What has mathematics done for biology?

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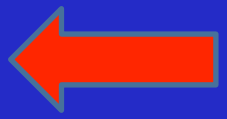
Mathematical Modelling

- In Vivo
- In Vitro
- Bioinformatics
- Mathematical Biology 

UK

Aberdeen; Bath; Birmingham; Bristol; Cambridge; Durham; Dundee; Glasgow; Heriot-Watt; Imperial College, London; Kings College, London; Liverpool; Leeds; Loughborough; Manchester; Newcastle; Nottingham; Oxford; Oxford Brookes; Reading; Sheffield; Southampton; Sussex; Surrey; University College, London; Warwick; York [27]

- BBSRC Institute in Norwich
- Barts Cancer Institute, Queen Mary University

Wolfson Centre for Mathematical Biology (60 percent maths, 40 percent biology)

+ 5 permanent faculty; 11 postdocs, 18+ students, 15+ visitors/per year
+ Computational Biology Group (David Gavaghan)

[joint seminar is about 60-70 people]

+ Oxford Centre for Industrial Applied Mathematics (OCIAM)
+ Oxford Centre for Gene Function
+ Wellcome Trust Centre for Human Genetics
+ Department of Statistics
+ Department of Zoology

++++ Doctoral Training Centres (David Gavaghan) ---- **A new way of training graduate students**

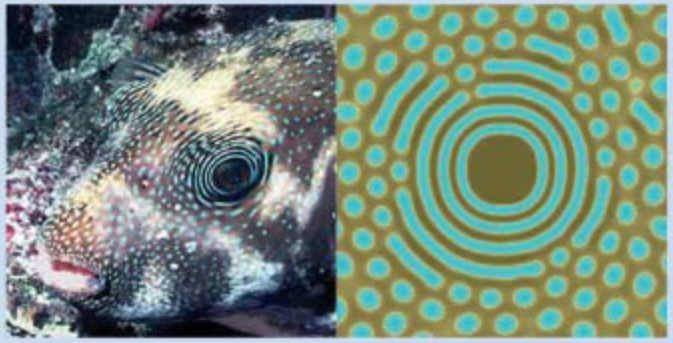
Developmental Biology

- Alan Turing's theory for pattern formation in 1952 – he proposed:
- (i) the idea of **morphogen**
- (ii) patterning principle

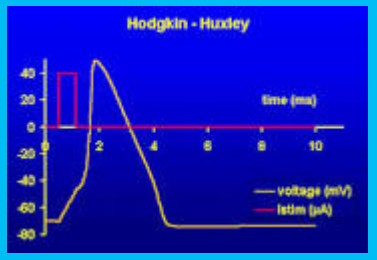
(Meinhardt):

short-range activation, long-range inhibition

c



Physiology



- Hodgkin and Huxley (1952): signal propagation in the squid giant axon
- Using a mathematical model they predicted details about the channels and gates through which ions pass – verified much latter experimentally
- Nobel Prize

Medicine

- Tumours need vasculature to grow (angiogenesis). Therefore reduce angiogenesis and cure cancer!

- BUT???? How come anti-angiogenesis and chemo/radio-therapy work so well????

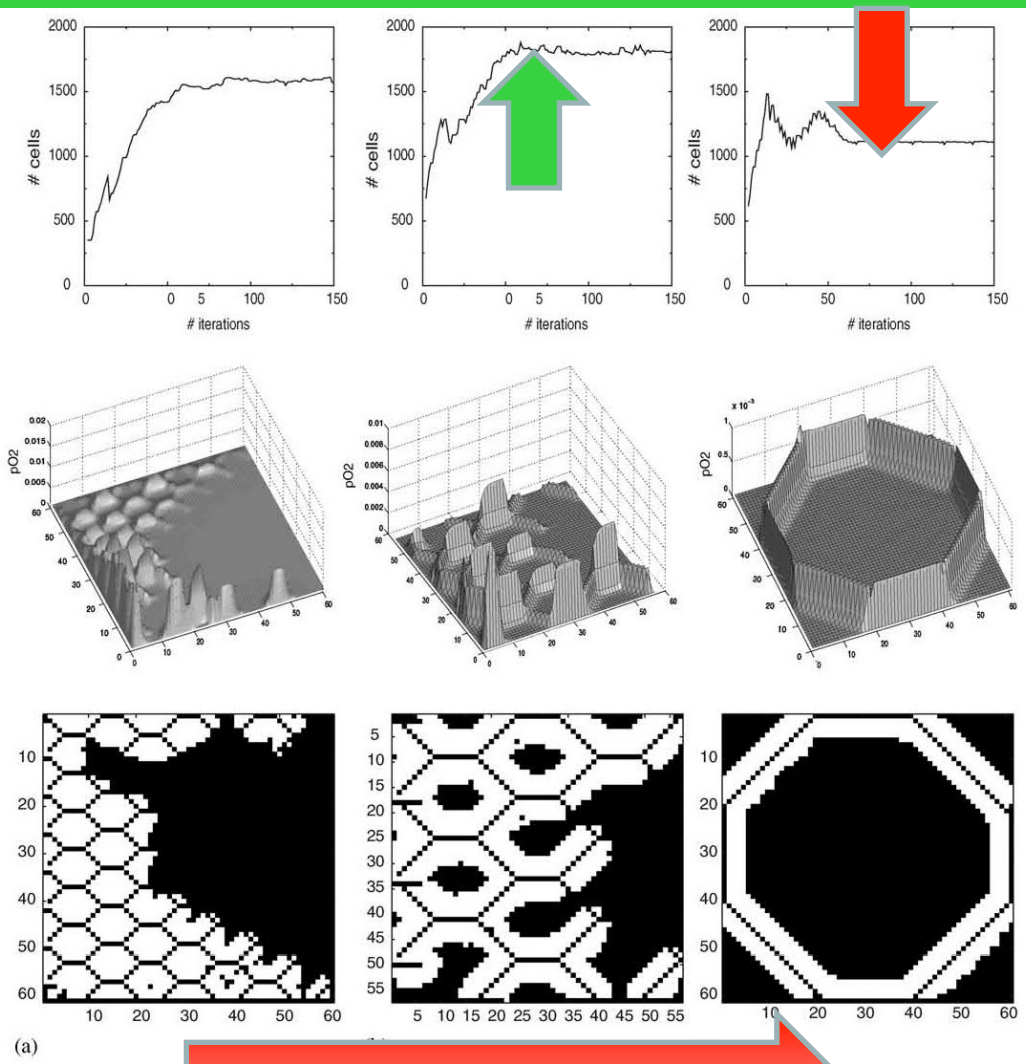


Fig. 10. Simulation for systems whose vascular networks have different sparsity, i.e. we have varied the *vascular density*, defined as the number of vessels per surface unit. In column (a) we have plotted the results for a system with vascular density = 114 vessels/mm^2, column (b) corresponds to vascular density = 24 vessels/mm^2, and column (c) corresponds to vascular density = 4 vessels/mm^2. The results plotted in the first row corresponds to the evolution of the size of cancer colony in time (where each iteration corresponds to 15 h, which is an estimation of the duplication time of our cancer cells), the second row, to the stationary distribution of oxygen (pO_2 in dimensionless units), and the third row, to the stationary cell distribution. In the middle set of figures, the vertical axis is the oxygen concentration. In the bottom panel of each column white spaces are occupied by cancer cells, whereas black spaces are either empty or occupied by vessels.

Vessel Normalisation

Now instead of using angiogenesis drugs to REDUCE tumour nutrient delivery, they are being used to ENHANCE it.

Developmental Biology: Migration of Cranial Neural Crest Cells

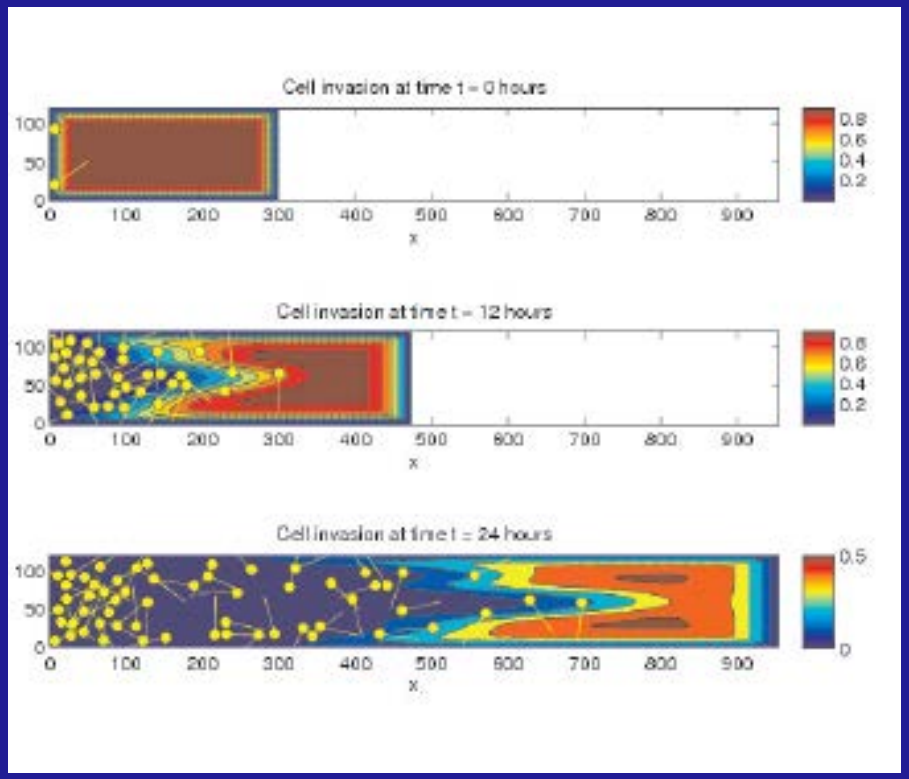
- Stowers Research Institute in Kansas

- NC cell population is crucial for proper development of the heart and peripheral nervous systems

- Is the cellular origin of the highly aggressive cancers, melanoma and neuroblastoma

Model and manipulation

- Can a chemoattractant (VEGF) produced by the overlying ectoderm be sufficient for robust invasion?



Model Prediction and Validation

- A single chemotactic gradient with a single cell type is not a feasible mechanism. There must be at least 2 cell types – one chemotactic, one not chemotactic.

- By FACS (flow cytometry analysis) and by LCM (laser capture microdissection) show significant differences in expression of 19 out of 84 genes.

- Leading NC cells have upregulated expression of cell guidance and navigation genes (cell guidance factor recptors [EphA4]; integrins (Itgb5); MMPs [MMP2]; cadherins [Cdh7]). Trailing cells have upregulated expression of cadherins distinct from leading NC cells.

Lead cells transplanted proximally

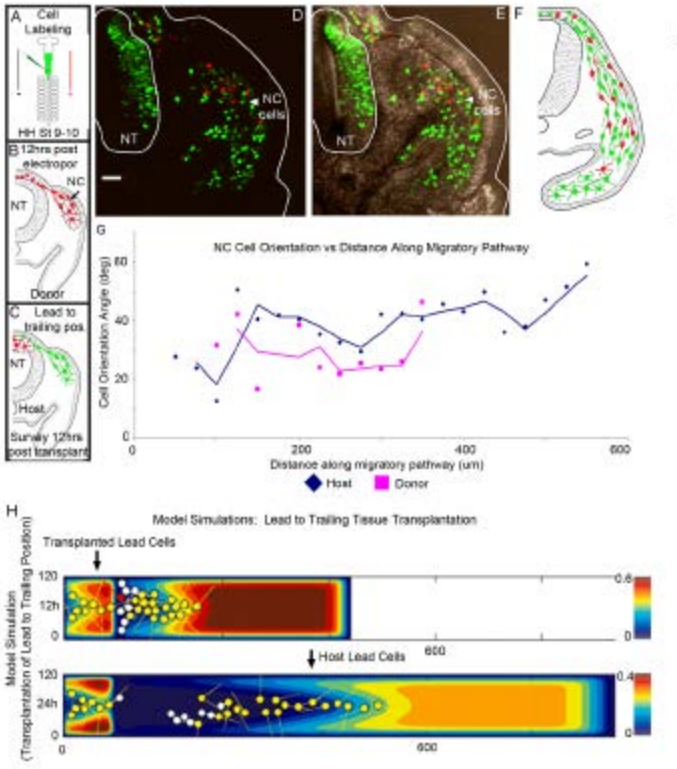


Fig. 5. Very few leading NC cells migrate after leading to trailing transplant. (A-C) Experiment schematic. (D,E) Transverse sections after tissue transplantation, also represented schematically (F). (G) Average nuclear orientation angles after trailing NC cell ablation [169 host cells (blue), 37 donor cells (pink), 3/13 embryos]. (H) Model simulation. Leaders (yellow), trailers that are following others (white) and trailers that are not following others (red). Scale bar: 50 μm. NC, neural crest cells; NT, neural tube; hr, hours.

Epidemiology: HIV Modelling in India

MATHEMATICAL BIOSCIENCES
AND ENGINEERING
Volume 6, Number 4, October 2009

doi:10.3934/mbe.2009.6.779
pp. 779–813

HIV/AIDS EPIDEMIC IN INDIA AND PREDICTING THE IMPACT OF THE NATIONAL RESPONSE: MATHEMATICAL MODELING AND ANALYSIS

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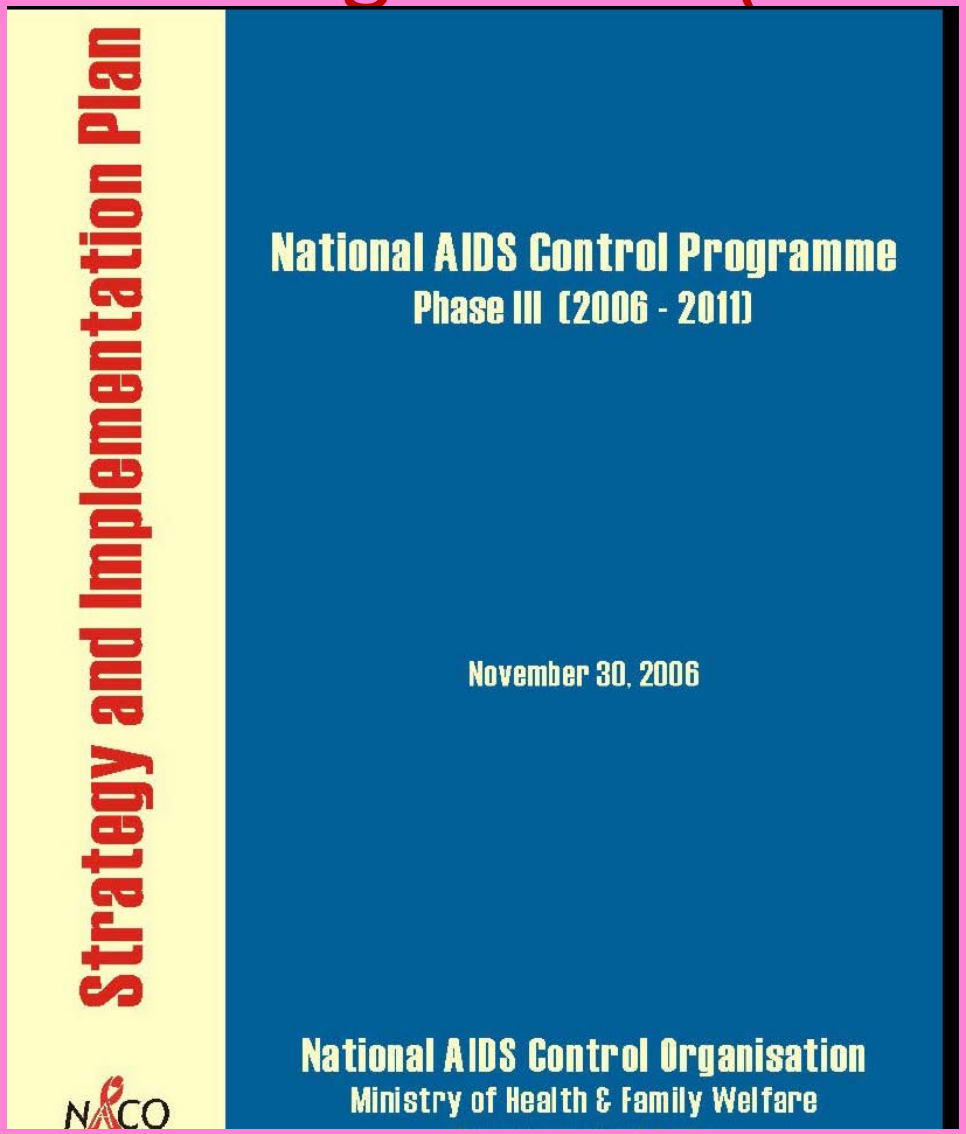

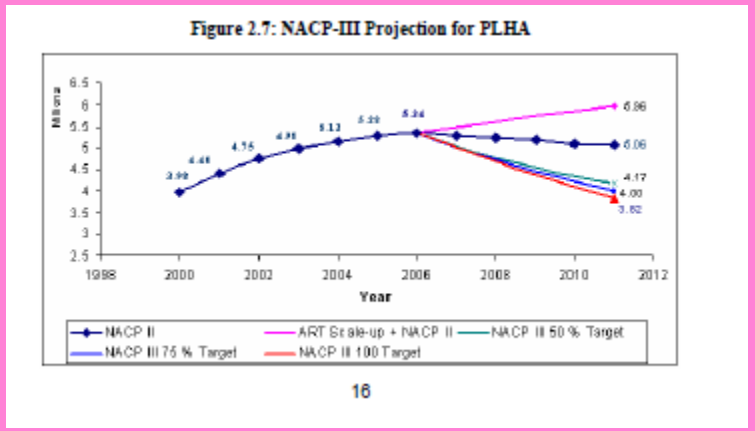

Model Predictions

- The model predicted that, should the interventions of NACP II be continued, there would be 2.08 million PLHA by the end of 2011. This value is very close to the data for 2011 released by the Indian Ministry of Health in 2012 showing the number of PLHA was 2,088,642.
- Subsequently the model predictions helped inform the mid-term review of the NACP III plan initiated by the National AIDS Control Organisation (NACO) of the Ministry of Health in 2009.