Imperial College London

DIAL-A-MOLECULE
An EPSRC Grand Challenge Network

EPSRC
Pioneering research and skills

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Dr.Reddy's
Agilent Technologies
domainex
the faster route to drug discovery
gsk GlaxoSmithKline
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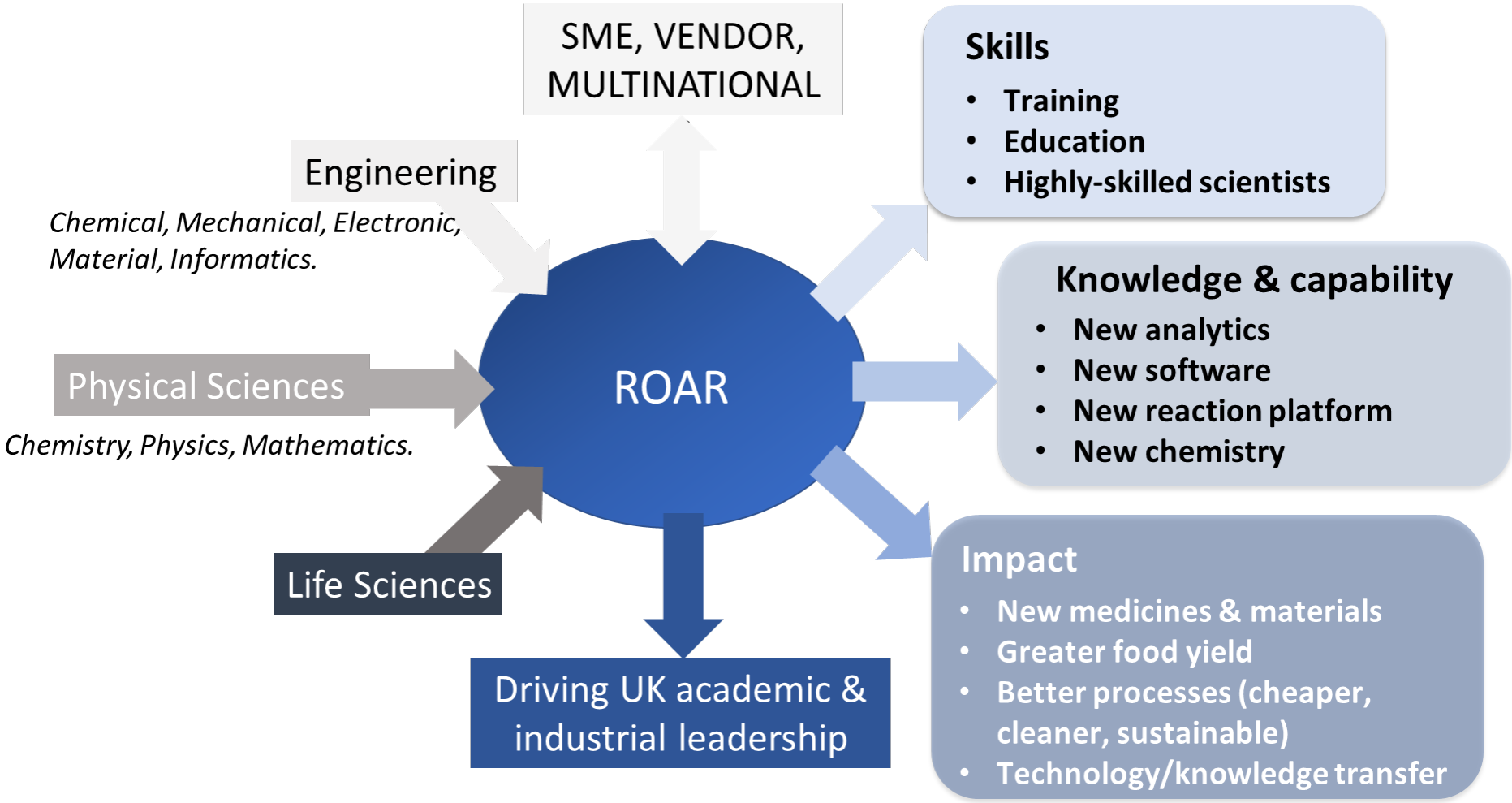
jmp Statistical Discovery™ From SAS.
METTLER TOLEDO

Centre for
Rapid, Online Analysis of Reactions
(ROAR)

Dial-A-Molecule Institute @ Imperial College London

UK's Flagship Facility for Synthetic Chemistry

Centre for Rapid Online Analysis of Reactions (ROAR)



http://www.imperial.ac.uk/rapid-online-analysis-of-reactions/

ROAR: Our Mission

- An infrastructure project – equipment AND expertise
- Training in key skills that are not currently provided in academic education
- Develop/discover the next generation of synthesis & analytics
- From fundamental studies to industrially-relevant problems
- Enables UK Academia and industry to take leadership in Molecular Sciences research

Who we are, and what we do

Prof. Mimi Hii
Director

Dr. Ben Deadman
Facility Manager

Dr. Paola Ferrini
Research Technician

TBA
Research Technician

- Provide access to state-of-the-art facilities
- Organise Training
- Showcase Technology

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Reaction Automation: Hardware

- First robot: automatic dispensing of solid/liquids
  - Mounted in a purge box
  - Ability to handle plates/vials
  - Powder dispense from vials and hoppers
  - Positive displacement liquid dispense (10 µL – 10 mL)
  - Analytical balance with integrated camera for dispensing mass up to 1200 g (0.1 mg resolution)
  - Ionizer to minimize static

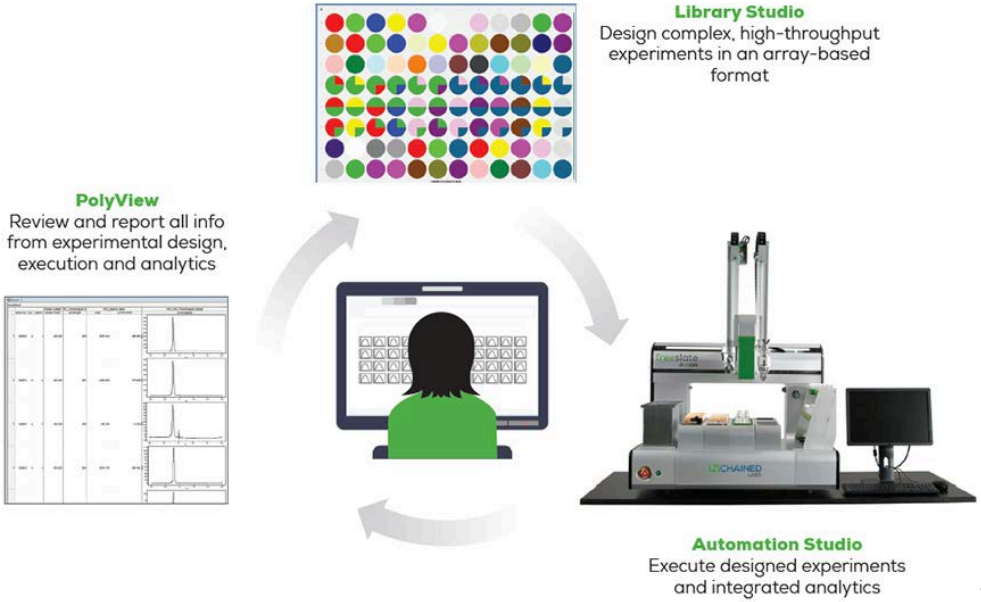
freeslate jr. configured for solid dispense

freeslate jr. delivering a plate from shoulder hotel to balance

1 Waste bin
2 Powder dispense hopper rack
3 Viscous liquid and solid dispenser
4 Vial/plate gripper
5 Tip rack
6 Balance with integrated camera
7 Vertical plate hotel

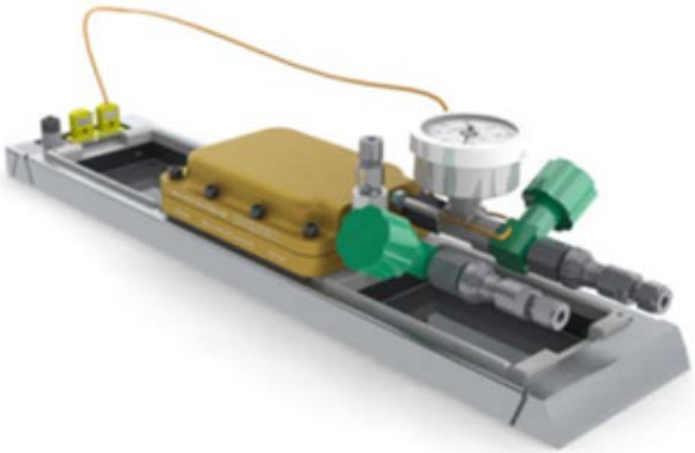
Reaction Automation: Hardware

- Second robot: High-Throughput Screening
  - Liquid dispense and aspiration
  - ca. 1,000 serial operations per day
  - 1 mL vials (96-well plate spacing) to 125 mL jars



Reaction Automation: Hardware

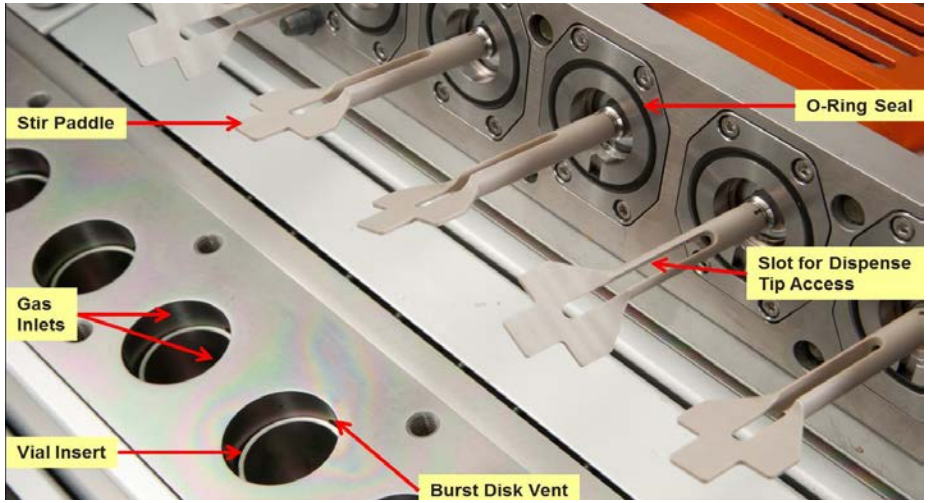
- Key features
  - Magnetic tumble stirring
    - Excellent mixing even in 96-well plate format
    - Will place additional tumble stirrers off-robot



  - -20 to 180 °C in 6 zones
  - Deck-Screening Pressure Reactor
    - 48 wells with magnetic stirring
    - Up to 200 psi (14 bar) at 180 °C (300 psi at 24 °C)

Reaction Automation: Hardware

- Third robot: Optimizing Sapling Reactor (OSR) module
  - 8 parallel reactors, 5-25 mL working volume
  - Additional heating/cooling/stirring plate/vial positions for screening
  - Overhead mechanical stirring
  - Independent temperature controls (-20 →200 °C)
  - Independent pressure controls (30-400 psi @ 150 °C)
  - Gas manifolds.
  - *Sampling while under pressurized atmosphere, including suspensions*



Analytical Support: Chromatography

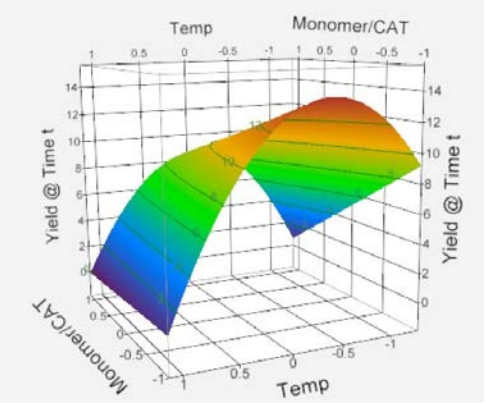
- Agilent 1290II/6530-DAD-QTOF
  - Binary pump
  - Multisampler (holds up to16 x 384 = 6144 samples, vials, 96- or 384 well plates)
  - Sample cooler
  - Multicolumn thermostat (up to 8 columns)
  - Diode-array detector
  - QTOF

- Agilent 1260II SFC/hybrid-DAD-MS
  - Quaternary pump
  - Multisampler (up to 6144)
  - Sampler cooler
  - DAD
  - Valve for SFC/uHPLC switching

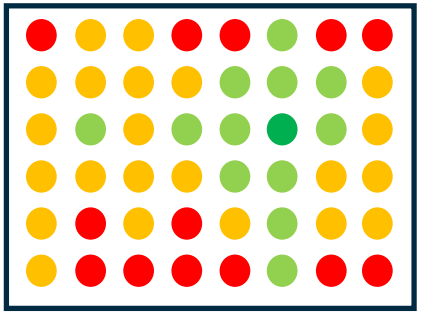
Note: This is in addition to the £4M Agilent Measurement Suite

Reaction Automation: Applications

- Optimisation of Continuous Variables
  - Multivariate optimization using Design of Experiments (DoE)
    - JMP providing licenses for DOE software
  - Solubility studies (possible)
    - For recrystallization
    - For formulation
  - Automate other testing protocols



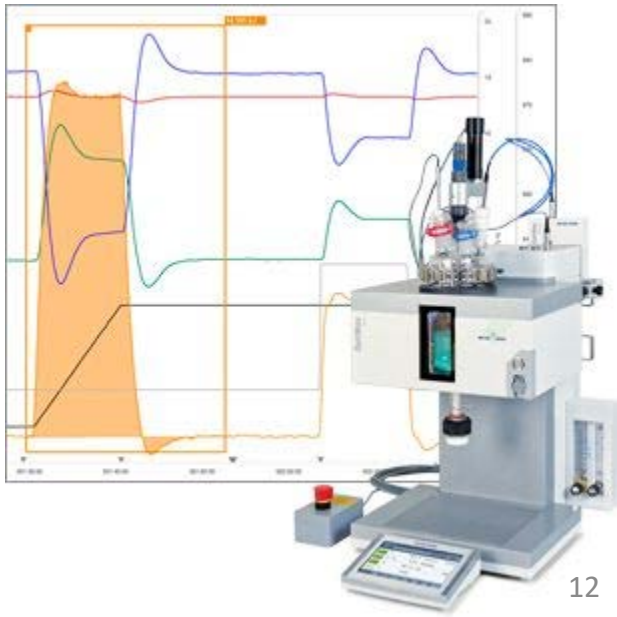
- Categorical Variable Screening
  - *e.g*. Ligand, solvent, and additive screens
  - Full factorial screens
    - 9 heated and stirred positions
    - Each position can hold 96 vials or 384 well plates
    - Potentially > 3,000 conditions screened at once!



Reaction Kinetics: Reactors

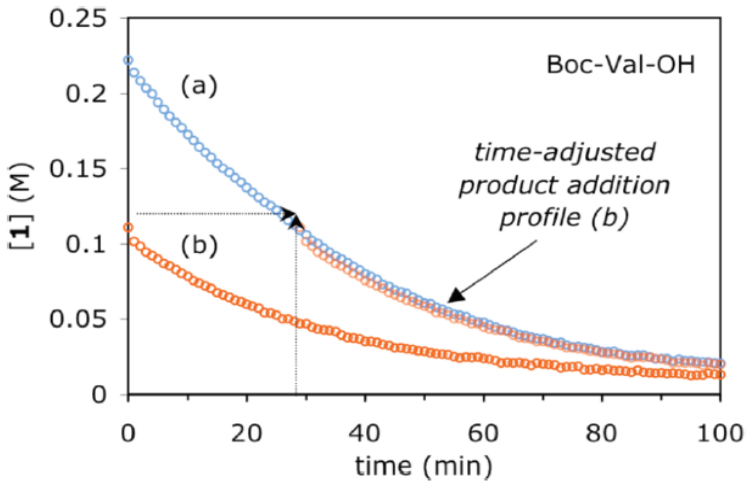
- Mettler-Toledo EasyMax station
  - 2-Position (25 mL – 100 mL)
    - or 6-position (3 mL – 25 mL)
  - Alloy C22 stirrer
    - or magnetic stirring

- OptiMax HFCal
  - Single Position (50 mL – 1,000 mL)
  - Automated dosing
  - Alloy C22 stirrer
- Automated dosing
- Multiple temperature control regimes
- PC Control and full data collection
- Reaction studies across scales



Reaction Kinetics: Analytics

- ReactIR
  - Batch probe
  - Temperature controlled flow-cell
- EasySampler
  - Automated sample collection and dilution for offline analysis (e.g. HPLC)
- Heat Flow Calorimetry
- PAT Control Box
  - Can take feed from other sensors (e.g. pH)
- Data is synchronised
- High-quality reaction data



Continuous Flow: Hardware

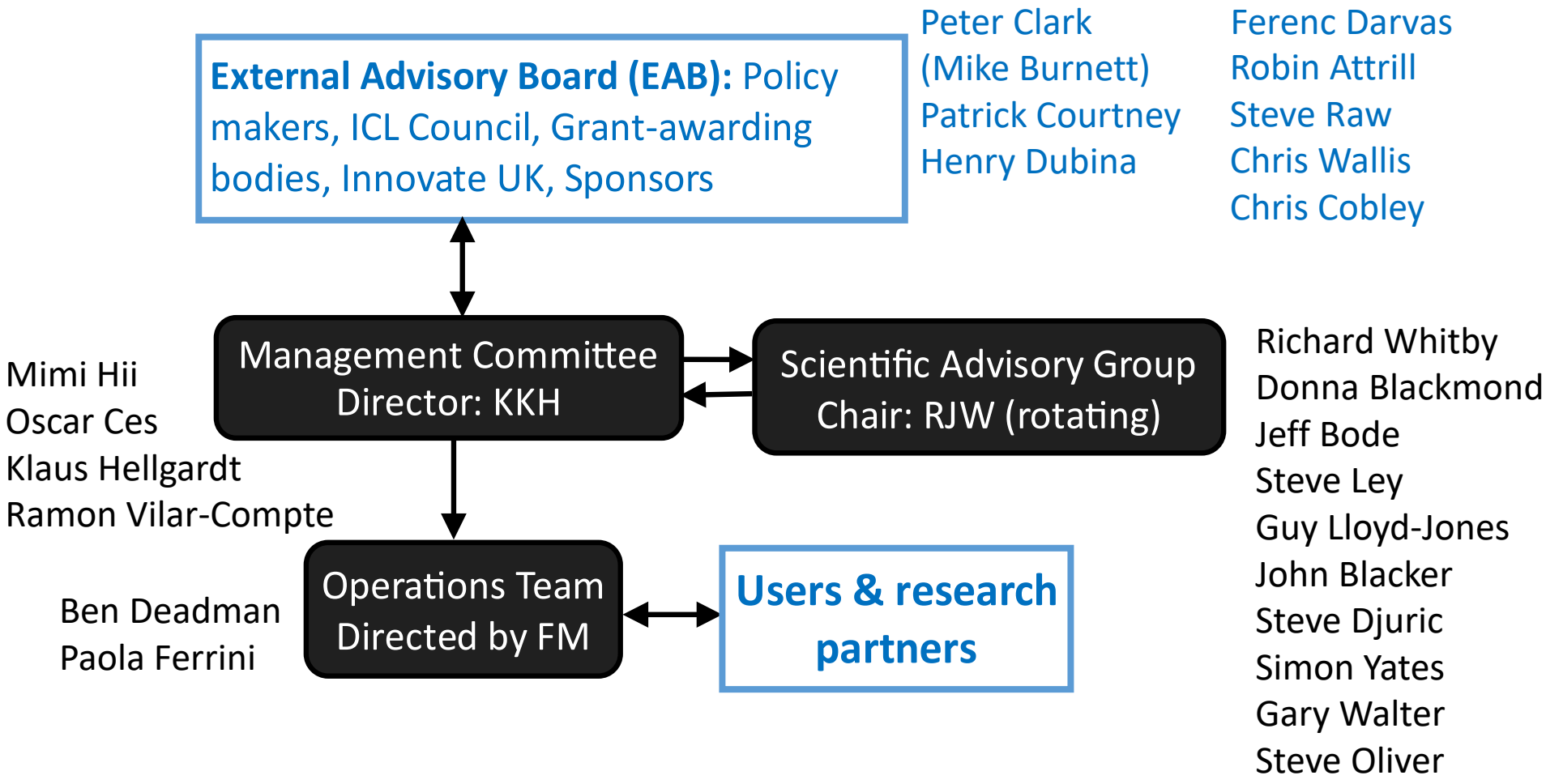
- Thalesnano: H-Cube Pro, Phoenix, Cat Cart Changer
- MT ReactIR-flow cell

- CF hydrogenation reactor with H_2-generator (up to 60 mL/min)
- 10-150 °C
- 1-100 bar
- 0.3-3 mL/min

- Standalone unit with BPR, HPLC pump, gas module and g-l mixer
- r.t. to 450 °C
- 1-200 bar
- 30/70 mm cartridges or 8 mL SS loop

Additional flow reactors being acquired through tender.

Organisation of ROAR



- Up to 50% for external users: 2171.5 h (290 days)/yr
- **Academic access is subsidised up to end of 2020**
- Commercial projects considered on a case-by-case basis

ROAR Access Process

1. Call for proposals
   - Join the ROAR mailing list
   - Calls released as facilities are commissioned
   - First calls expected Q4 2018
2. Contact us (ROAR@imperial.ac.uk) to discuss your requirements
3. Proposals evaluated by the Scientific Advisory Group
4. During your ROAR visit
   - We will provide support
   - All data is collected (ELN)
5. After your ROAR visit
   - Help with interpretation of your results.
   - Feedback
   - (For academic projects): Data deposited in an open access repository.

More Information

ROAR website

www.imperial.ac.uk/rapid-online-analysis-of-reactions/

ROAR website

ROAR mailing list

http://eepurl.com/duaxZf

Contact us

ROAR@imperial.ac.uk