

Nothing is written to a system of record or sent to the lab without approval.

BUILT IN FROM DAY ONE

- **Read before write** — retrieval is read-only
- **Numbers from code** — words from the model
- **A scientist signs off** — before anything leaves
- **SaaS, VPC or on-premise** — in your perimeter

WHY IT MATTERS

Four gaps in today's discovery workflow

Each one is answered by a different part of the platform.

SCOUT

One question, several systems

TODAY

Four systems, joined by hand.

WITH SIGMATIC

One conversation reaches them all.

PIPELINES

The same analysis, every time

TODAY

The method lives in one person's head.

WITH SIGMATIC

Same steps, every run, auditable.

LAB CONNECTION

A loop that reaches the bench

TODAY

Results end as an email to the lab.

WITH SIGMATIC

Requests the experiment, reads it back.

YOUR ASSETS

Methods and models that stay yours

TODAY

Licensed tools and models out of reach.

WITH SIGMATIC

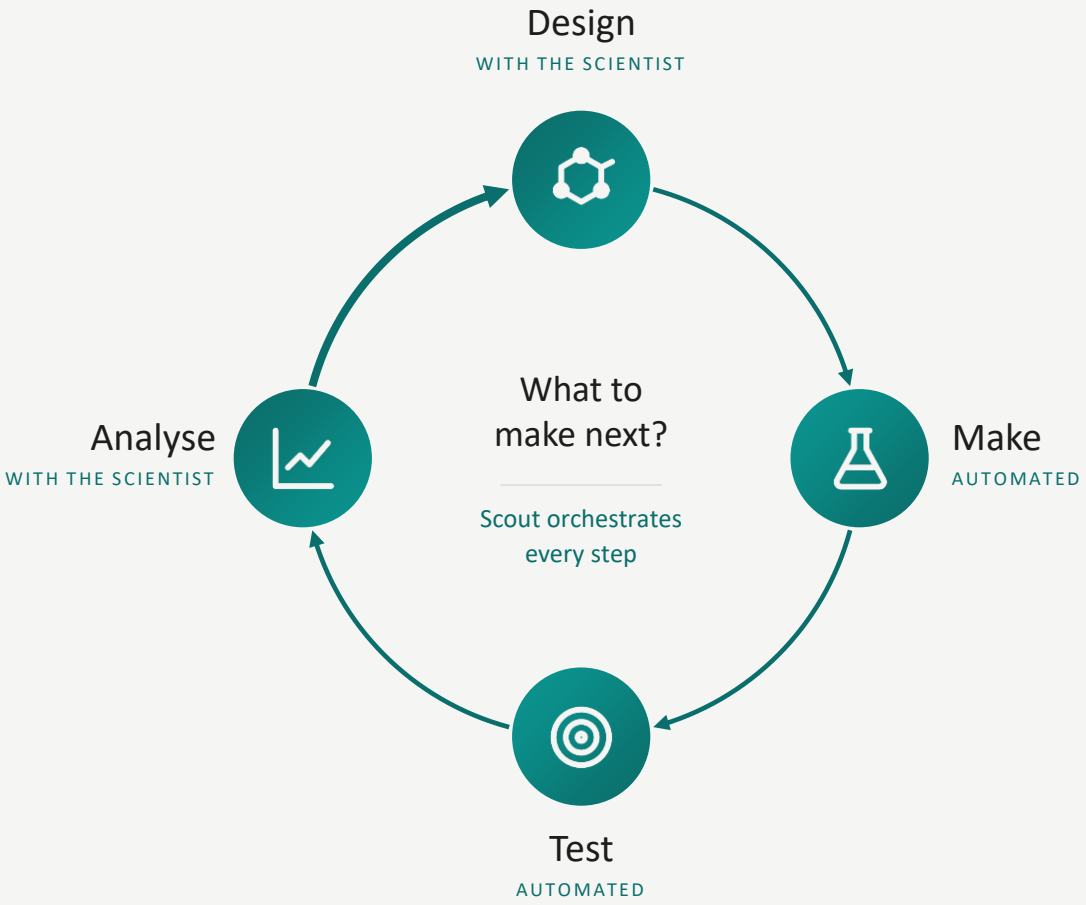
Run as agents; models stay yours.

THE OUTCOME Less failure early. A higher probability of success on what moves forward.

THE STORY WE FOLLOW

The decision at the centre of each DMTA cycle

Scout orchestrates the whole cycle. We follow one decision through two campaigns.



TODAY, A SCIENTIST PULLS IT TOGETHER BY HAND

- SAR
- Assays
- Registration
- Predictions
- Literature

WE FOLLOW IT THROUGH TWO CAMPAIGNS

01 — Co-scientist

Interactive: expand a hit

02 — AI-led

Autonomous: new chemical matter

CAMPAIGN 1 · INTERACTIVE CO-SCIENTIST

ATR inhibitors in ATM-null cell models

Five ATR inhibitors, four biallelic ATM-null A549 clones, 109 dose–response observations.

01

CAMPAIGN 1 · INTERACTIVE CO-SCIENTIST

Triaging ATR inhibitors in ATM-null cell models

Five inhibitors profiled across five engineered A549 models; two recommended for confirmation.

THE PIPELINE

01 SCIENTIST — Ask

Reproducible sensitivity window in ATM-null models?

`Scout`

02 SCOUT — Retrieve

7 models, 109 dose–response points, read-only.

`BioELN` `ChemELN`

03 SCIENTIST — Direct

Prioritise on binding, druggability, off-target liability.

`Scout`

04 SCOUT — Profile

Docking into 9L40, druggability, 47-target panel.

`PDB` `Vina` `ADMET`

05 SCIENTIST — Request

Biochemical ATR assay on the two named compounds.

`Lab`

06 SCOUT — Analyse

Dose–response back, fitted values and QC flags.

`Code`

TODAY

Export, dock, check liabilities, join by hand.

WHAT THE SCIENTIST GETS

- Compounds ranked, with sources
- What the data does not support
- An assay request, awaiting approval

SYSTEMS CONNECTED

`BioELN` `ChemELN` `LIMS` `RCSB PDB` `AutoDock Vina` `Druggability` `Off-target panel` `Lab request`

MODE

Interactive co-scientist

The chemist steers at every turn, not just at the ends.

SHARE IN SILICO

WHO DECIDES

The scientist, at three of the six turns.

WHY CO-SCIENTIST HERE The scientist redirects between every Scout turn.

ASK IT IN SCOUT “Take those compounds through in silico prioritisation, then tell me which two should enter confirmation.”

The interactive session, from cell data to a biochemical assay

Five ATR inhibitors, genotype-stratified models, and a confirmation assay sent only on approval.



THE STEPS

01 Ask
Sensitivity window in ATM-null models?

02 Retrieve
7 models, 109 responses, read-only

03 Profile
Docking (9L40), 47-target panel

04 Request
HTRF ATR assay, on approval

05 Analyse
Dose–response read back

Amber: the scientist · teal: Scout

CAMPAIGN 1 · THE RESULT

What the cycle recommended, and what it held back

Ceralasertib and berzosertib forward; elimusertib's 10.07× window held back on a single replicate.

COMPOUND	WINDOW	REPLICATION	DRUGG.	logS	FLAGS	DISPOSITION
Ceralasertib	4.58× / 4.88×	2 experiments, 6 replicates	50	−2.73	7	Recommended
Berzosertib	3.10×	1 experiment, 6 replicates	35	−4.99	9	Recommended
Elimusertib	10.07×	1 experiment, single replicate	50	−3.47	9	Held back
Camonsertib	—	partial-loss model only	50	−2.31	4	No comparison
VE-821	—	incomplete curve, two concentrations	20	−5.05	4	No window

PAINS clear on all five. Druggability is a weighted composite of PAINS, solubility and ADMET, and every compound returns LOW trust: these are predictions, not measurements.

CAMPAIGN 2 · AI-LED

Factor Xa: alternatives to rivaroxaban from PDB 2W26

Structure-anchored scaffold hopping with shape, pharmacophore and docking, led by Scout.

02

CAMPAIGN 2 · AI-LED

Structure-anchored scaffold hopping from Factor Xa (PDB: 2W26)

Search bounded at ECFP4 ≤ 0.35 to rivaroxaban, MW 300–550 Da, cLogP 1.0–5.5, with a ≤ 2.0 Å redocking control.

THE PIPELINE

01 SCIENTIST

Objective

Novel, developable FXa leads from 2W26.

Scout

02 SCOUT

Plan

Ensemble: novelty, selectivity, PK.

Ensemble

03 SCOUT

Verify

Structure checked; search bounds set.

RCSB RDKit

04 SCOUT

Screen

Shape, pharmacophore and docking.

FastROCS Orion Vina

05 SCIENTIST

Review

Directions triaged, limits stated.

Report

SYSTEMS CONNECTED

RCSB PDB OpenEye Orion FastROCS Plus RDKit AutoDock Vina PLIP ProLIF ADMET

MODE

AI-led research

An objective across cycles.

SHARE IN SILICO

WHO DECIDES

The scientist: objective and review.

TODAY

Weeks of hand-offs; one hypothesis explored.

WHAT THE SCIENTIST GETS

- Three directions, each a test
- Every library accounted for
- What is not yet advanceable, stated

WHY AI-LED HERE A search too wide to supervise by hand.

ASK IT IN SCOUT "Find novel, developable leads for a new Factor Xa programme as alternatives to rivaroxaban."

orion a Cloud-native Platform

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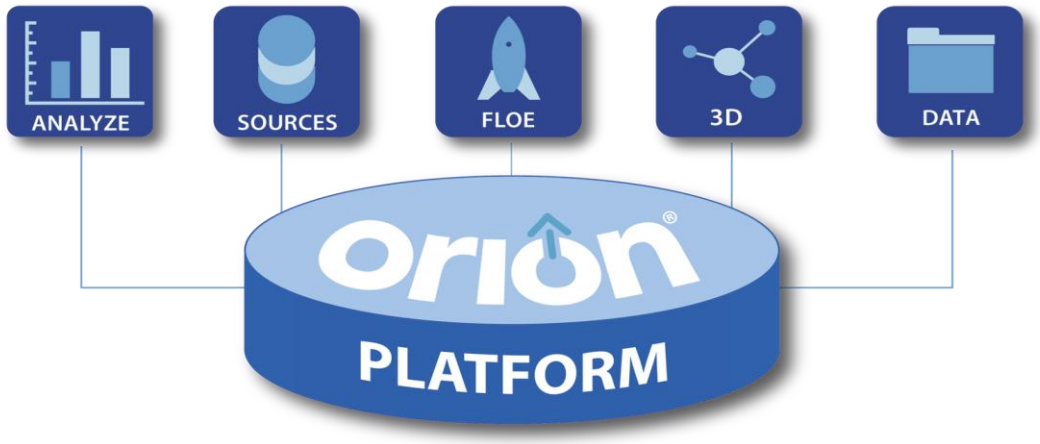
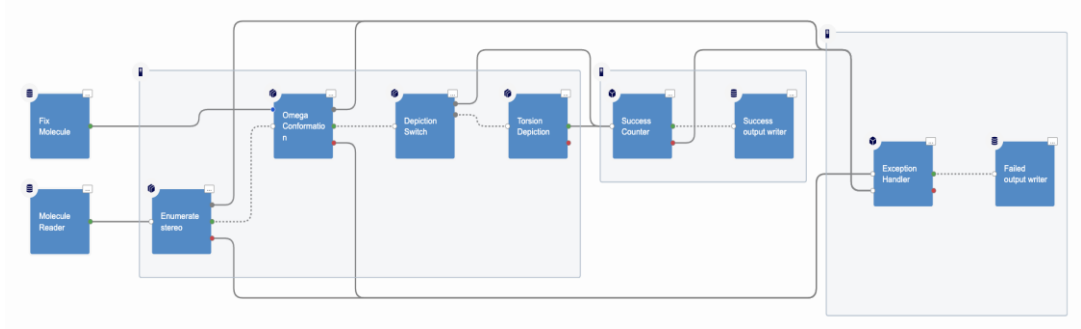


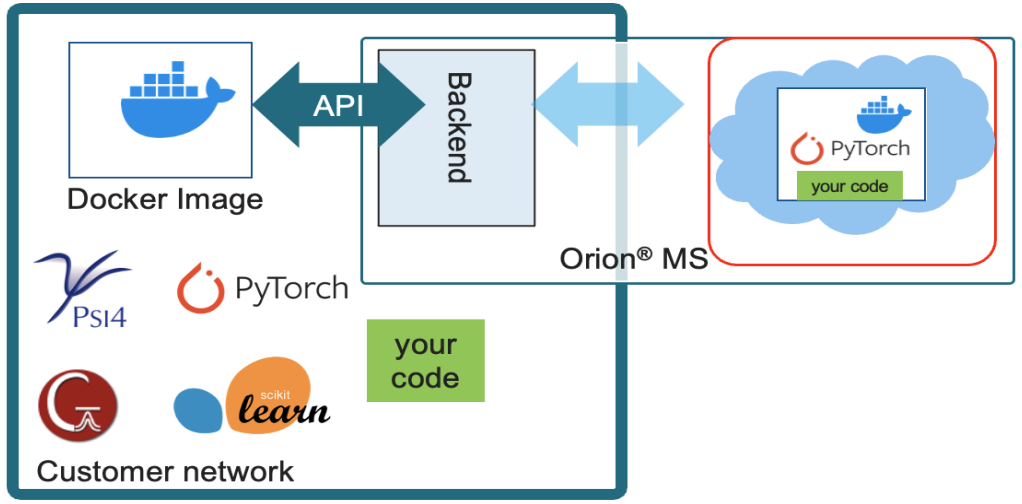
Fully Integrated Environment for Molecular Modeling and Design



Calculations Powered By the Cloud (100's GPUs, 10,000's CPUs)



Calculations Run at Scale using Parallization with Cubes and Floes

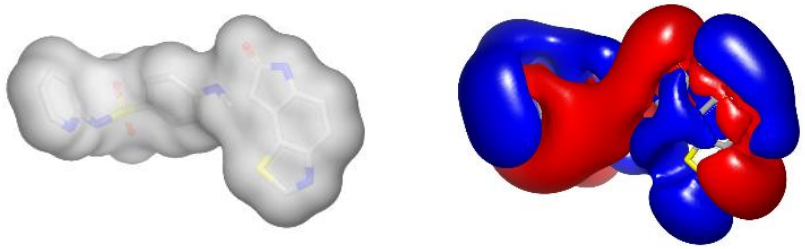


Via Docker and our API you can make your software cloud-native

Innovated Methods for Virtual Screening

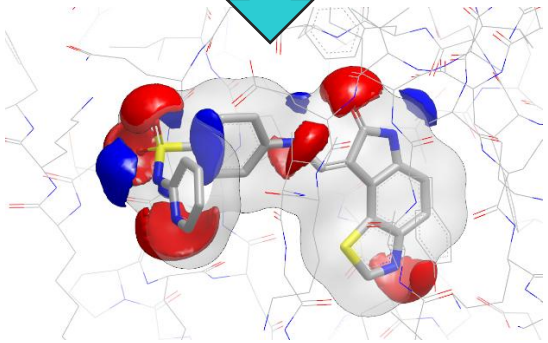
Ligand-Based 3D Similarity Methods – Why 3D?

The two fundamental molecular properties

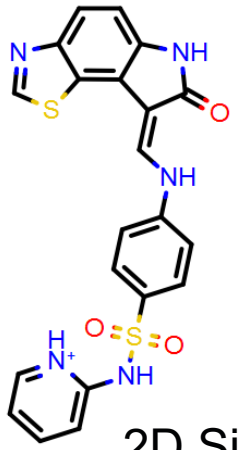


Shape

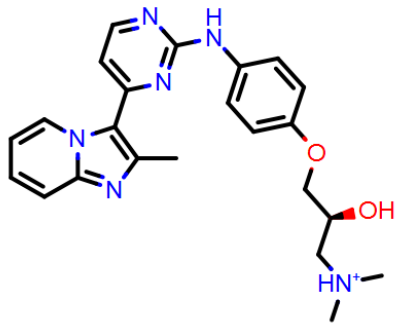
Electrostatics



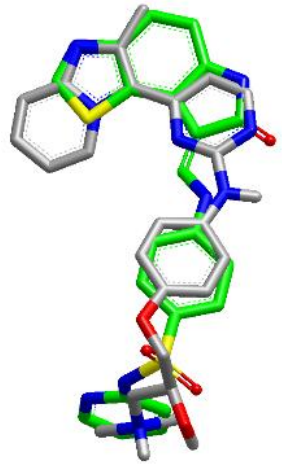
CDK2
IC_{50} = 10 nM



CDK2
IC_{50} = 10 nM



3D Overlay



2D Similarity = 0.12

3D Shape Similarity = 0.77

Similarity in shape and electrostatics → **similarity in biology**

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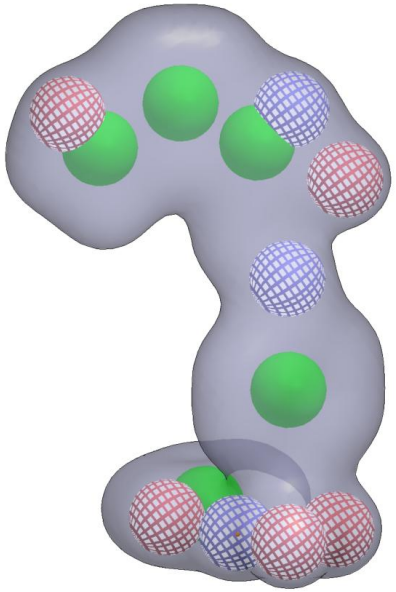
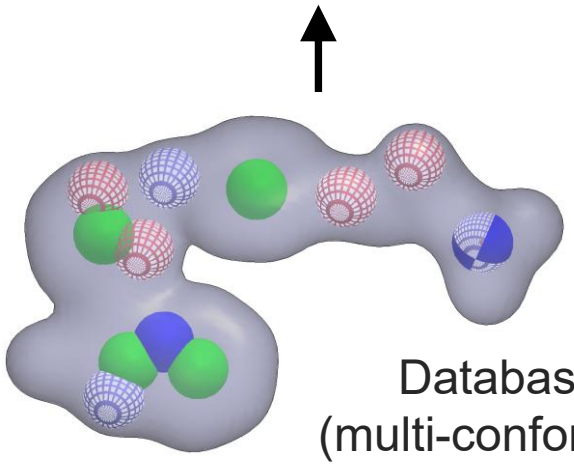
Innovated Methods for Virtual Screening

Ligand-Based 3D Similarity Methods – How ROCS works

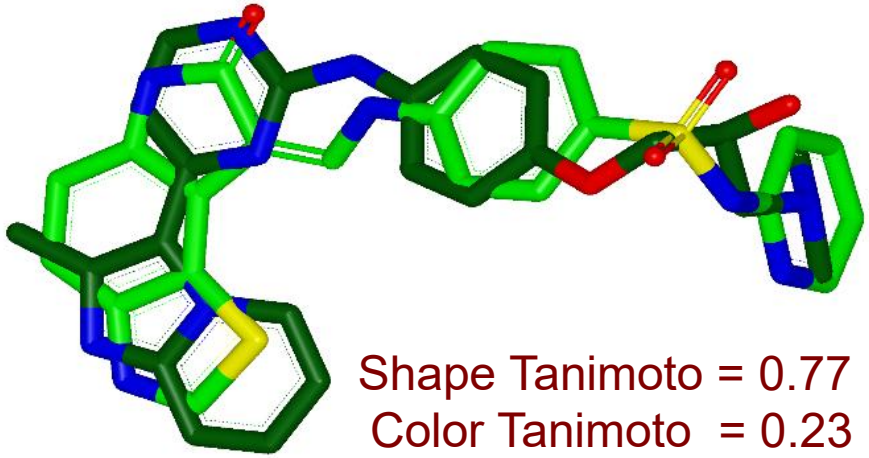


Query

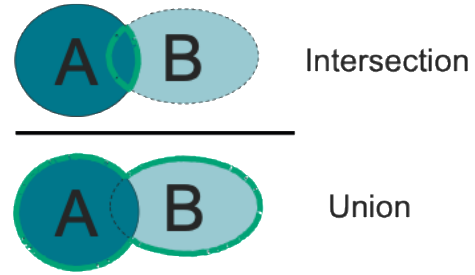
Overlay and optimize alignment rigidly



Database (multi-conformer)



Shape Tanimoto = 0.77
Color Tanimoto = 0.23
TanimotoCombo = 1.00



***ROCS (Rapid Overlay of Chemical Structures)**

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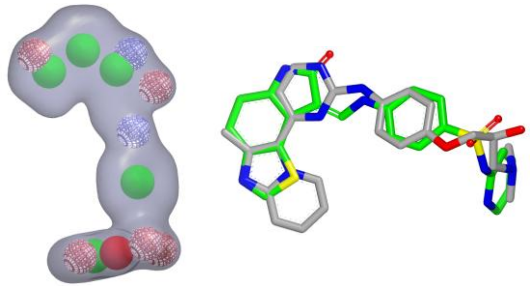
Hit-ID Module Innovated Methods for Virtual Screening in orion

Ligand-Based 3D Similarity Methods

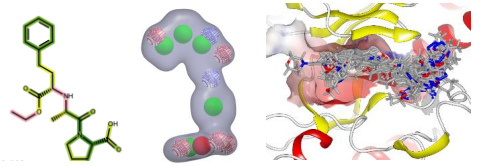


Molecule Search/ FastROCS/ROCS X

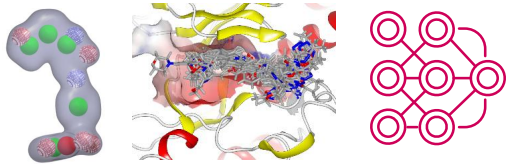
(0-$)

Hybrid Methods

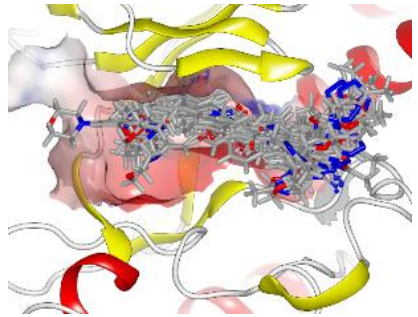
FastROCS Plus ($) – *FastROCS search followed by hitlist rescoring*



Gigadock Warp ($$) – *Subset docking followed by FastROCS similarity for all to top hits, then ML docking scores + full docking*



Structure-Based Methods



Gigadock

($-$$$$)

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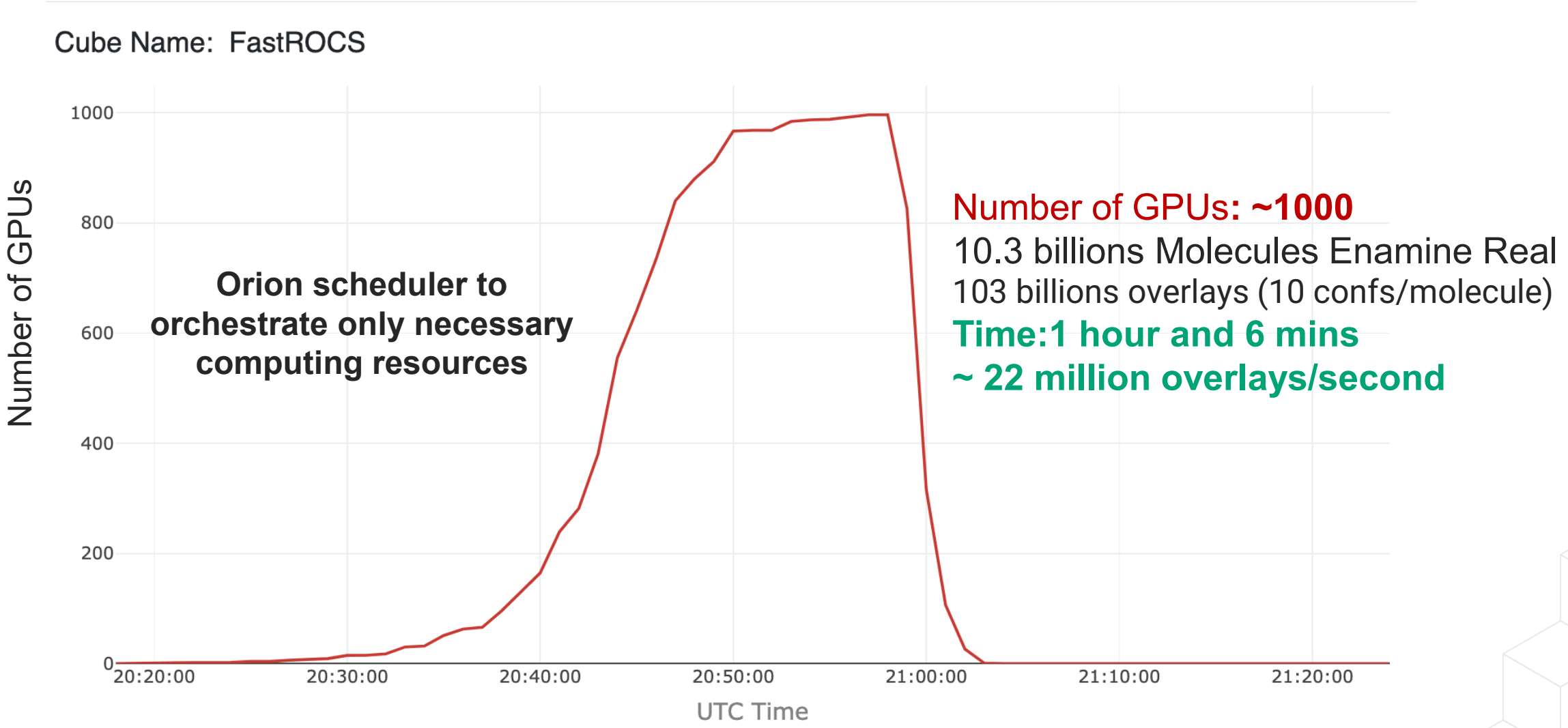
FastROCS Plus Screens 10 Billions Enamine in an *Hour*



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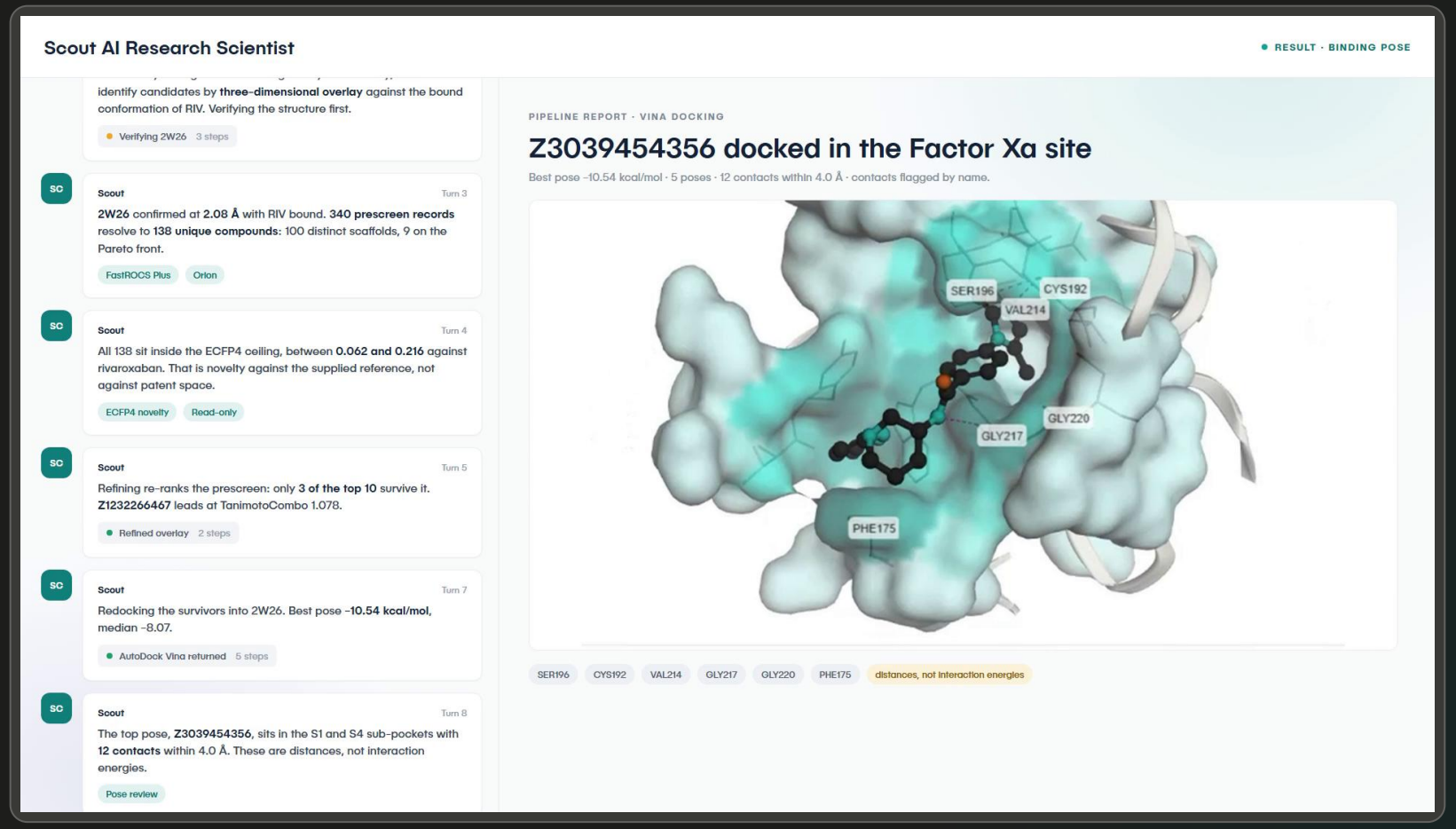
The Factor Xa search, end to end

Five steps from the objective to triaged chemistry directions, across a three-task ensemble.



THE STEPS

01 Objective
Novel FXa leads beyond rivaroxaban

02 Plan
Three-task ensemble

03 Verify
2W26 holo, 2.08 Å; bounds set

04 Screen
Shape, pharmacophore, docking

05 Review
Directions triaged, limits stated

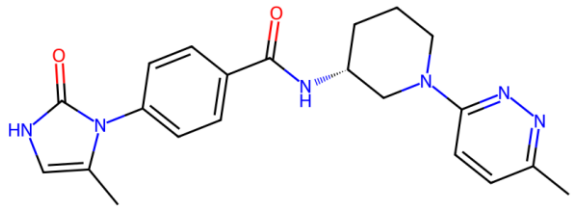
Amber: the scientist · teal: Scout

CAMPAIGN 2 · THE RESULT

Three candidates worth exploring

All novel against rivaroxaban, all reproducing the query shape, each with a named next experiment.

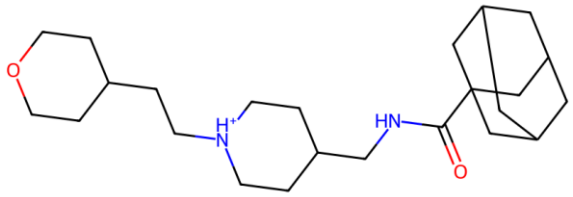
340	138	100	9
RECORDS SCREENED	NOVEL CANDIDATES	DISTINCT SCAFFOLDS	ON THE PARETO FRONT



Z1232266467

Refined rank 1

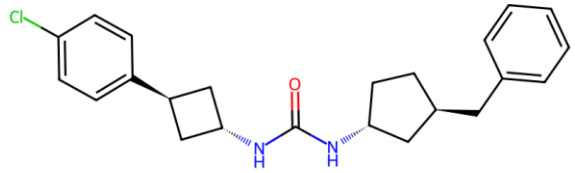
TanimotoCombo	1.078
Shape / colour	0.822 / 0.256
ECFP4 to RIV	0.200
MW / cLogP	392.5 / 1.97



Z4493814656

Refined rank 2

TanimotoCombo	1.077
Shape / colour	0.767 / 0.310
ECFP4 to RIV	0.188
MW / cLogP	389.6 / 2.43



Z5392689995

Refined rank 3

TanimotoCombo	1.059
Shape / colour	0.797 / 0.263
ECFP4 to RIV	0.160
MW / cLogP	382.9 / 5.30

NEXT Restore the pose coordinates to audit the S1 and S4 contacts, then measure Factor Xa inhibition on these three.

CONSIDERATIONS

What to weigh when you adopt an agentic platform

Two of these four layers are what a demo shows you. The other two are the ones that take years to get right.



ABOVE THE LINE · WHAT A DEMO SHOWS

Agentic orchestration

- Agent and tool integration
- Planning and reasoning
- Automated workflow execution

Data and scientific knowledge

- Scientific knowledge integration
- Integrated data access and pipelines
- Continuous learning and adaptation

BELOW THE LINE · WHAT TAKES YEARS TO GET RIGHT

Trust and governance

- Audit and traceability per agent
- Compliance, security and provenance
- Observability and monitoring

Platform and infrastructure

- Resource orchestration
- Scalability across a programme
- Extensibility: API, MCP, CLI

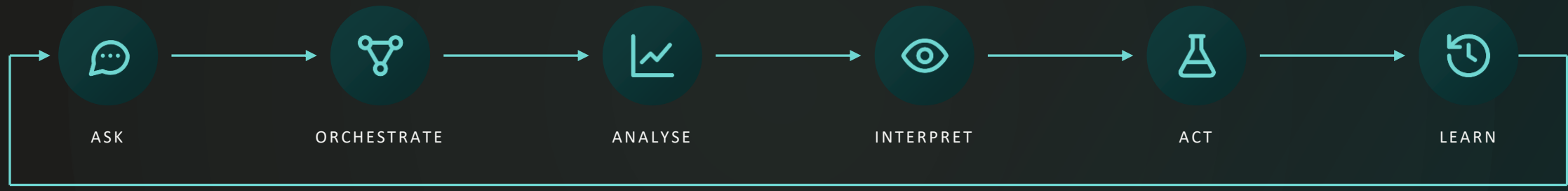
The questions worth asking of any platform are the ones below the line.

LOOKING AHEAD

Where this goes next

The scientist sets the question. The cycle closes around it, and delivers traceable results on every cycle.

THE CYCLE, END TO END



01

An AI scientist per programme

It takes the next cycle, not the next task.

02

One conversation, every system

Data, in silico, lab and record in one place.

03

Work that shows itself

Drafted, traced and approved before it leaves.

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Questions

Thank you.

COME AND TALK TO US

Booth 14

Bring a programme and we will talk through what it takes.

OR TRY SCOUT NOW

30-day trial