

CHIMERA

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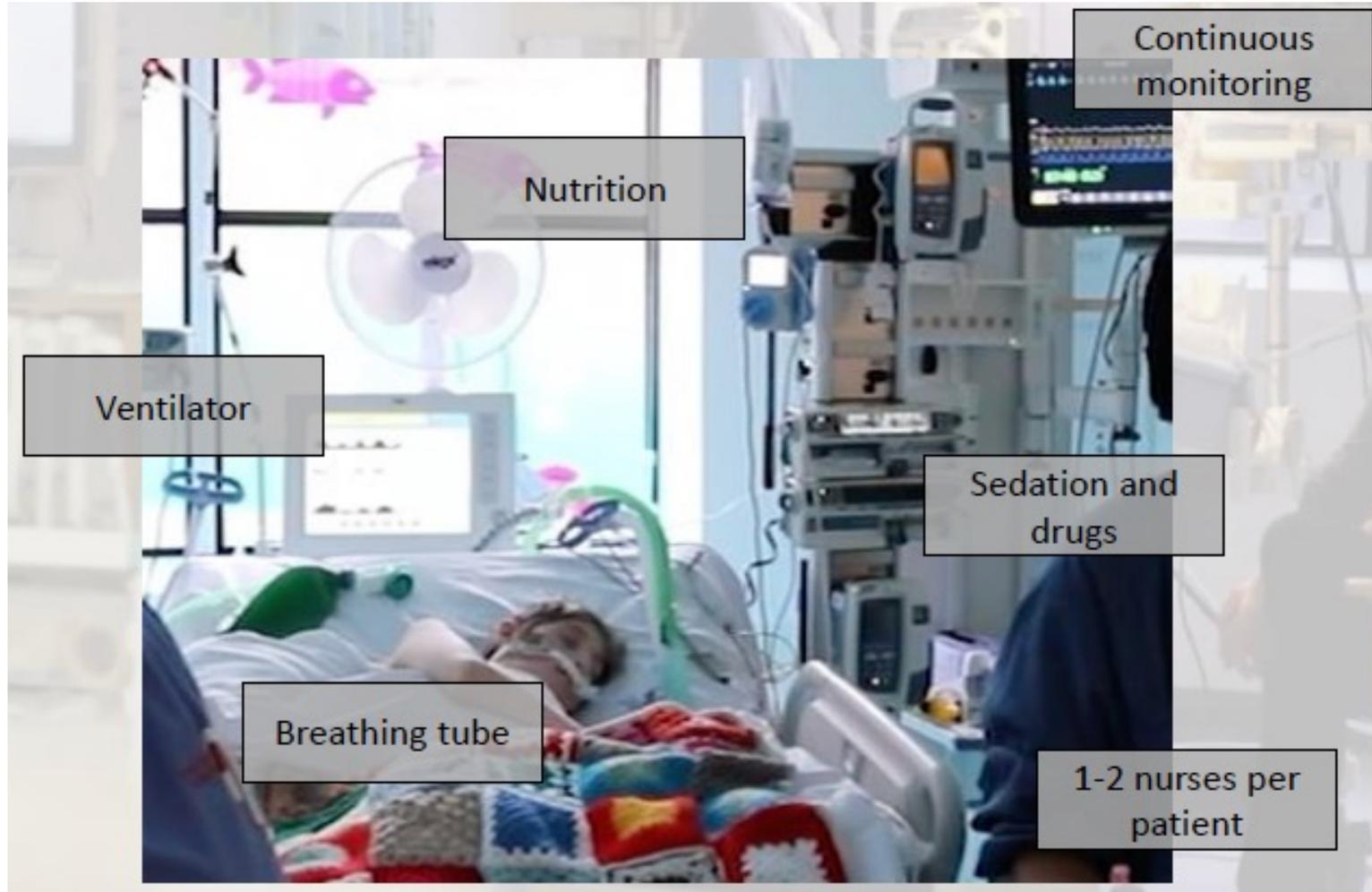
noun

Collaborative Healthcare Innovation through
Mathematics, Engineering and Artificial
Intelligence

Rationale

- Each year (before COVID-19) around 20,000 children, 30,0000 adults in the UK need intensive care
- All these patients are monitored continuously at the bedside
- BUT the wealth of these physiological data are not currently used to inform clinical decision making
- Need for multidisciplinary, sophisticated modelling
- Ambition to broaden to wealth of physiological data collected by patients and hospitals





- Heart rate
- Blood pressure
- Breathing rate
- Oxygen saturations
- Carbon dioxide levels
-

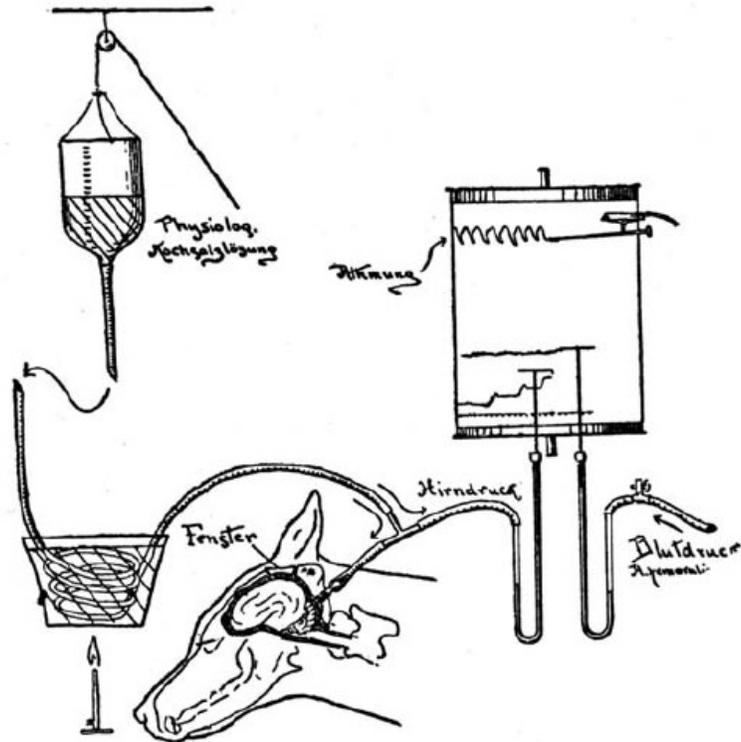


... but only fraction of data used to make treatment decisions

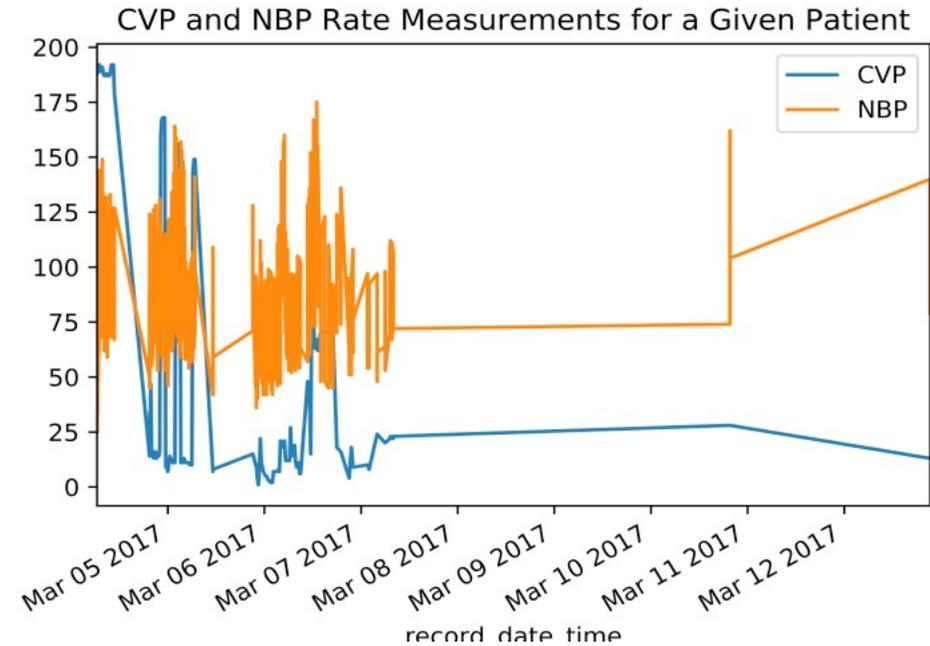
Continuous data generation in ICU patients (e.g. every 5 seconds)...

Admission Documents	Progress notes	Consult Notes	Discharge/Transfer	Child Protection Checklist	ECLS	ICU Chart	Cares	Ward Chart	Neonatal Care	RRT	Labs	Resus	Patient Monitoring	CATS flowsheet	Graphs	How To	MDT - Test	Test-Do not u...	
Flowsheet (Paeds)																			
04/04/2019																			
Weight (Working)	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000	25.000
Height (Working)																			
Head circumference (cm)																			
Tri Weekly Weight (Kg)																			
No. of Days on ITU		1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Date/Time Fit For Discharge																			
Heart Rate	123	125	125	133	128	124	123	121	119	117	117	117	122	117					
Heart Rhythm	NSR	NSR	NSR	Sinus tach	Sinus tach	NSR	NSR	NSR	NSR	NSR	NSR	NSR	NSR	NSR					
Art BP	111/53 (68)	90/53 (66)	89/51 (63)	103/69 (81)	101/43 (58)	104/58 (70)	99/50 (62)	97/48 (60)	86/45 (56)	87/46 (57)	81/45 (55)	80/42 (54)	83/45 (55)						
NBP	91/54 (64)																		
Temp. 1	Oes. 37.0	Oes. 36.9	Oes. 36.9	Oes. 37.0	37.0	Oes. 37.0	Oes. 37.4	Oes. 37.4	Oes. 37.2	Oes. 37.2	Oes. 37.0	Oes. 36.9							
Temp. 2	Ax. 37.0					Ax. 37.4													
Temp. 3																			
Bair Hugger																			
Respiratory Rate	22	25	25	25	22	22	20	18	20	18	18	18	17						
Capillary Refill	2-3 Secs		2-3 Secs		2-3 Secs	< 2 Secs	< 2 Secs	< 2 Secs	< 2 Secs	< 2 Secs	< 2 Secs	< 2 Secs							
General Colour	Normal		Normal		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal						
CVP																			
Intra-abdominal pressure																			
Cardiac Output																			
Cardiac Index																			
NIRS Channel Right Forehead																			
NIRS Channel 3 Somatic																			
Pupils, Left			2: Briskly		: Pinpoint	3: Briskly			3: Briskly			3: Briskly							
Pupils, Right			2: Briskly		: Pinpoint	3: Briskly			3: Briskly			3: Briskly							
Sedation Score			-5			-5			-5			-5							

Some of the Challenges...



Most physiology knowledge developed from animal experiments



Two different blood pressure readings – note data recording failure or withdrawal

Patient data are noisy with artefacts – needs clinical interpretation

Some of the Opportunity.....



University College London Hospitals
NHS Foundation Trust



Great Ormond Street
Hospital for Children
NHS Foundation Trust

Data Availability:

- **GOSH** (three ICUs, paediatric, neonatal, cardiac) – 51 beds for babies and children up to 16 years old
- First hospital in Europe to implement a system to record bedside monitor data every 5 seconds (2015)
- Access to 5,500 records (admissions Jan 2016 – Dec 2018)
- **UCLH** – 35 bed adult ICU
- Founding partners of the Critical Care Health Informatics Collaborative – 45,000+ admissions from 11 adult ICUs at 5 UK teaching hospitals

Opportunity to Impact on Critical Care:

- Early warning signs for patient deterioration
- How to set patient-specific ventilator parameters
- When should you extubate a patient?
-

Our Broad Aims

- Use real patient data
- Develop data-driven models of human physiology
- Develop an understanding of patient physiology during critical illness and recovery
- Improve methods for patient treatment
- Build an internationally-recognised, multidisciplinary and multisector Hub focused on these questions



Work Packages (WPs)

WP1 – statistical learning from clinical data

WP2 – iteratively testing and improving biomechanical models

WP3 - learning biophysical model structure and parameters with neural networks

WP4 – multidisciplinary workshops, clinical and industry engagement

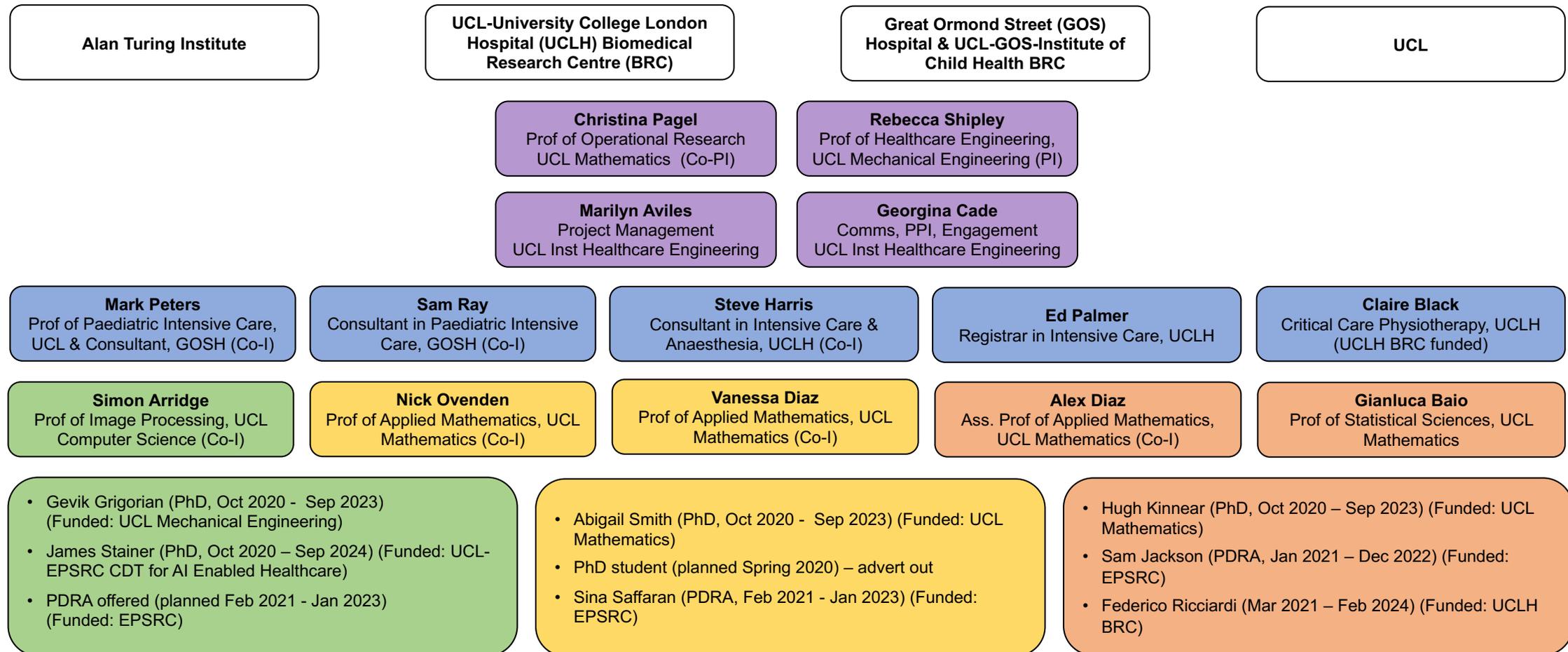
WP5 – data curation, infrastructure, ethics, open-source data and model platforms

WP6 – patient and public engagement, dissemination

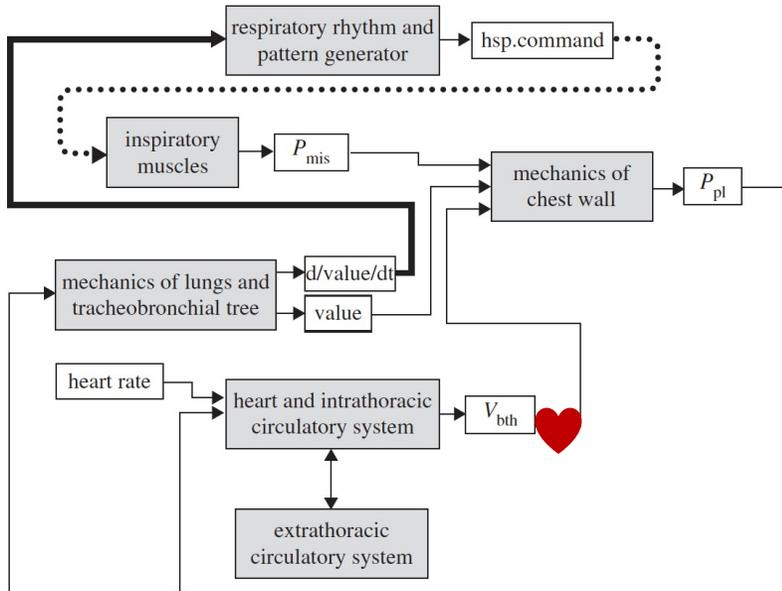


The team so far

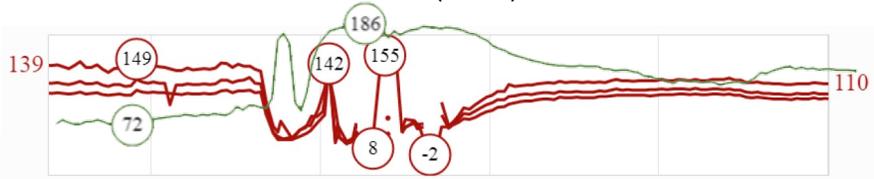
-  Management, partnership building, engagement, dissemination (WP4,5,6)
-  Critical care, clinical data (WP4,5)
-  Statistical analysis and learning (WP1)
-  Biomechanical modelling (WP2)
-  Machine learning (WP3)
-  Project partners and host institution



Learning Physiology Models

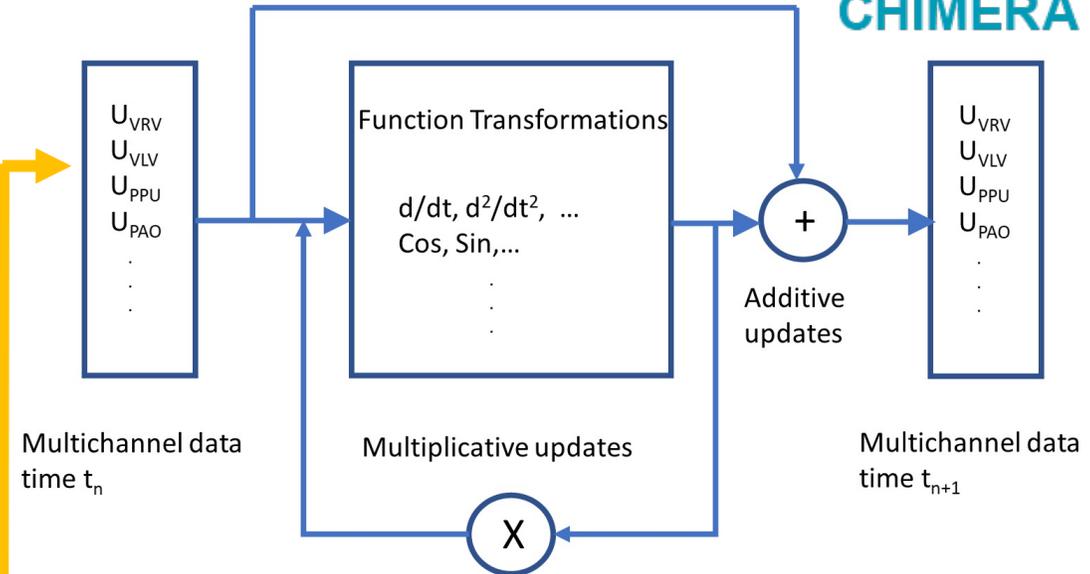


Jallon et al. *Phil Trans R Soc* (2009) **367**, 4741-4757

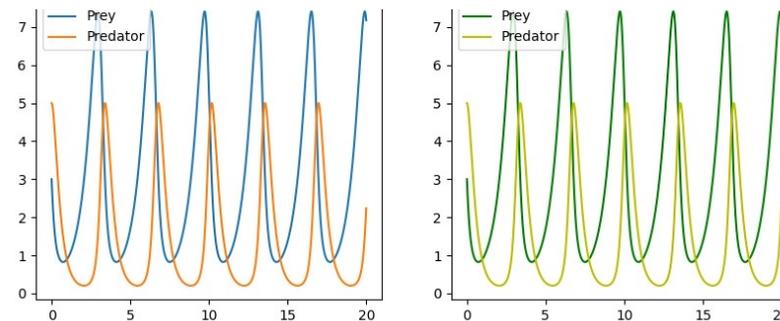


Example individual patient data streams from GOSH PICU: heart rate, blood pressure (systolic, diastolic, mean), recorded every 5 seconds for duration of patient stay. Additional data streams include:

- Respiratory rate
- Blood oxygen saturation
- Blood volume
- End tidal carbon dioxide measurement
- Temperature



Example : Learned Lokta-Volterra Equations



Output:

- ✓ Better understanding of physiology
- ✓ Predictive tools to inform clinical intervention based on individual's data

Computational Stats

Objectives include:

- Identify and characterize the most important parameters from available patient data.
- Design algorithms for efficient parameter inference within statistical models for classification and regression.
- Work alongside mathematicians and clinicians to calibrate their human physiology models, which are often computationally expensive.
- Develop new calibration algorithms to accommodate the sequential nature of the available data.
- Methods development:
 - Rare-event simulation
 - Bayesian emulation and history matching
 - Time series classification and feature selection

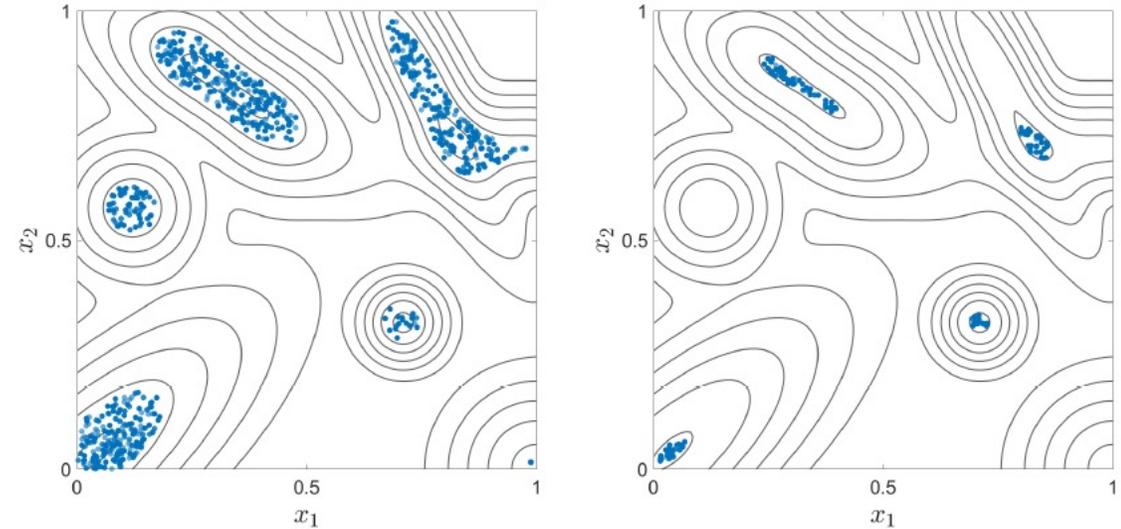


Fig. 1. Iterative selection of input configurations for model calibration.

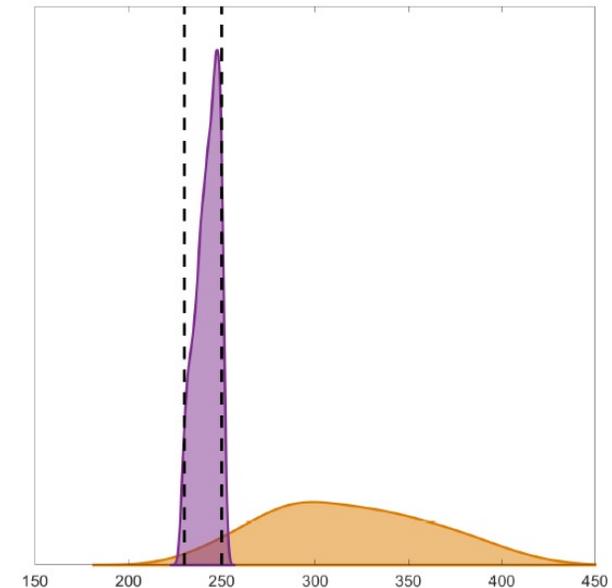


Fig. 2. Model output after calibration (pink) lies within the desired range, unlike the non-calibrated output (yellow).

Plans and Activities



- Started Jan 2021
 - Hub building - multidisciplinary team meetings, data infrastructure and ethics
 - Monthly seminar series – internal and national speakers – all welcome!
 - UCL website: <https://www.ucl.ac.uk/chimera/>
 - Twitter: @uclchimera
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- Multidisciplinary workshops starting in year 2
 - Flexible funding to develop new collaborations, projects, initiatives
 - Proactively looking to collaborate – get in touch!

Acknowledgements



Engineering and
Physical Sciences
Research Council

NIHR | University College London Hospitals
Biomedical Research Centre



University College London Hospitals
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NIHR | Great Ormond Street
Hospital Biomedical
Research Centre



Great Ormond Street
Hospital for Children
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The
Alan Turing
Institute