Modelling Solid Tumour Growth

Lecture 5: Summary and Future Directions

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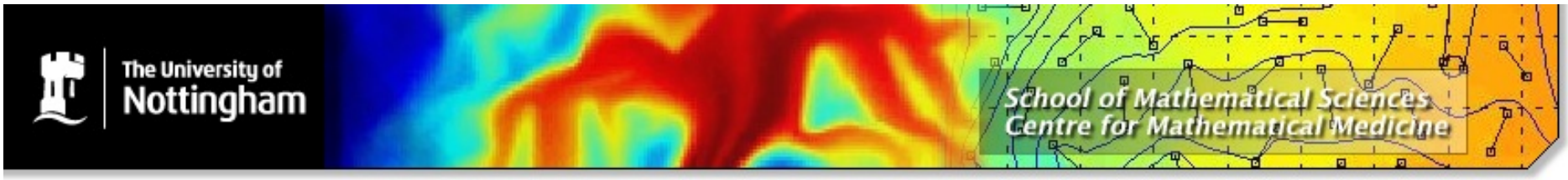


Outline

- Summary of Previous Lectures
- Current Modelling Challenges
- Therapeutic Challenges

Summary of Previous Lectures

- Avascular Growth
  - ODE models - spatially-averaged models
  - 1D PDE models - radially-symmetric models
  - 2- and 3D PDE models - symmetry-breaking or invasion
- Angiogenesis
  - PDE models - analytically tractable in 1D
  - Probabilistic models - realistic simulations in 2- and 3D

Current Modelling Challenges

- Cellular heterogeneity within tumour:
  - clonal cell populations, vasculature, ECM
- Coupling mechanical effects and growth:
  - stress may influence proliferation/death
  - proliferation/death may influence stress
- Coupling across spatial scales:
  - subcellular, cellular and macroscale phenomena are linked
  - this may involve developing hybrid models in which PDE/ODE models are coupled to discrete models
- Specialising models to describe specific aspects of tumour growth
  - e.g.gliomas and ductal carcinoma in situ (DCIS)

We will discuss briefly

- gliomas (Swanson et al.)
- DCIS (Franks et al.)
- multiscale model of vascular tumour growth (Alarcon et al.)
- genetic engineering of macrophages (Owen et al.)

Modelling Gliomas

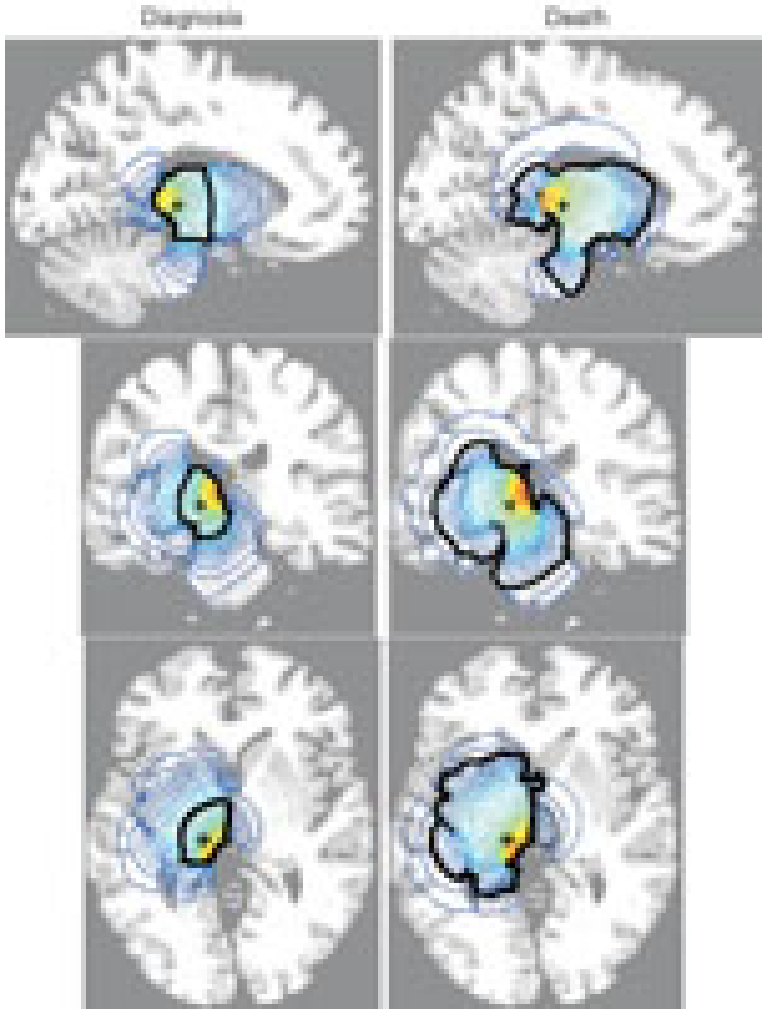
- Let c = tumour cell density at location x and time t

- Assume that c satisfies

$$\frac{\partial c}{\partial t} = \nabla.(D\nabla c) + \rho c$$

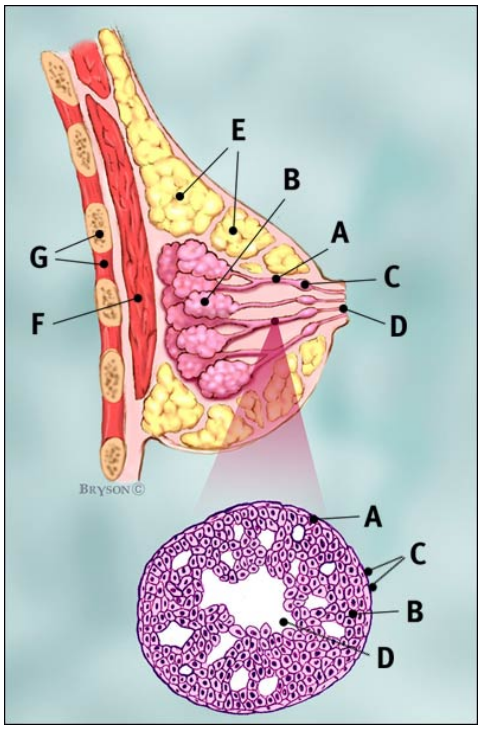
where the diffusion coefficient D and cell proliferation rate ρ may vary with spatial location ie from grey to white matter

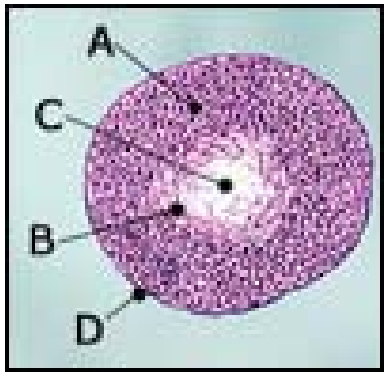
Modelling Gliomas

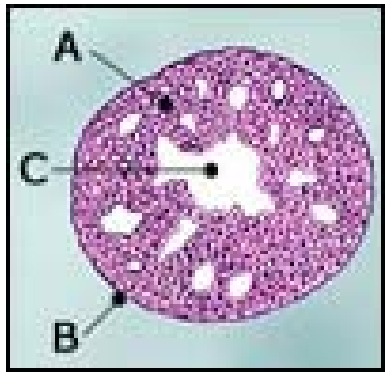


Series of images showing predicted spread of gliomas from detection to patient death

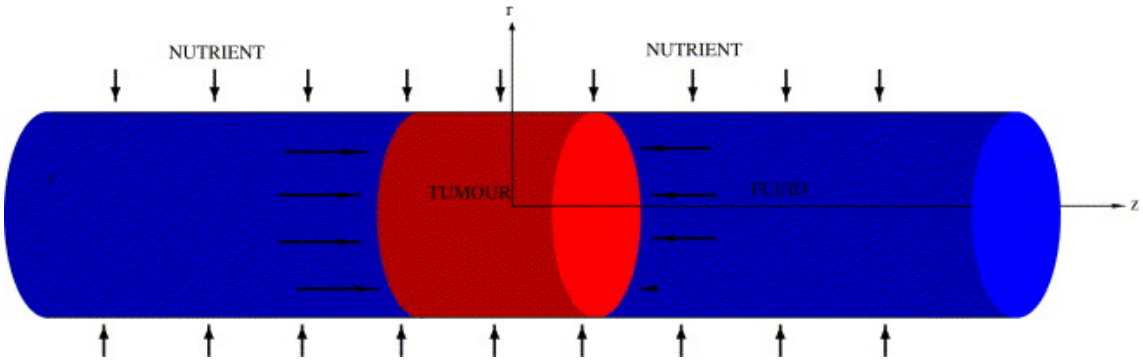
DCIS







DCIS

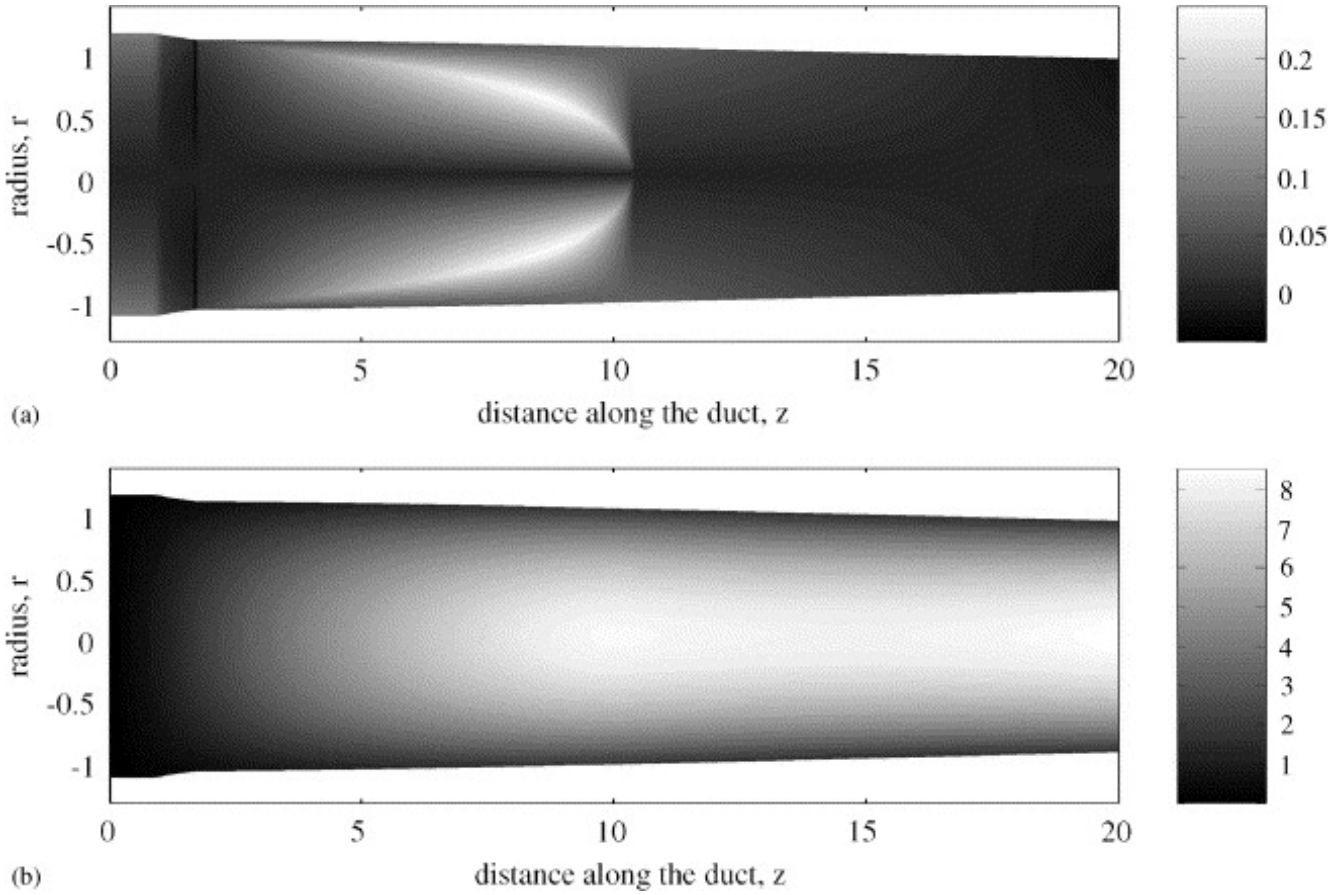


A schematic diagram showing the initial configuration of the duct and tumour

Model Framework

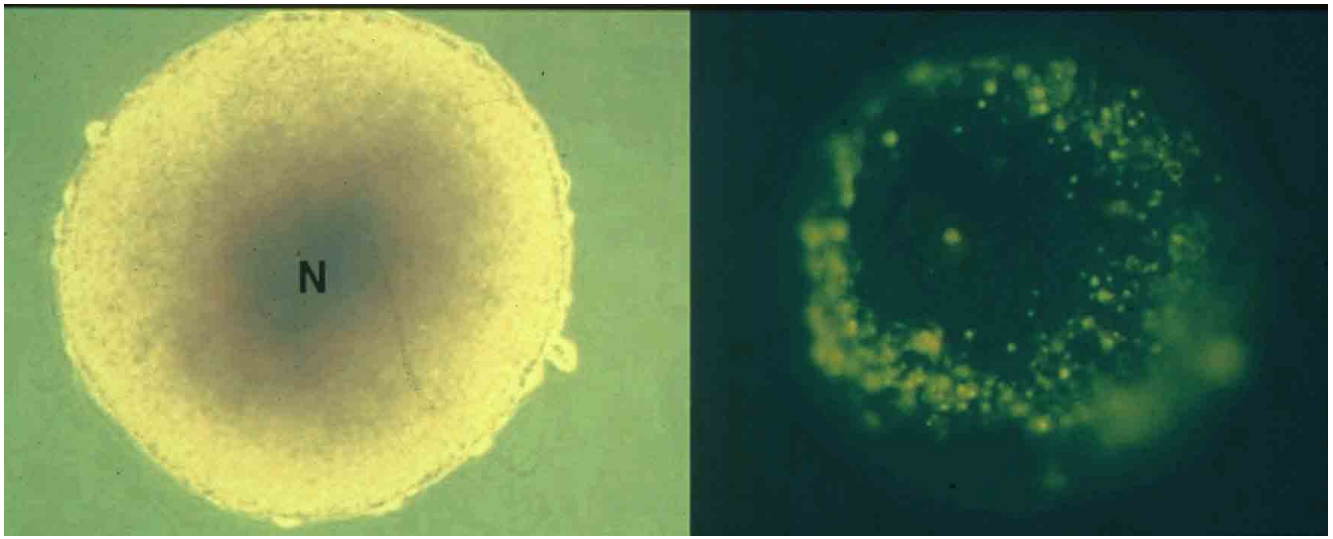
- Nutrient-limited model of avascular tumour growth within cylindrical duct
- Mechanical model of membrane deformation
- Models coupled via conditions on duct wall: expansive forces caused by net tumour growth balance forces that develop in membrane

DCIS



Series of plots showing (a) the radial velocity and (b) the axial velocity of the tumour cells at $t = 2$

Genetically Engineered Macrophages

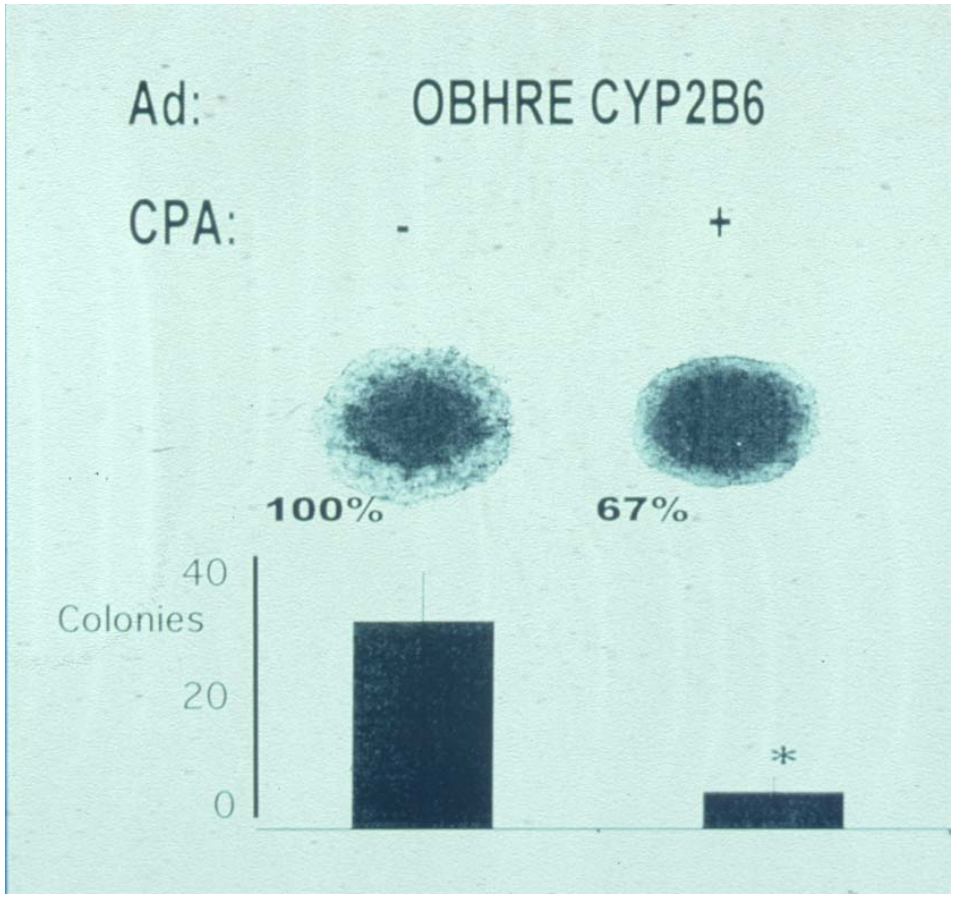


Macrophages are white blood cells which accumulate in hypoxic tumour regions

Genetically Engineered Macrophages: The Aim

- Extract and genetically engineer a patient's own macrophages
- Inject modified macrophages back into patient
- Macrophages migrate to hypoxic regions where they release chemicals which
  - kill tumour cells
  - halt the growth of new blood vessels

Genetically Engineered Macrophages: The Reality



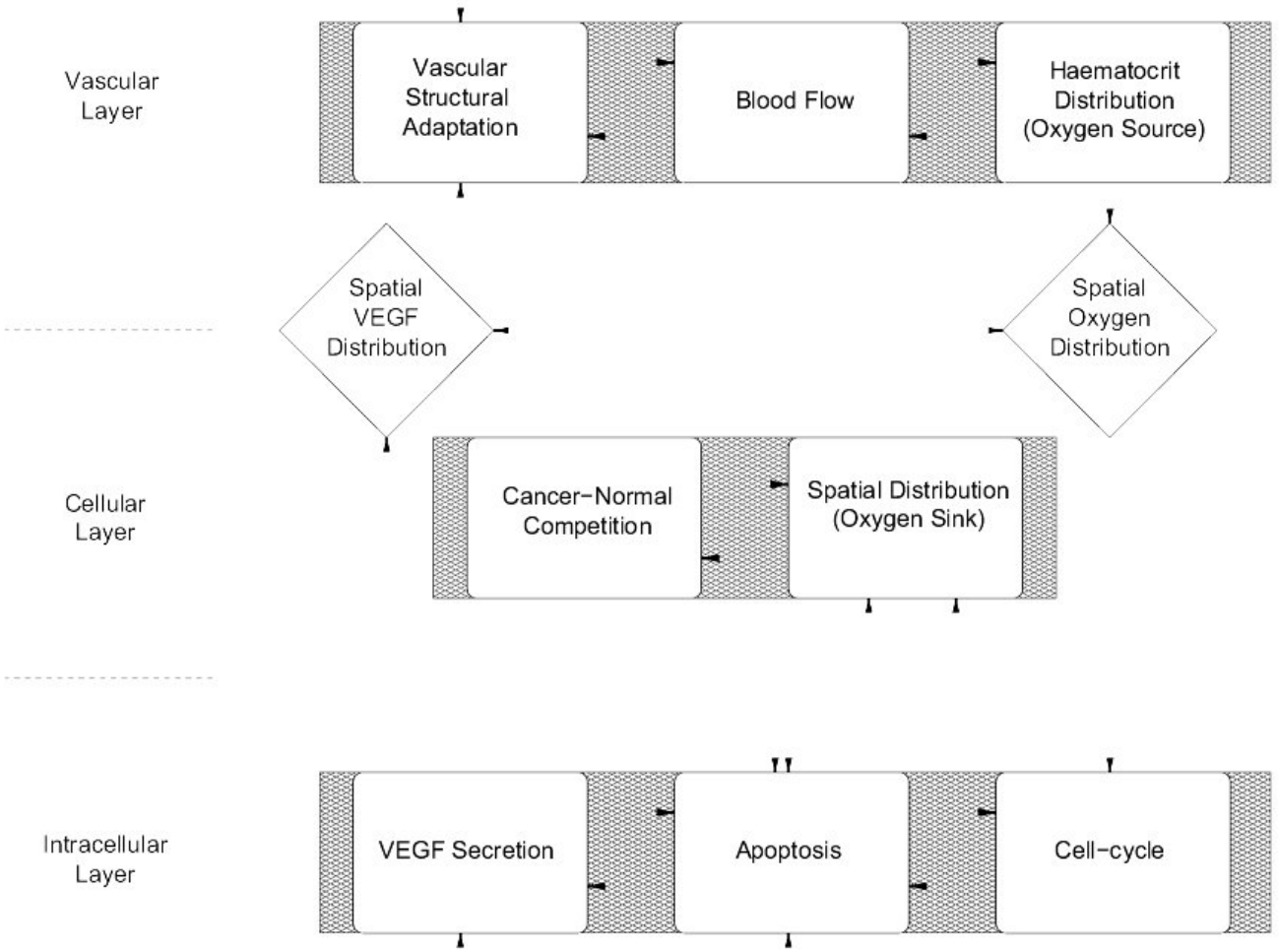
Laboratory results are promising

Genetically Engineered Macrophages: The Reality

Many issues that need to be resolved are being studied using a combination of mathematical modelling and experiments

- Can engineered macrophages displace normal macrophages (and tumour cells)?
- How many macrophages needed for optimum response?
- What drugs should be used?
- Coordination with other therapies?

Multiscale modelling of vascular tumour growth

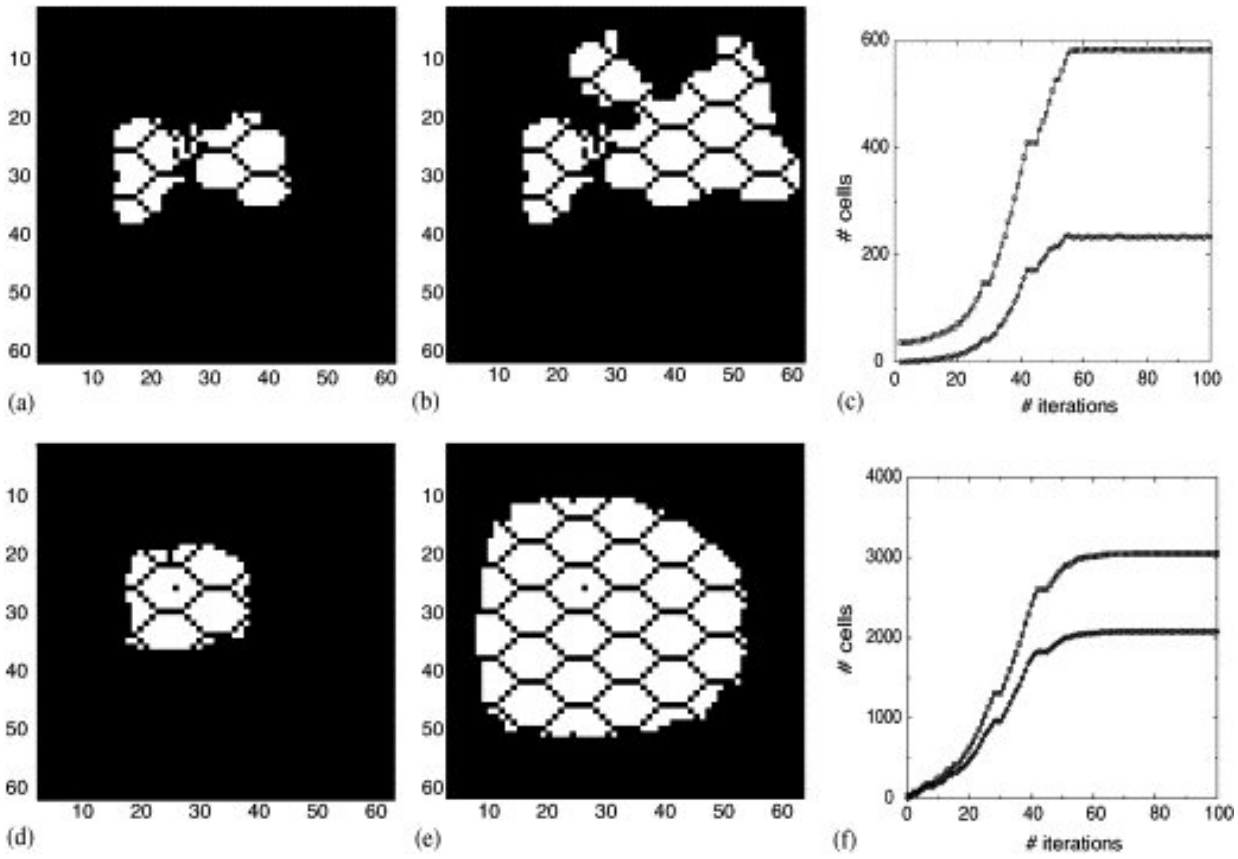


Schematic representation of our hybrid cellular automaton

Multiscale modelling of vascular tumour growth

- The subcellular level: ODE model of cell cycle based on the proteins cyclin and CDK (Tyson and Novak, 2001)
- The cellular level: 2D hybrid cellular automaton for vessels, tumour cells and normal cells; reaction-diffusion equation for oxygen, with distributed sources (vessels) and sinks (cells)
- The vessels: hexagonal network of blood vessels; pressure drop imposed across domain; Kirchoff's laws to determine flow in each vessel; vessel radii adapt to demands of surrounding tissue

Multiscale modelling of vascular tumour growth

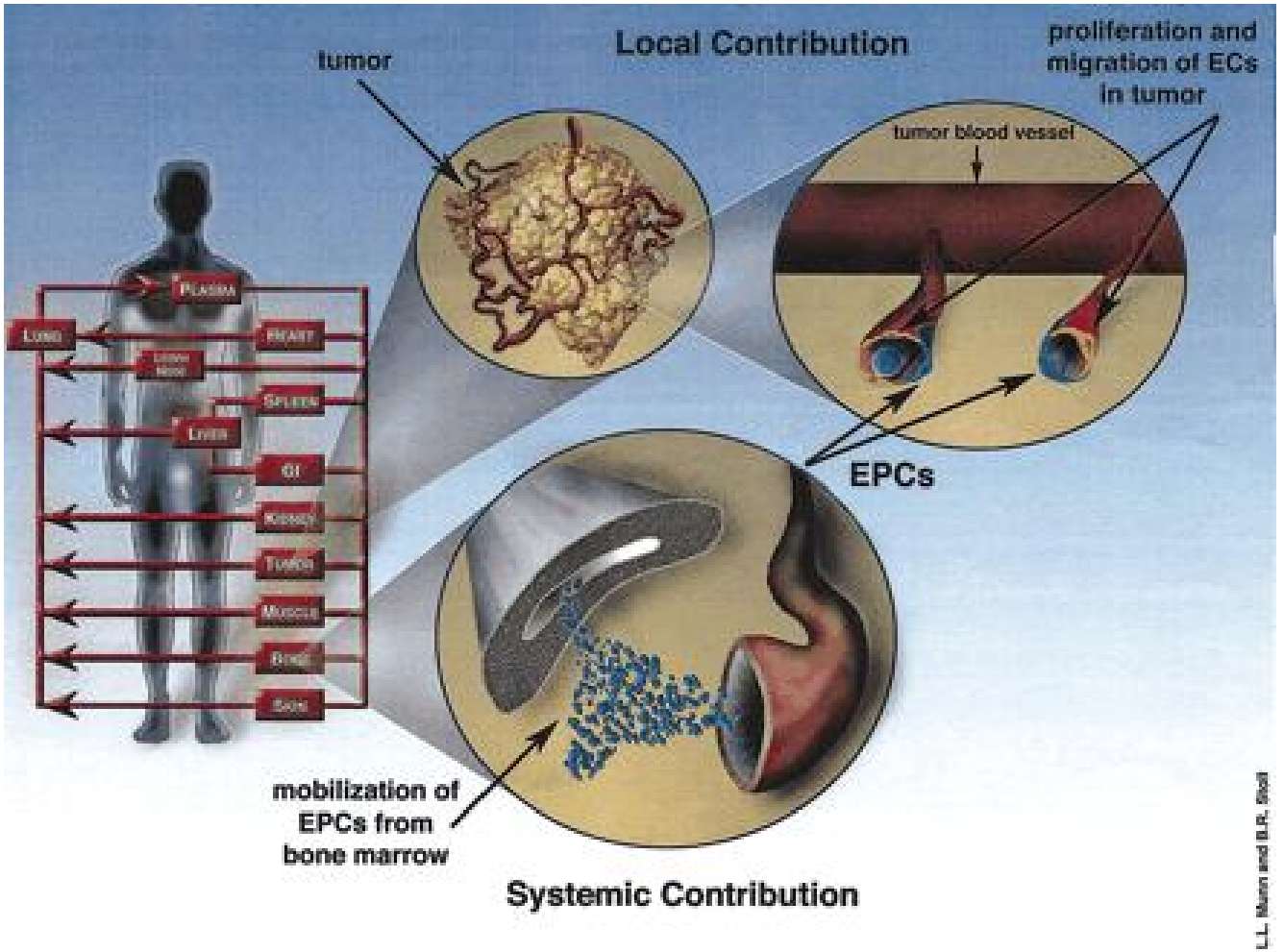


Tumour growth in homogenous and inhomogenous environments. **Key:** heterogenous (upper panels); homogeneous (lower panels). In (c) and (f), squares represent total number of tumour cells (proliferating + quiescent), diamonds denote quiescent cells.

Therapeutic Challenges

- Gene-based and viral therapies
- DNA condensation
- Anti-angiogenic treatments
- Hyperthermia
- Magnetically-tagged drugs

Therapeutic Challenges



Effective anti-angiogenic therapies will need to account for recruitment of EC stem cells to tumour sites.

Summary

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▶ Modelling solid tumour growth is an exciting and challenging area of mathematical research.

▶ In order to be of clinical value, these models need to become more specific (eg particular tumour, particular mutation).

▶ Many parts of the cancer jigsaw have now been identified (ie subcellular, cellular and macroscopic phenomenon).

▶ Mathematics provides framework with which to assemble the jigsaw and thereby to help improve our understanding and treatment of cancer

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