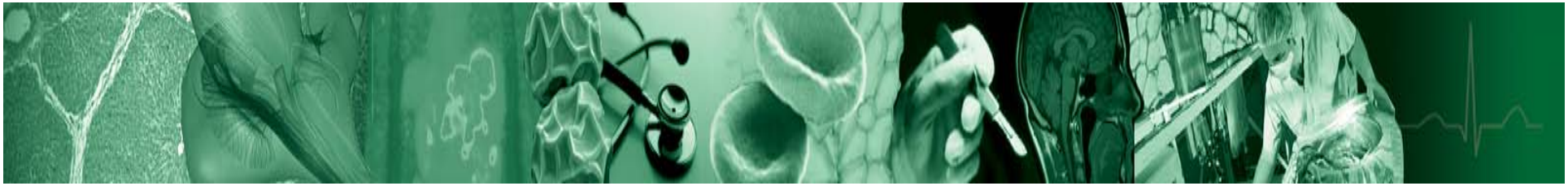
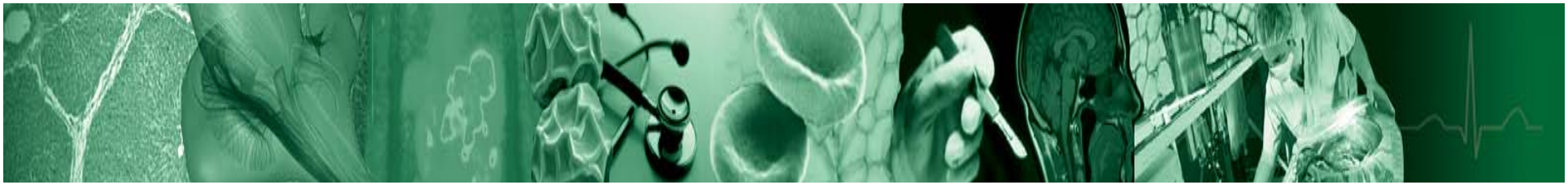


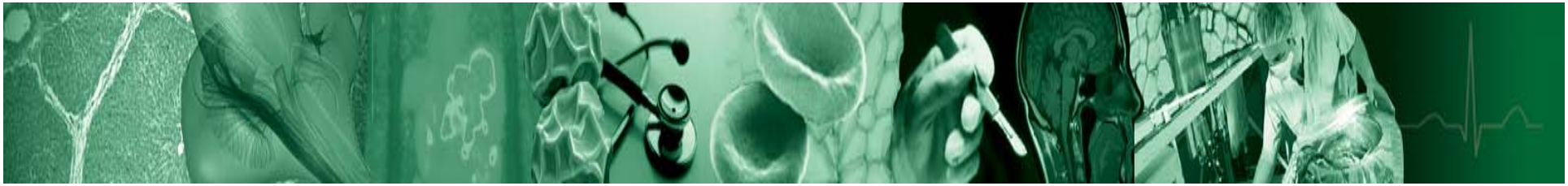
What is the state of the art in experimental validation of multi-scale models?

Stephen Payne
Institute of Biomedical Engineering
University of Oxford, U.K.

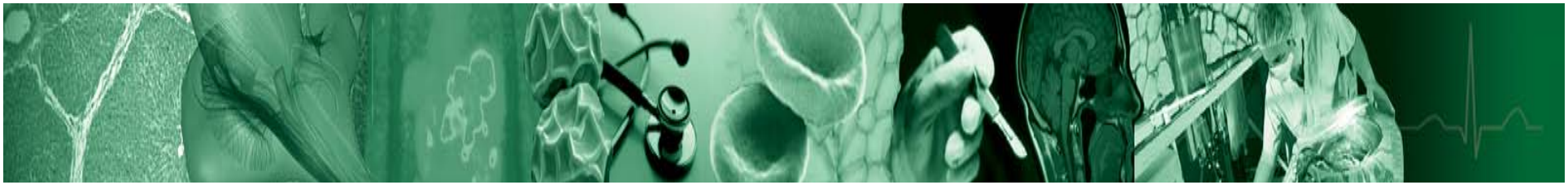


Overview

- Introduction
- Validation in principle
- Validation in practice (an example)
- Conclusions



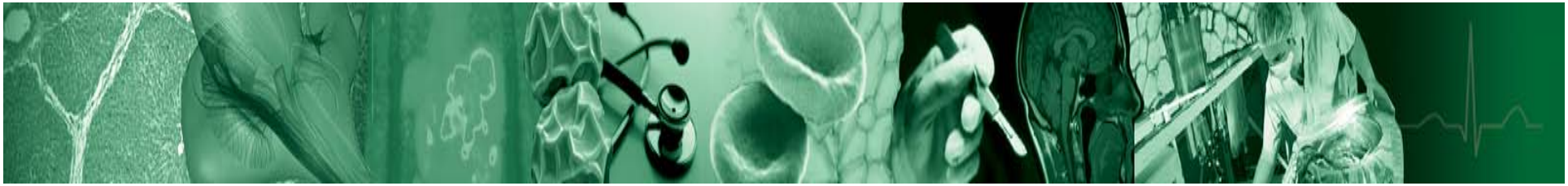
Introduction



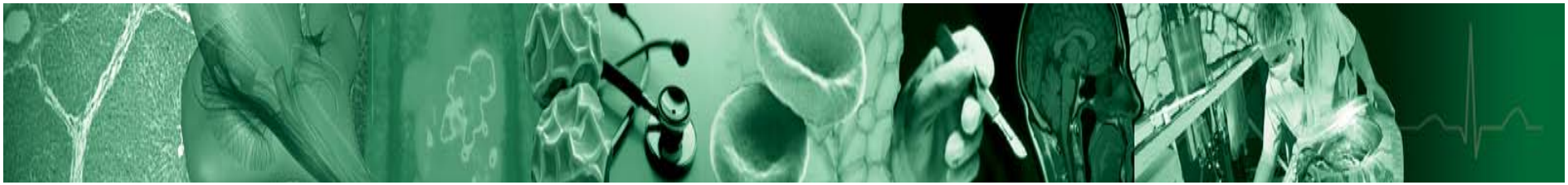
Problems and dangers

- Over-confidence
  - Models explain everything
- Over-scepticism
  - Models tell us nothing

- Over-simplistic approach
  - Poor understanding of what can be done
- Over-complication
  - Too much detail, too little understanding



Validation in principle



What does a model need?

- Models as ‘containers of [dis]belief’
- Models contain information + ignorance
  - Structural
  - Numerical

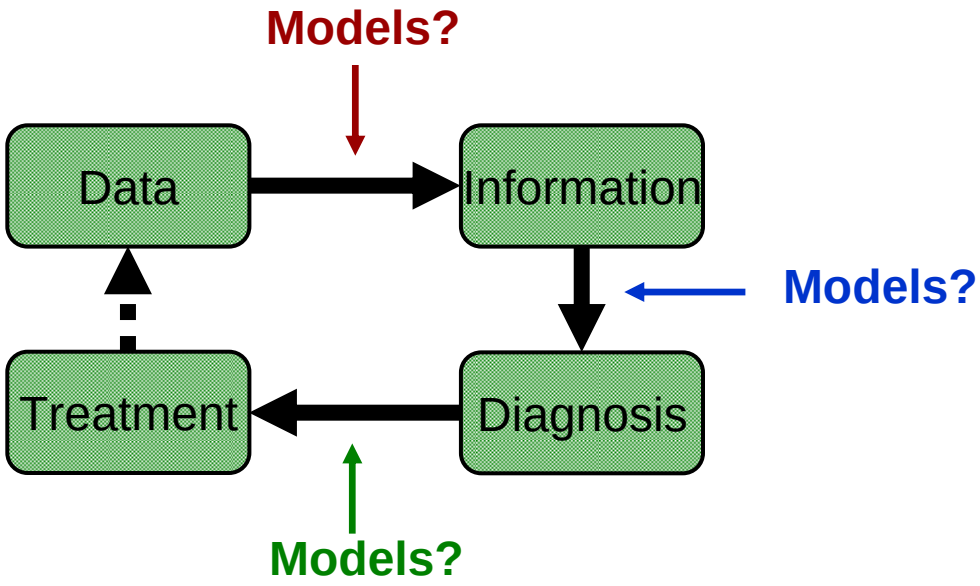
- So we need to ask two questions
  - Is the model the right one?
  - Are the parameters correct?
- Is this enough?

Model design

- Three stage process:
  1. What is the model for?
     - *What question are we trying to answer?*
     - *What clinical value are we trying to add?*
  2. What clinical data will be available?
     - *How much information can we get?*
  3. How complicated should the model be?
     - *How much do we include?*
     - *What do we leave out?*

The clinical cycle

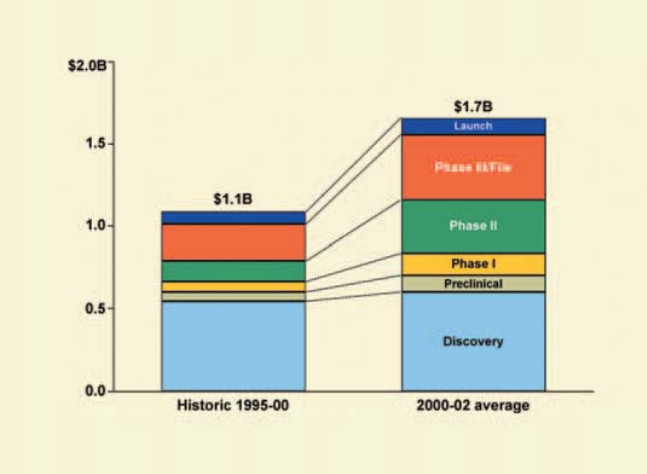
- How do models fit into this cycle?



- How to convert data into useful information?
- How can this information help in diagnosis?
- How can this assist in treatment?

Diagnosis -> Treatment

- Drug development is expensive.

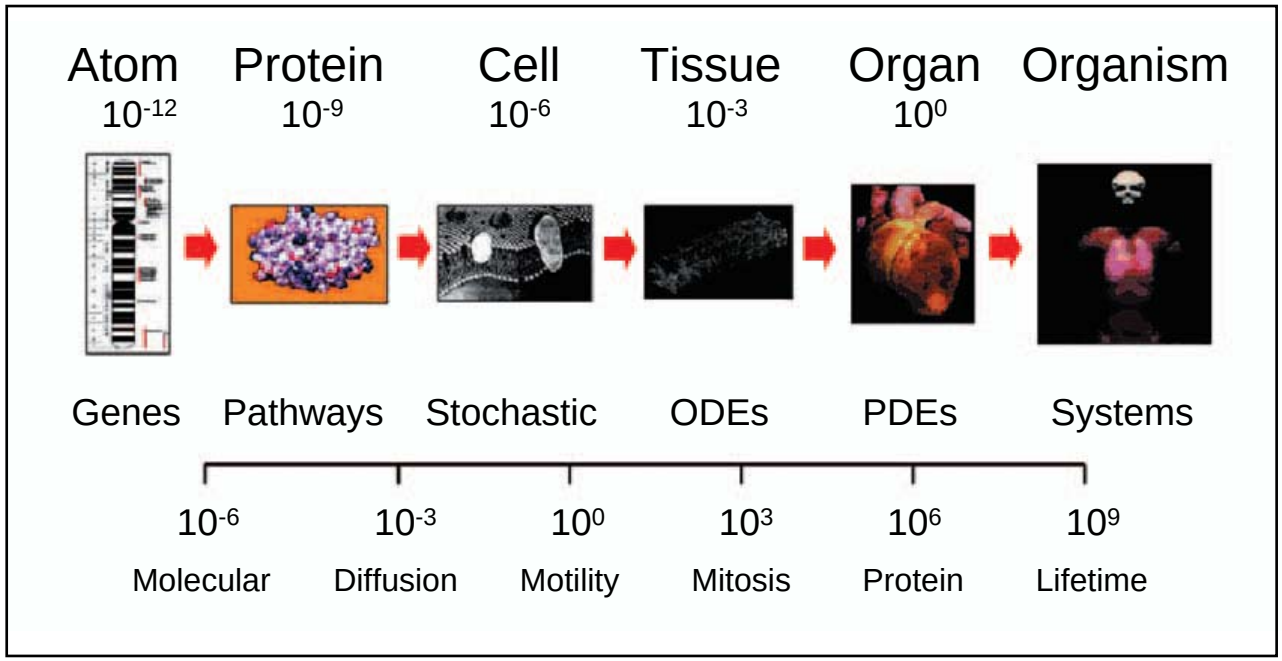


- Stroke drug development success rate is '*remarkably dismal*'.
  - 85 promising drugs trialled: 2 beneficial.

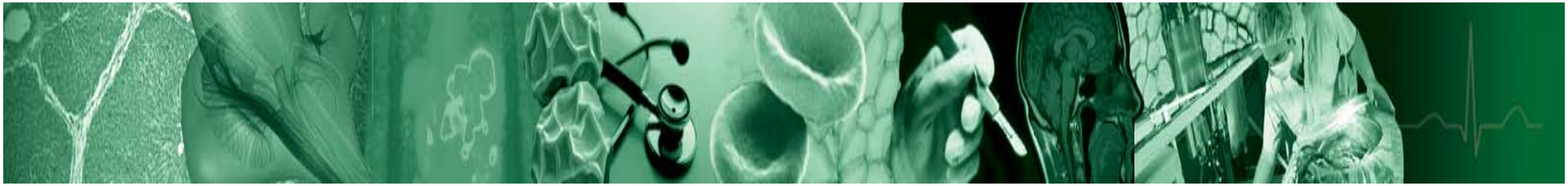
Kidwell et al., Stroke, 2007

Multi-scale models

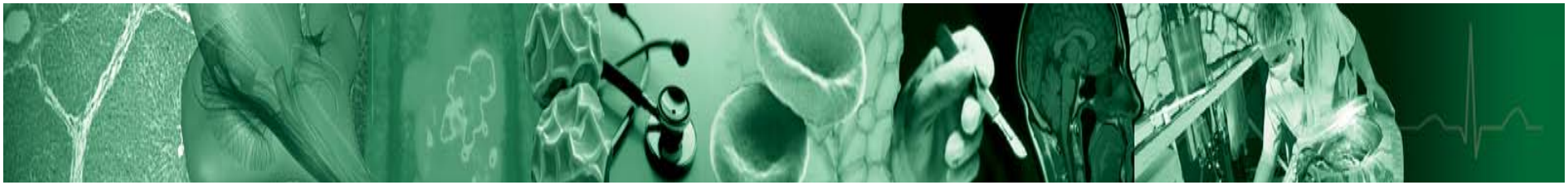
- Combination of different scales



- Combination of ‘fundamental physics’ and more ‘heuristic biology’

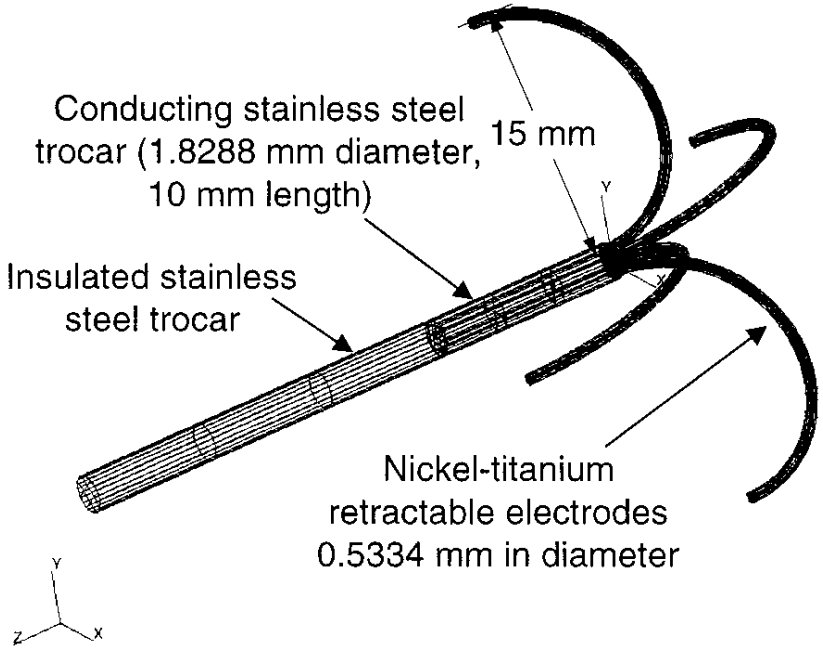


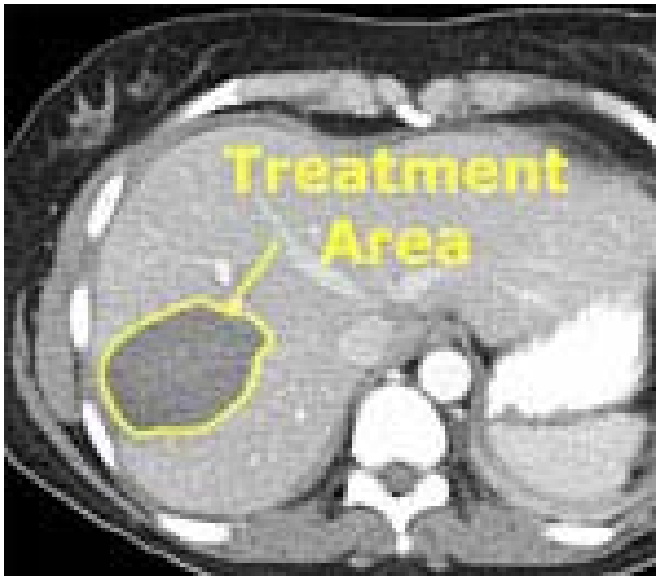
Validation in practice



IMPPACT

- ‘Image-based Multi-scale Physiological Planning for Ablation Cancer Treatment’
  - Heating/killing liver tumours.





IMPPACT

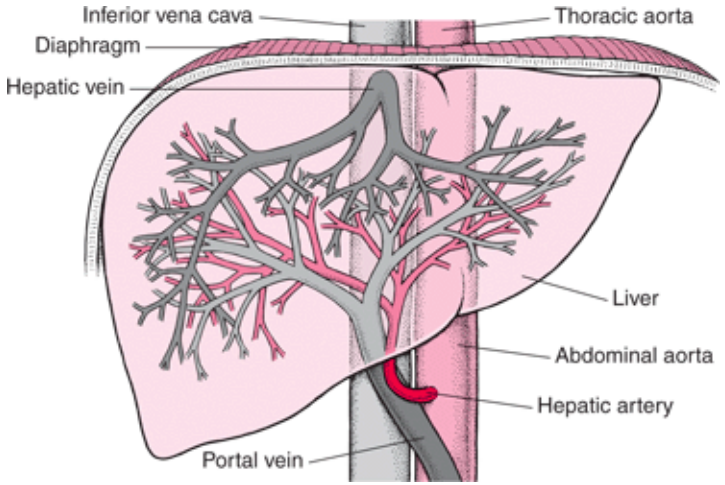
- Good news

	RFA	Surgical resection
Suitable cases	>75%	<25%
5 year survival rate	Up to 89%	~70%
Inpatient recovery time	2 days	2 weeks

- Bad news
  - 5 year survival rate:
    - 3-4 years experience: 89%
    - < 2 years experience: 45%

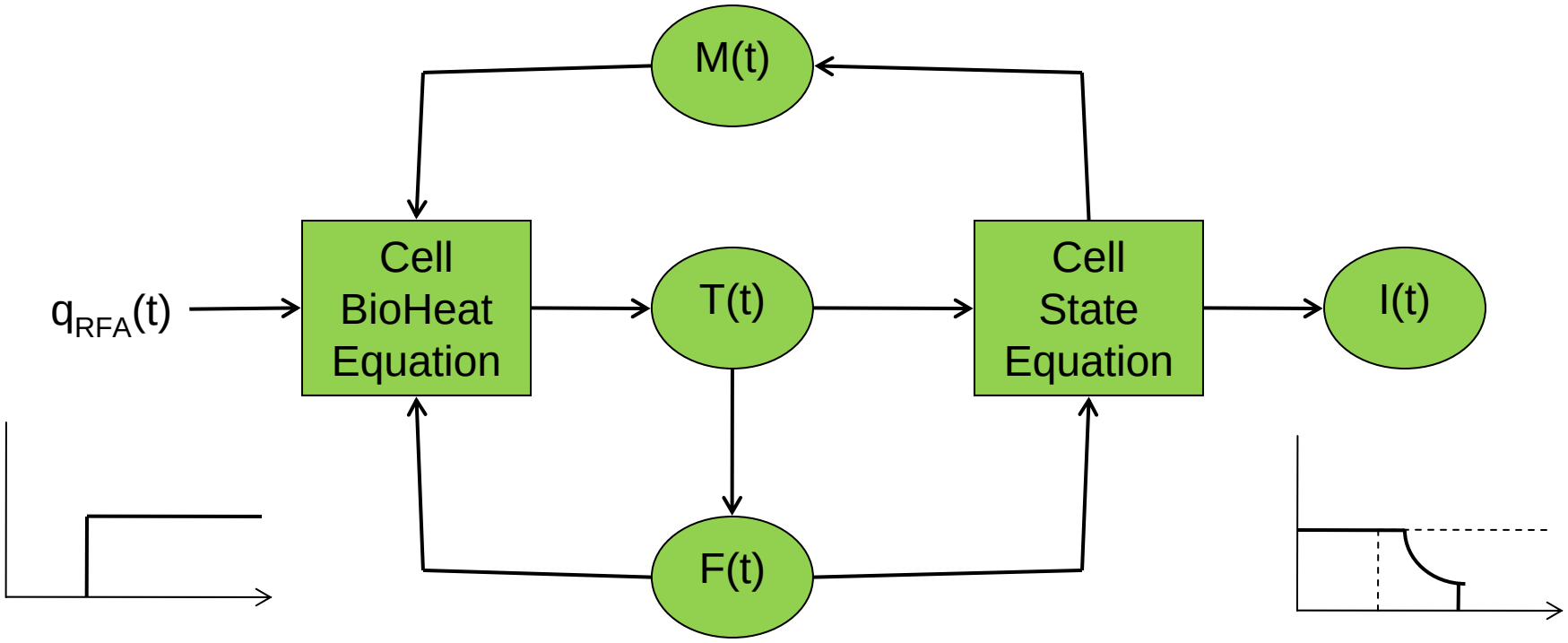
IMPPACT

- Clinical needs:
  - Training tools
  - Standardisation of techniques
- Basic question:
  - ‘How hot and how long?’



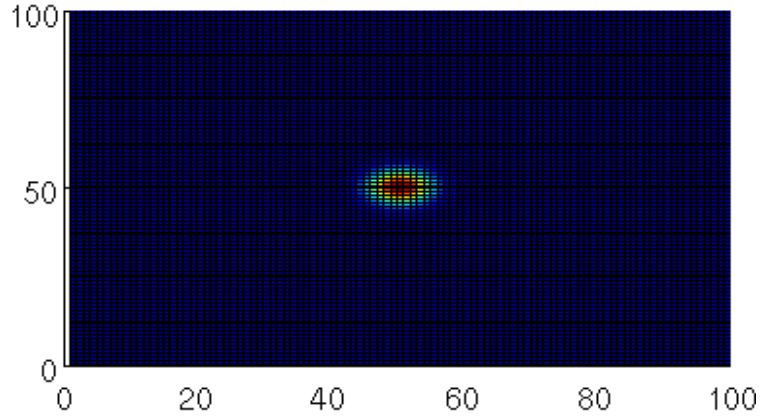
- Project aim to develop simulator as clinical training and support tool

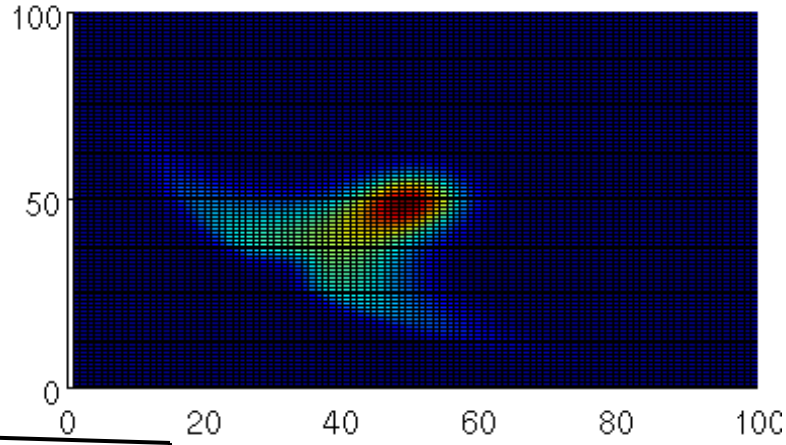
Cellular level

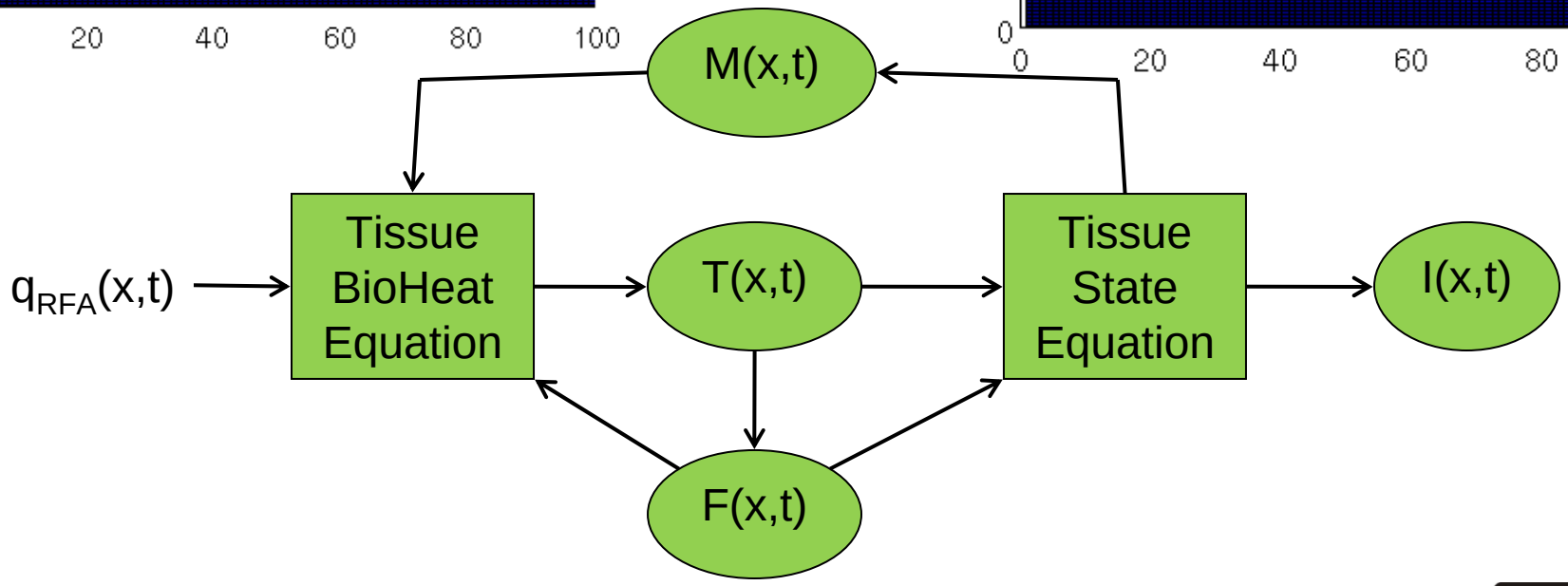


Combination of fundamental physics and more heuristic biology
Biology based on what we can measure (cell state)

Tissue level



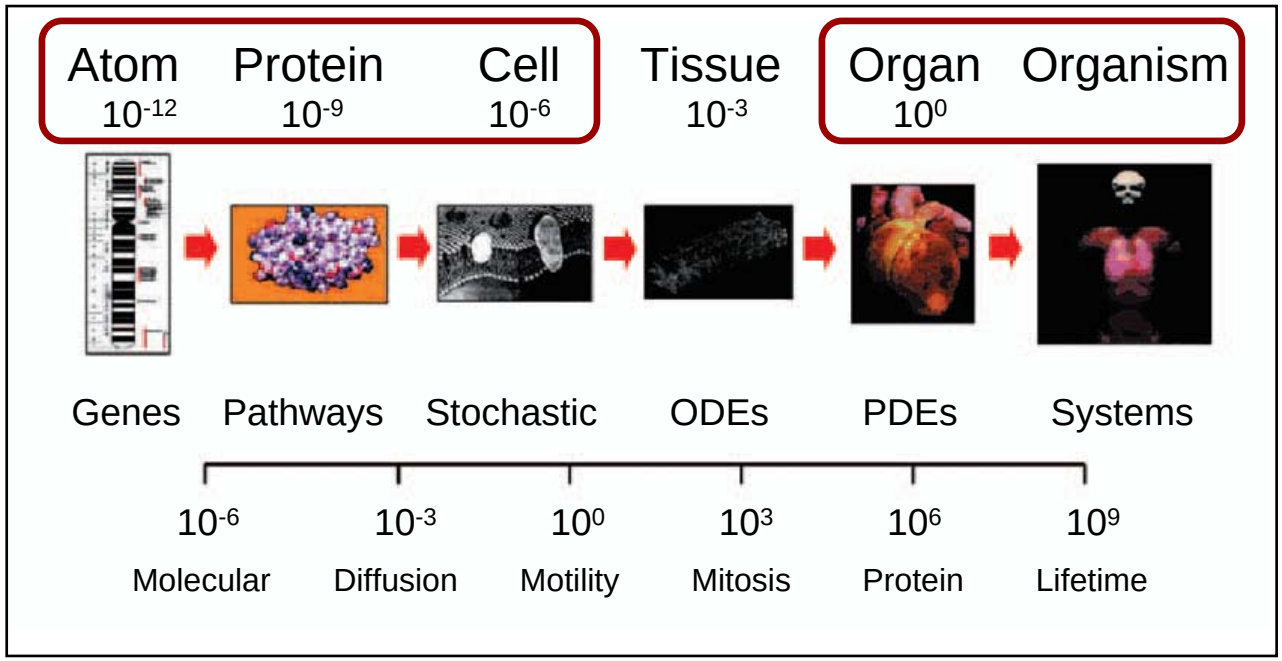




Combination of fundamental physics and more heuristic biology
Biology based on what we can measure (tissue state)

Multi-scale models

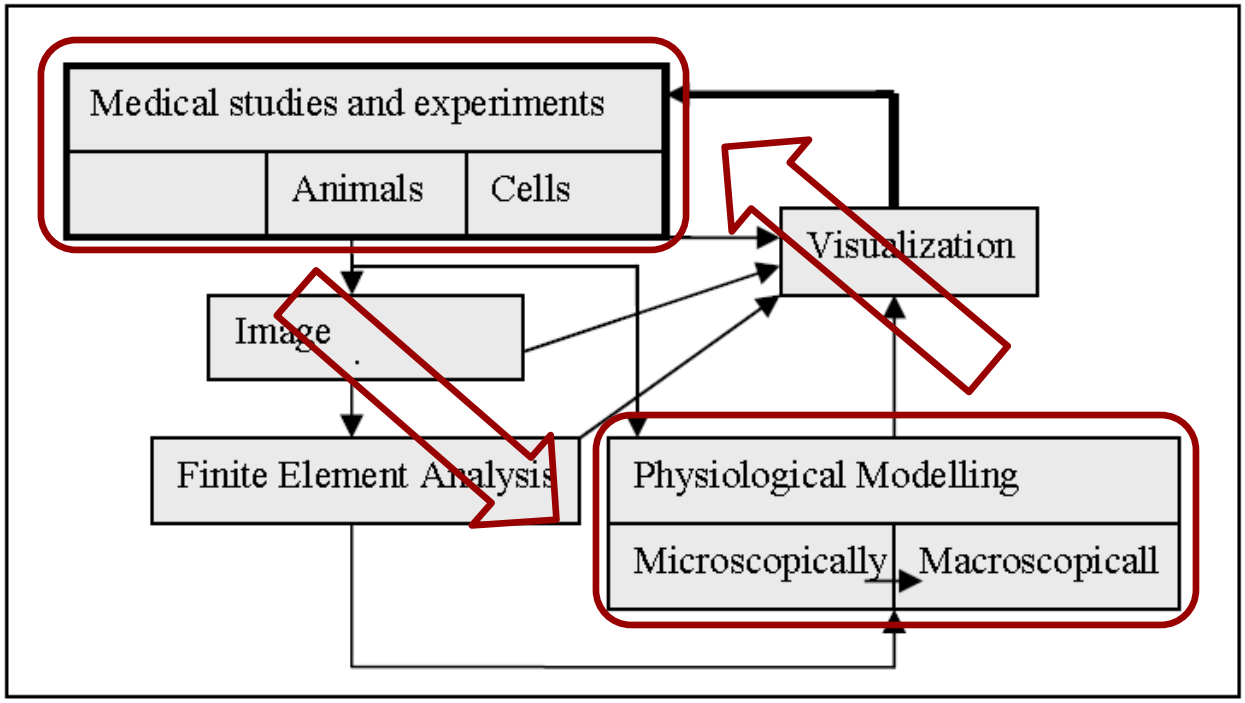
- Tissue level bridges the gap across scales



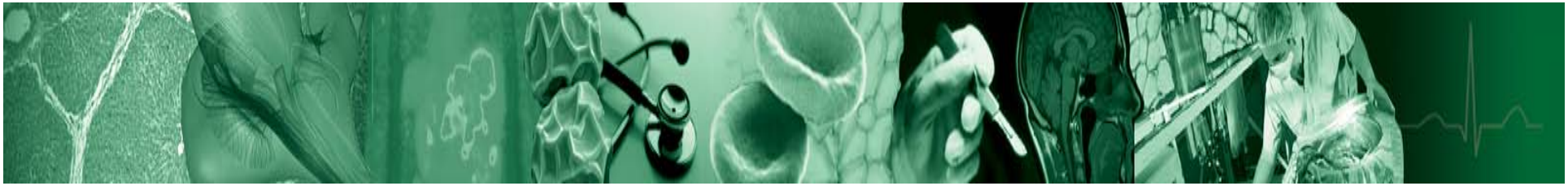
- Characterisation of model at one level interacts with next
- Validation of model at one level interacts with next

Multi-scale iterative models

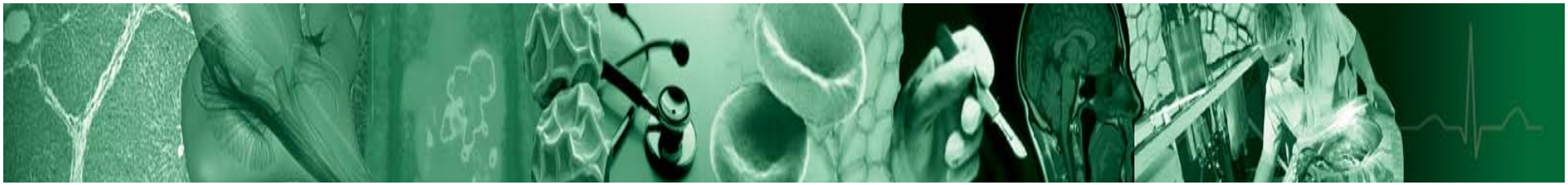
- This has to be *iterative*



- Models are not static
- Both data-driven and data-driving



Conclusions



What can we conclude?

- Modelling based on what we want to know
- Modelling/validation are an iterative process
- Multi-scale modelling + validation are:
  - Crucial (to believe the results)
  - Helpful (to understand what is happening)
  - Difficult (too little information)
- Realism rules