

Systems Biology Across Scales:

A Personal View

XXVI. Waves in Biology:

From cells & tissue to populations

Sitabhra Sinha

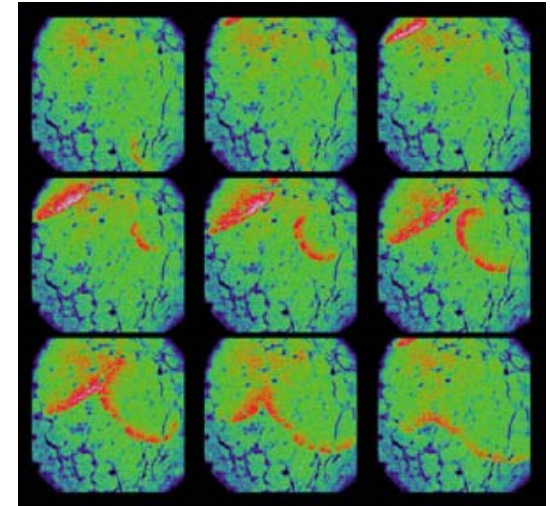
IMSc Chennai

Spiral Waves in Biological Excitable Media

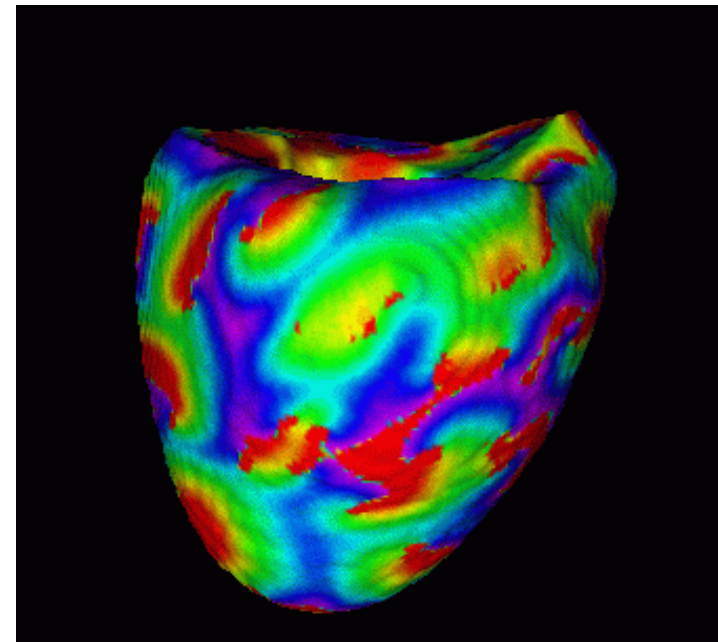


Aggregation of
Dictyostelium
Discooidium amoebae
by cAMP signalling

Ca^{++} waves in
cytoplasm of
Xenopus
oocytes



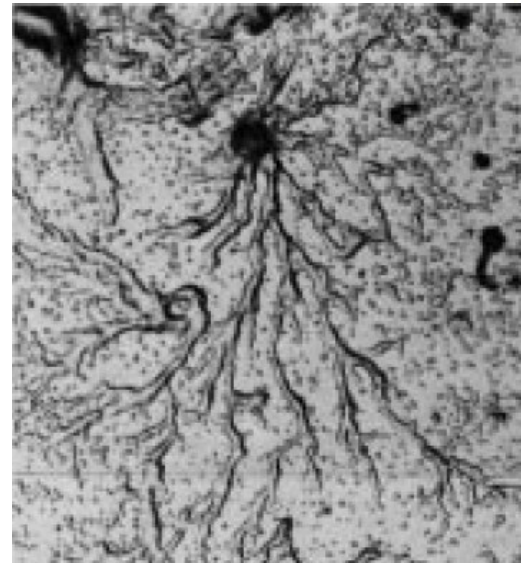
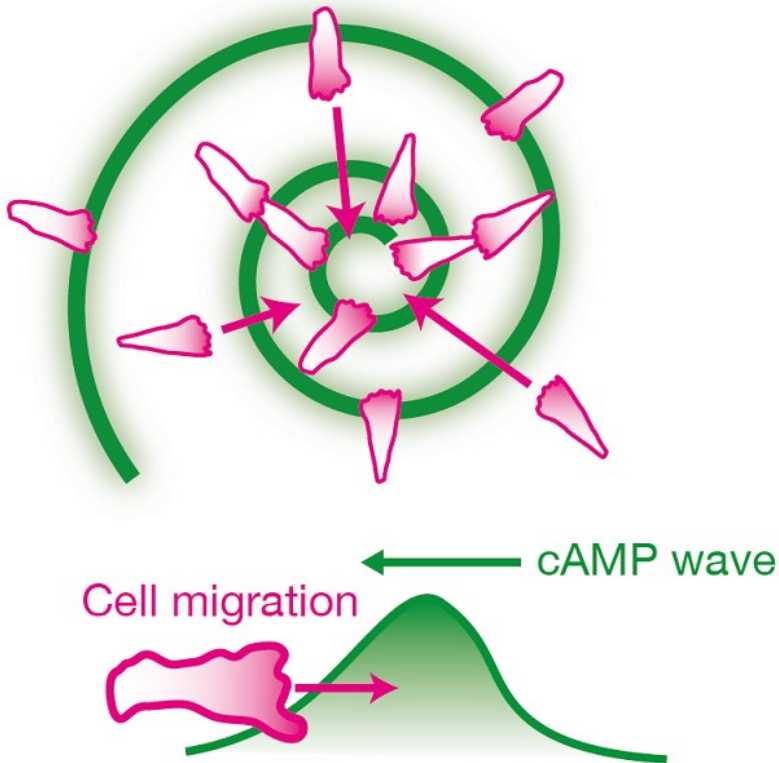
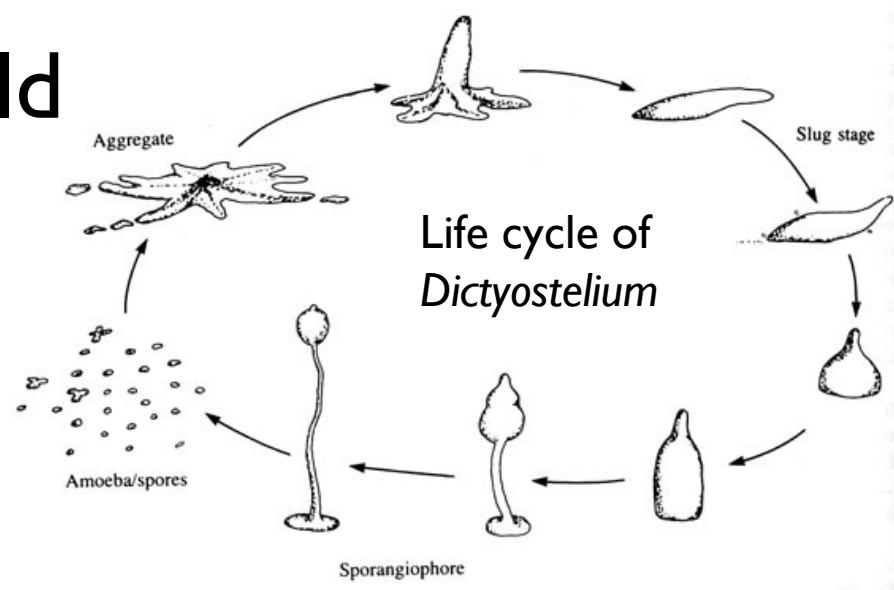
Electrical activity
in heart



Spiral Waves in Slime Mold

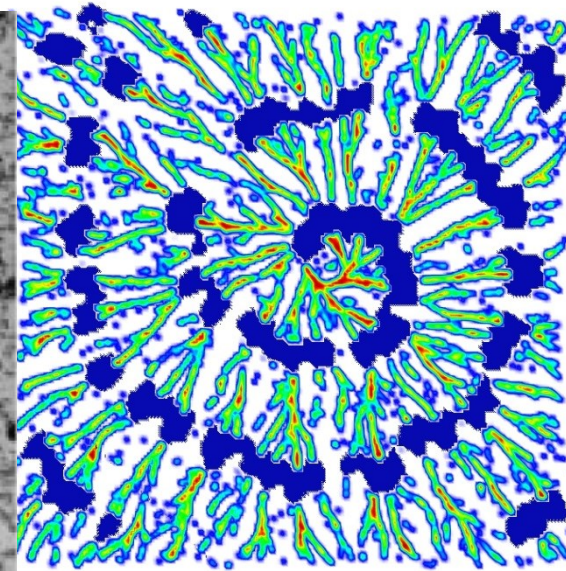
Normally slime mold exist as individual single-celled amoeba – but when starvation conditions arise they suddenly aggregate into a multi-cellular body.

Dictyostelium cells aggregate by moving towards the propagating waves of chemoattractant cyclic AMP (cAMP)



Claviez et al. (1986)

Normal cell aggregation patterns in experiments



Dallon and Othmer (1997)

Streaming cell density patterns in model (cAMP wave shown in blue)

Anatomical reentry & spiral waves



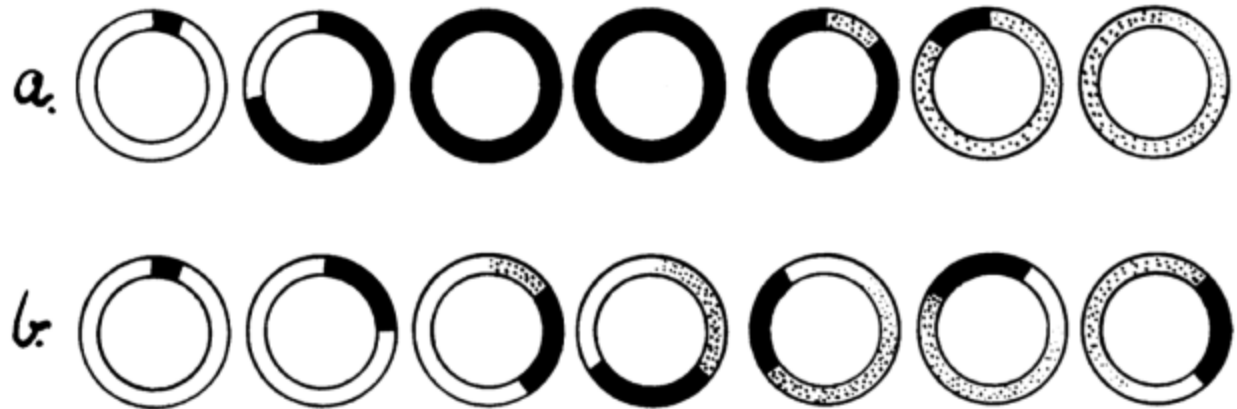
G R Mines

The earliest understanding of the formation of the spiral was as a 1-dimensional reentrant wave, i.e., the continuous circulation of a single pulse of activity around an inexcitable region resulting in persistent periodic activity of tissue even when individual cells comprising it are not capable of oscillation (Mines, 1913)

If wave returns to its initial position while the latter is still in the refractory state, the excitation dies out



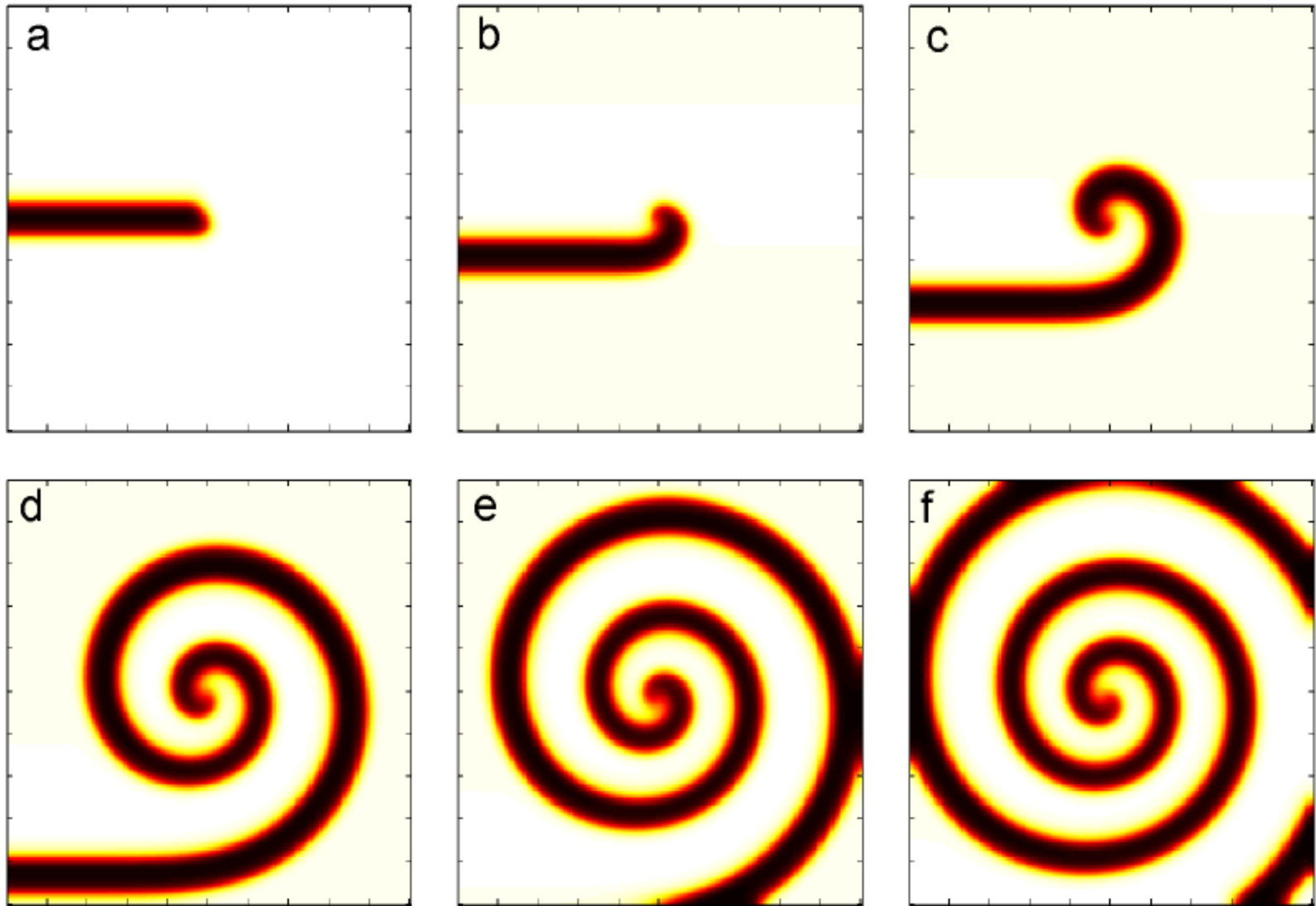
Schematic diagram of a ring of cardiac excitable tissue created by Mines from a tortoise heart



if initial position recovers by the time the wave comes back, reentrant activity becomes persistent

A self-sustaining wave of excitation circulation around the system, resulting in successive contractions of V_1, V_2, A_1, A_2 respectively was observed.

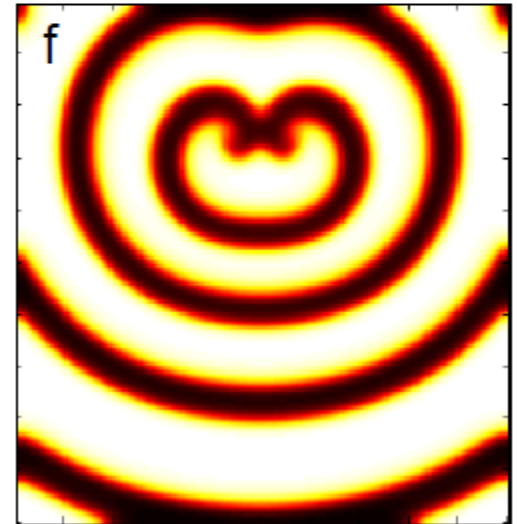
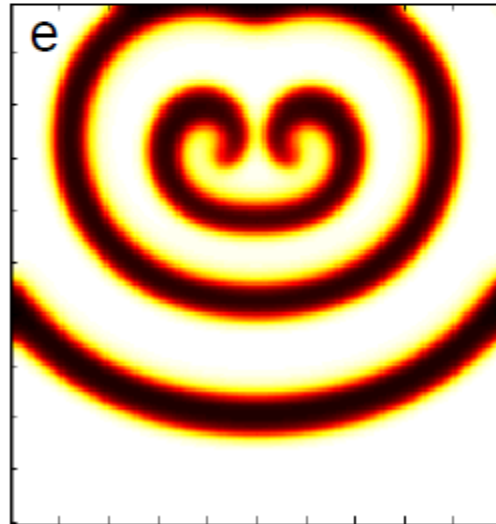
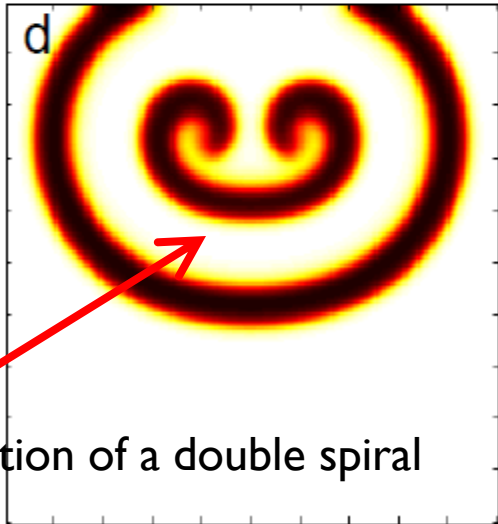
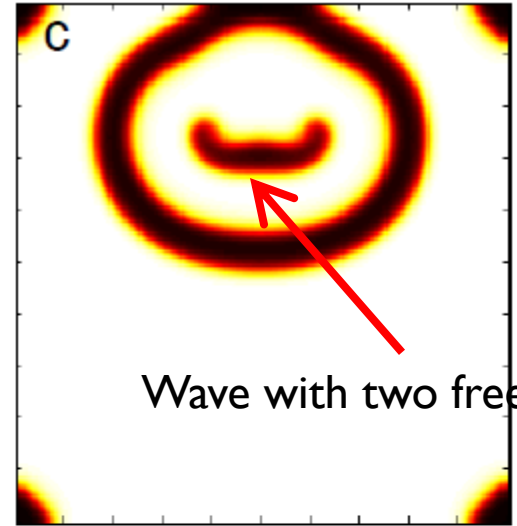
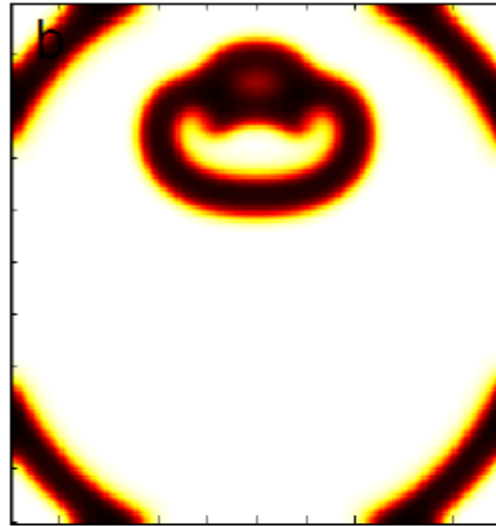
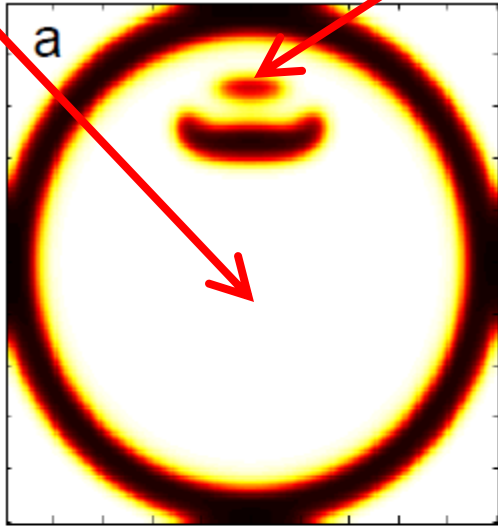
Spiral wave from a broken excitation front



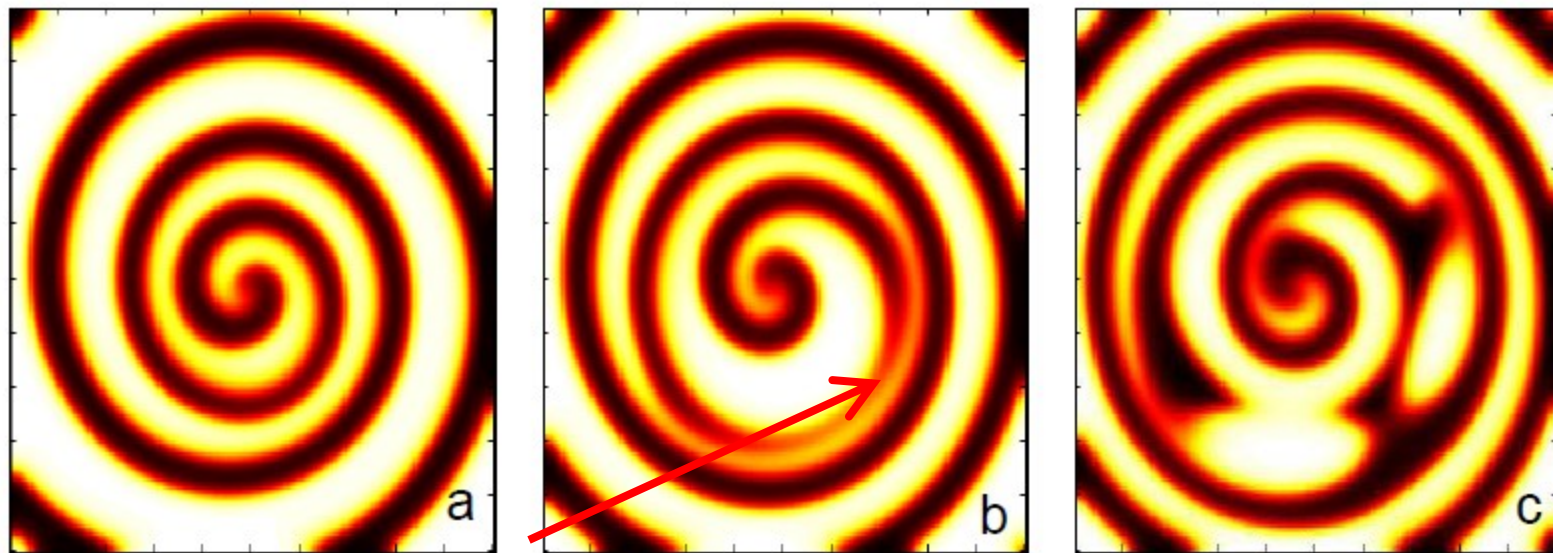
Spiral wave from T1-T2 stimulation protocol

First stimulus applied at time T1 in center of domain

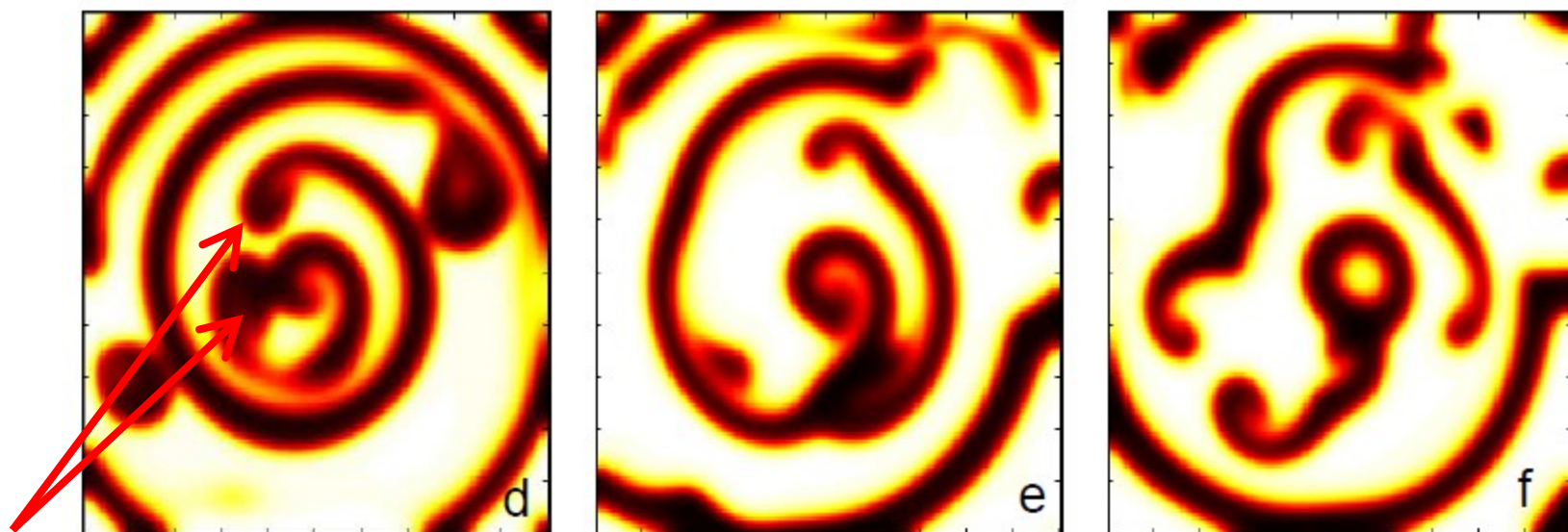
Second stimulus given at time T2 in a region that is not fully recovered



Spatiotemporal chaos from spiral breakup



wavefront colliding with inexcitable region



rise of new spiral wave fragments

From excitable to oscillatory media

A close cousin of excitable media models are...

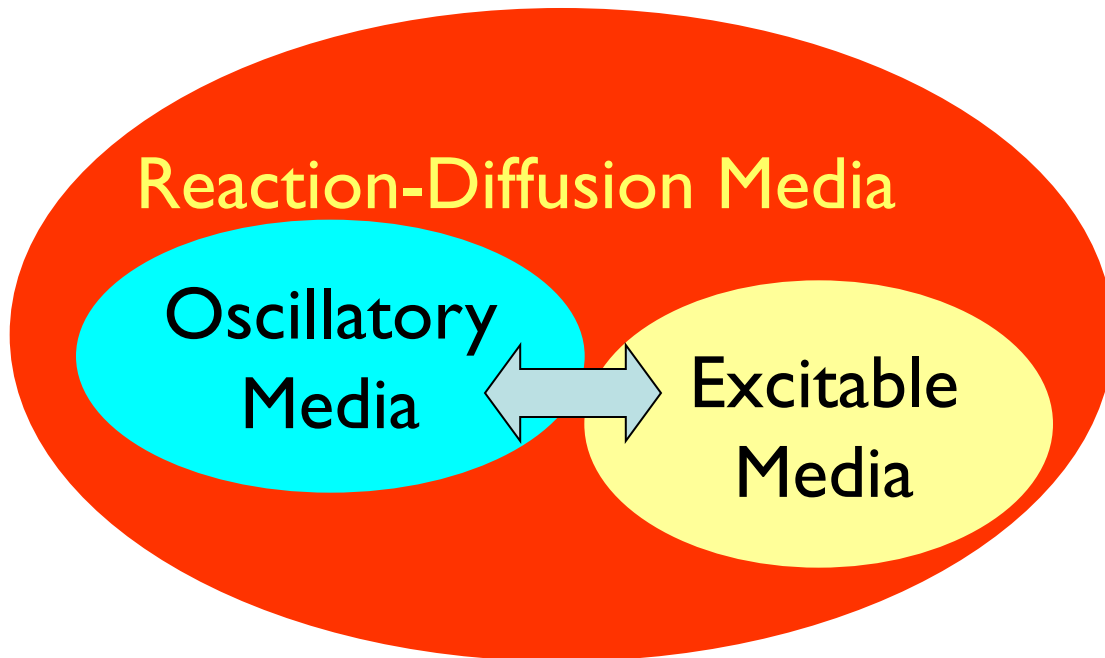
Oscillatory media...

obtained by making both the resting and excited states unstable

Also exhibit spiral waves !

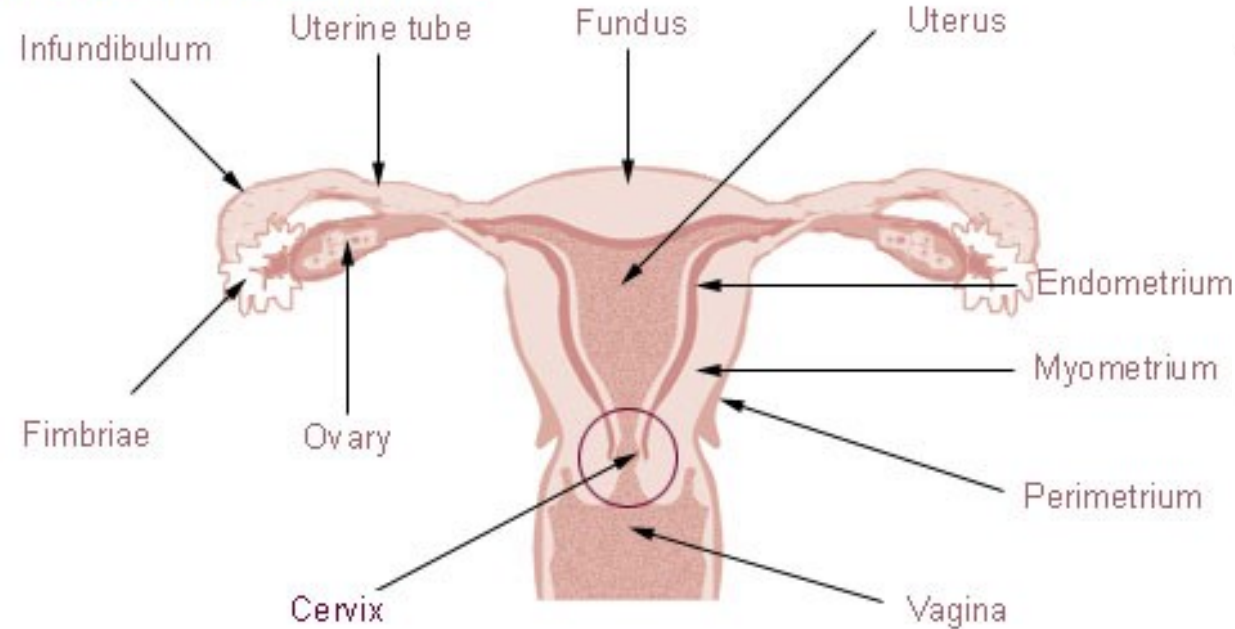
Many biological systems that show regular, periodic oscillations are modeled by oscillatory media

Some switch between excitable & oscillatory

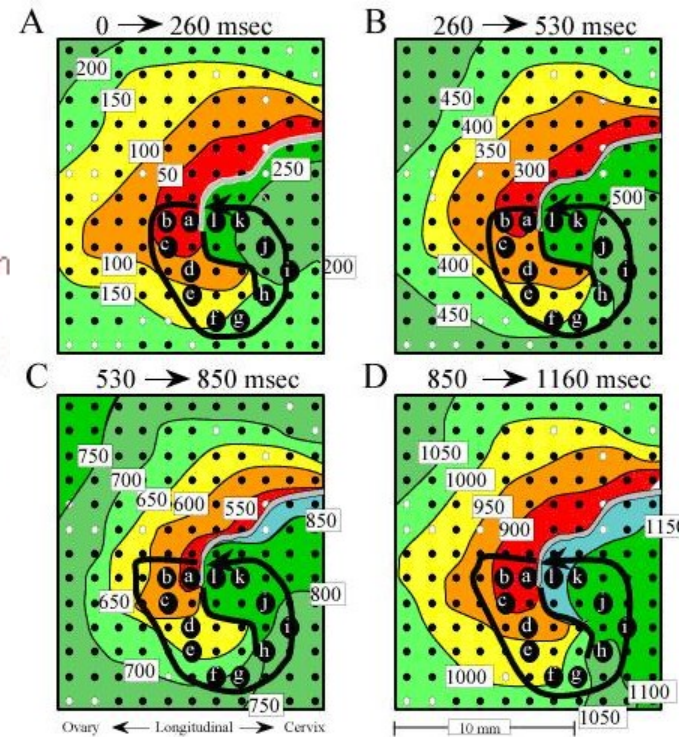


Coherent excitation in pregnant uterus

Uterus and Uterine tubes



Spiral waves observed in pregnant uterine tissue



Lammers Lab

The Pregnant Uterus: an excitable media

Increase in excitability with developing pregnancy

Increased spatial synchronization in excitation leads to coherent contractions → onset of labor (childbirth)

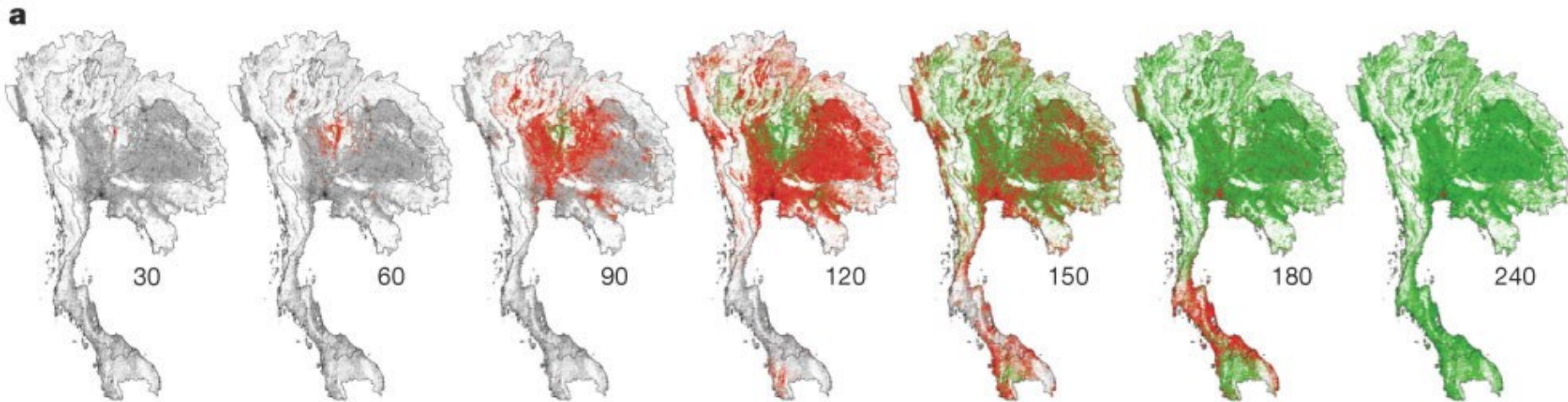
Spreading Waves in Epidemics

Contagion spreading can be represented in an excitable media context

Susceptible, S : resting state

Infected, I : excited state

Recovered or Removed, R : refractory state



Red : new cases

Green : areas where the epidemic has finished

Ferguson et al, Nature, 2005

Snapshots (30 - 240 days) after first case of an uncontrolled outbreak of transmissible avian flu in people living in Thailand.

Fisher Waves: Wave of advance of advantageous genes in spatially dispersed population

R A Fisher, *Annals of Human Genetics* (1937)

Let p be the frequency of the mutant gene, and q that of its parent allelomorph, which we shall suppose to be the only allelomorph present. Let m be the intensity of selection in favour of the mutant gene, supposed independent of p . Suppose that the rate of diffusion per generation across any boundary may be equated to

$$-k \frac{\partial p}{\partial x}$$

at that boundary, x being the co-ordinate measuring position in the linear habitat. Then p must satisfy the differential equation

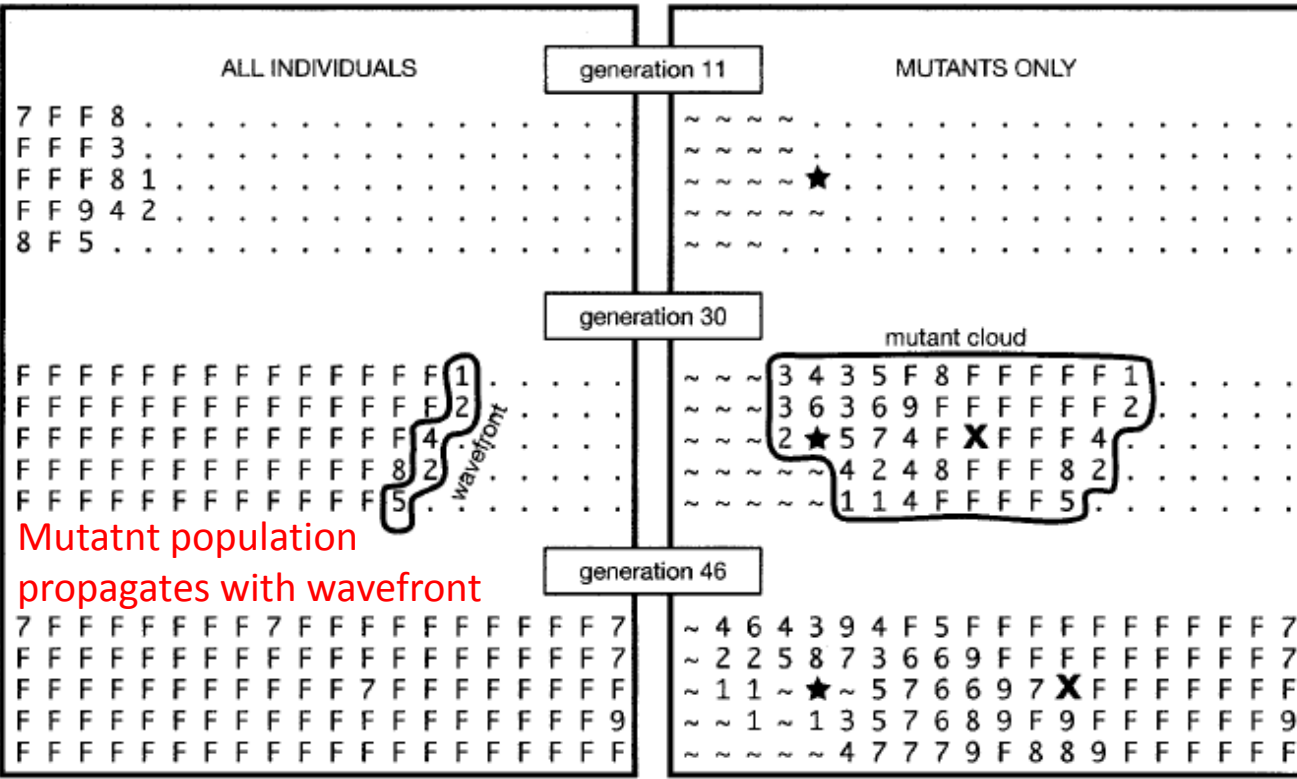
$$\frac{\partial p}{\partial t} = k \frac{\partial^2 p}{\partial x^2} + mpq, \quad \dots\dots(1)$$

where t stands for time in generations.

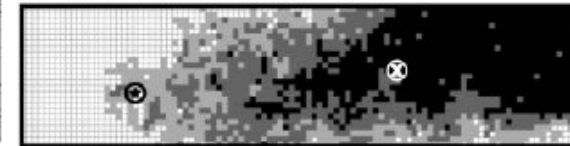
The Mutation Traveling Phenomenon

C.A. Edmonds, A. S. Lillie, and L. L. Cavalli-Sforza, PNAS USA **97** (2004) 975

Expansion of population and subsequent dispersion of a mutant subpopulation - within it shown at three time points (measured in terms of generations)



Mutant population propagates with wavefront



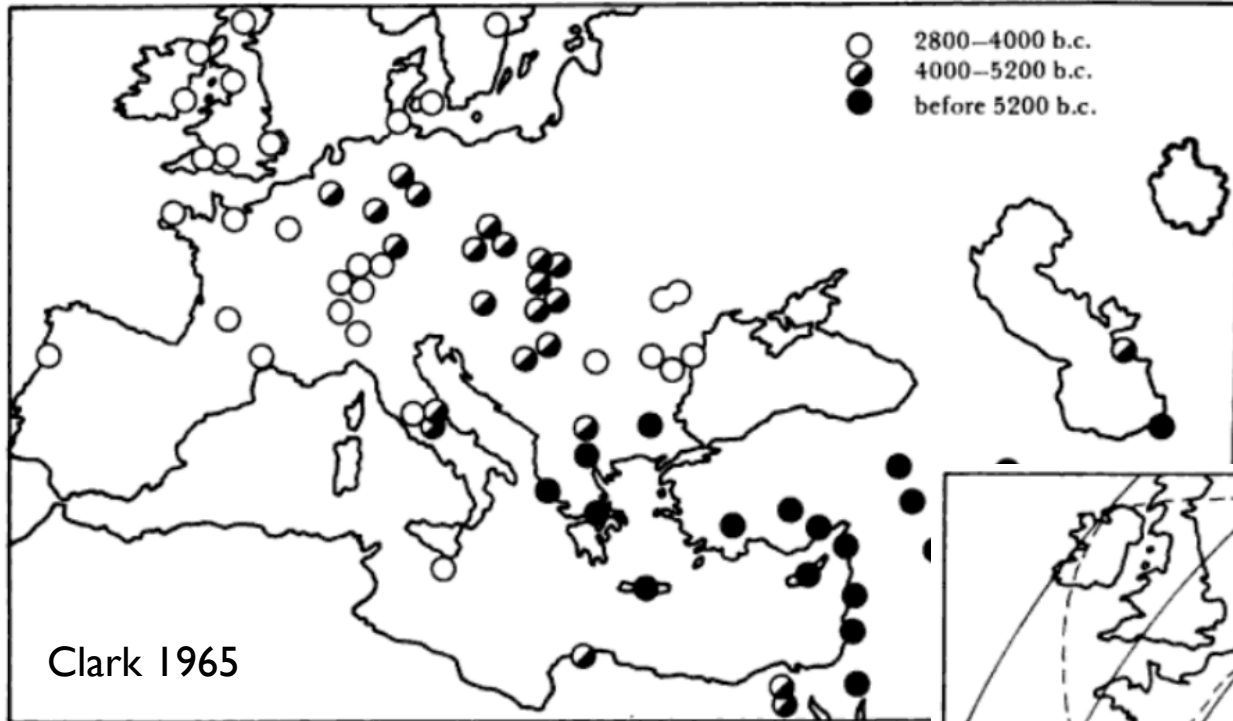
End-result of different simulations with mutations seeded at random locations

(* indicates place of origin of mutation, x indicates mutant centroid)

The Neolithic Transition Wave

Neolithic revolution:
change from hunter-gatherer to agricultural lifestyle
allowing large populations to be sustained

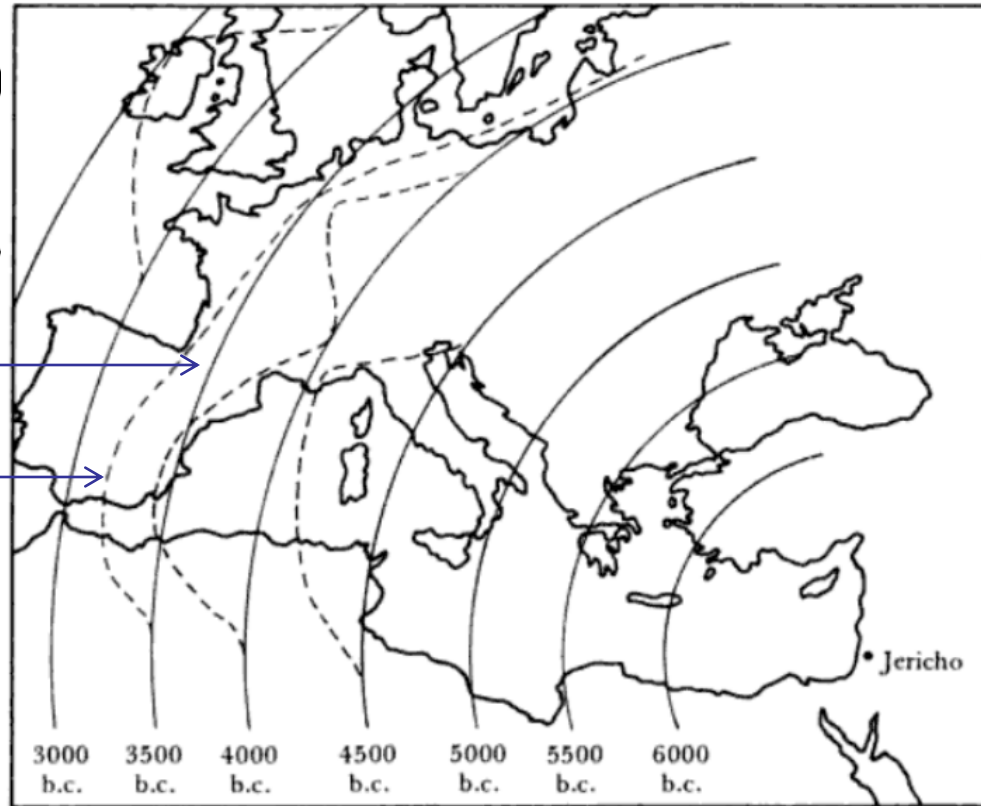
Spread of agriculture into Europe from southwest Asia according to radiocarbon dating



Clark 1965

Predicted from constant speed propagation model

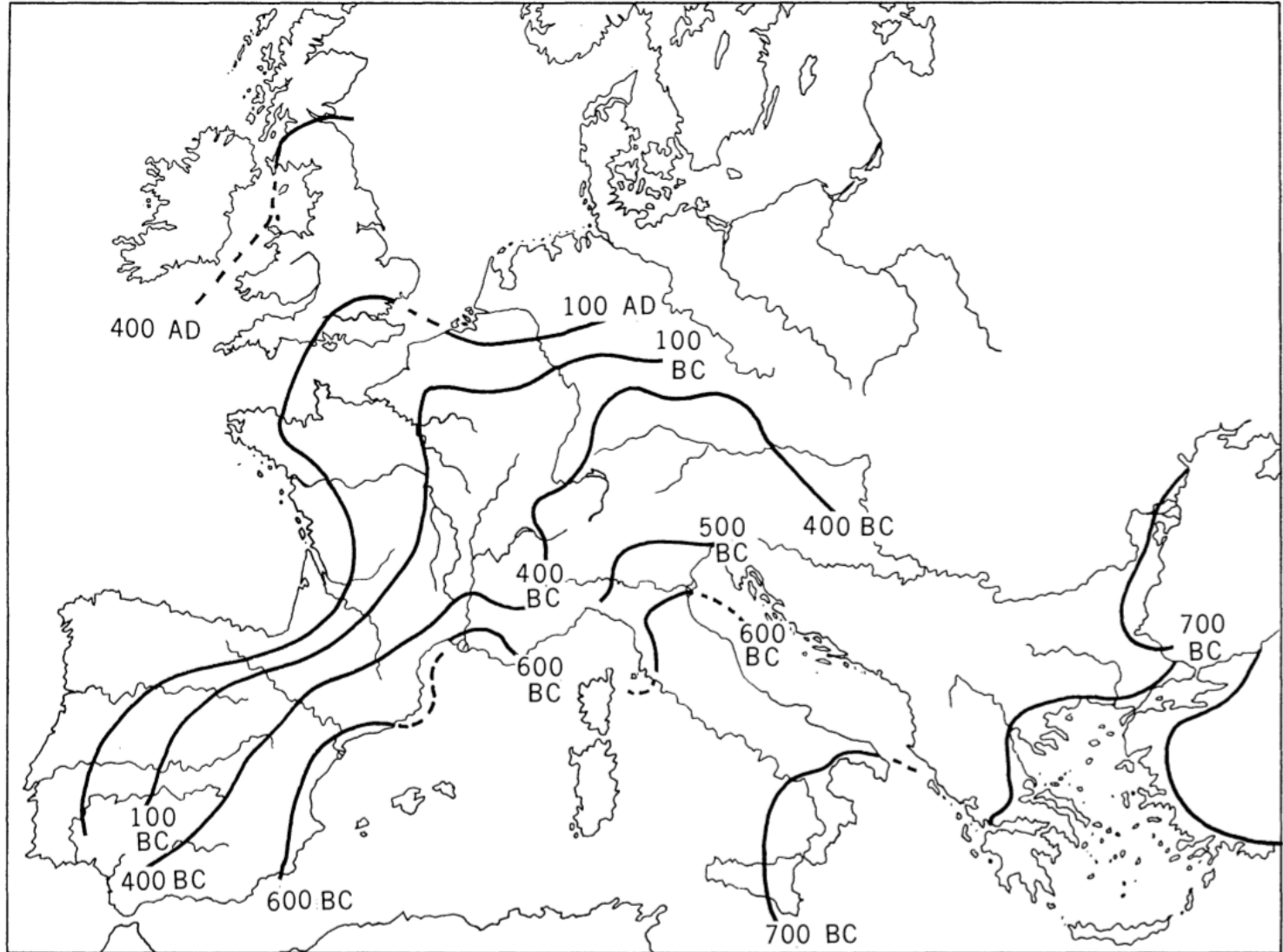
Regional Variation



“Wave of advance” of the farming way of life into Europe
(Ammerman and Cavalli-Sforza, 1971)

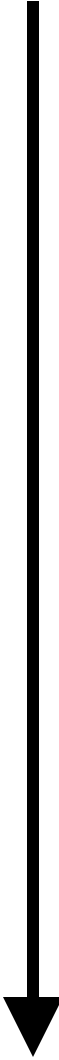
Cultural Diffusion:

Wave of advance for 'polis' (city)



Pounds 1996

Dynamical patterns in excitable/ oscillatory media at all scales

- 
- **Intracellular:** Ca^{++} waves
 - **Cellular:** signal propagation between neurons
 - **Groups of cells:** synchronization of beta cell activity in pancreas
 - **Tissue:** coordination of muscle activity in ventricles
 - **Organ:** coherent contractions in pregnant uterus
 - **Populations:** population dispersal (Fisher waves); spreading waves of epidemics