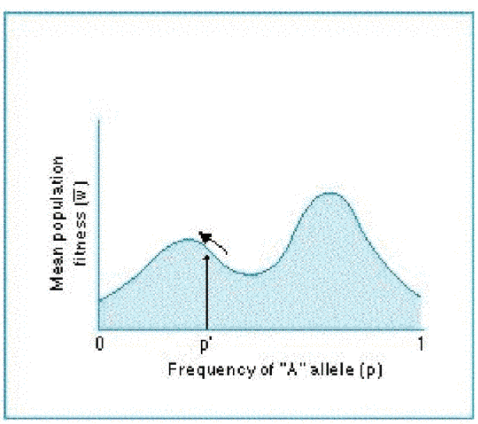
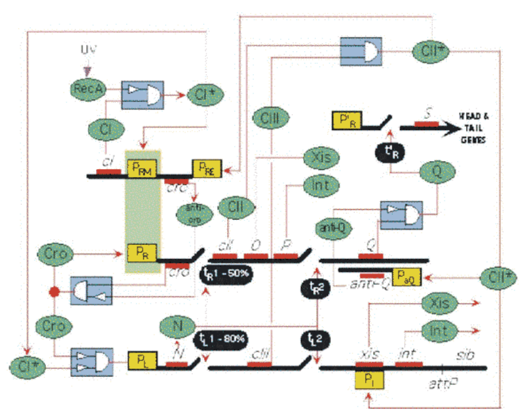
Programmed Cell Death and Evolutionary Cheating:

Could Ageing Solve the Puzzle?

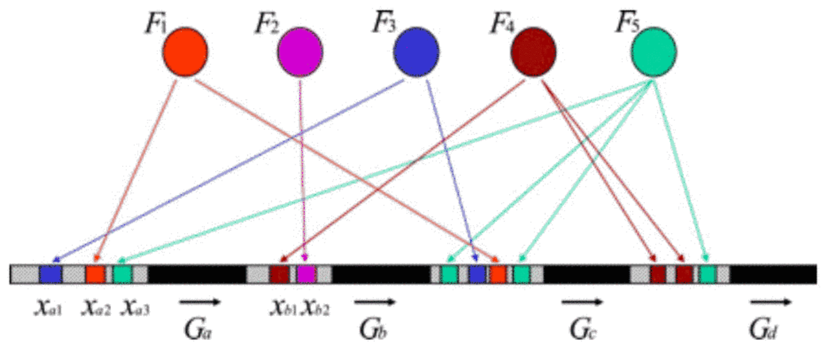
Anirvan Sengupta
Physics Dept. and BioMaPS Inst.
Rutgers University

The gap between evolutionary theory and systems biology





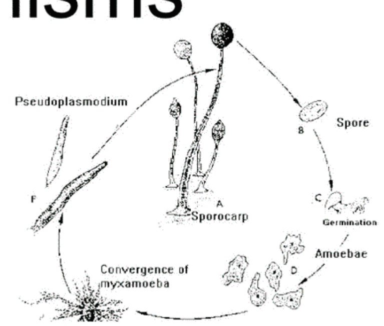
Evolution of Regulatory Elements

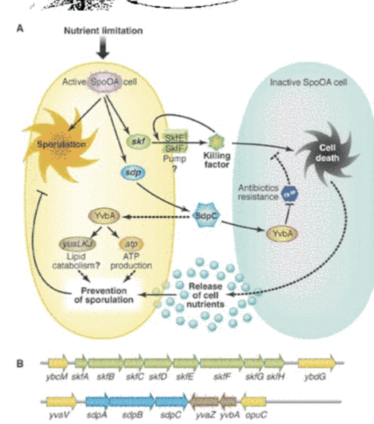


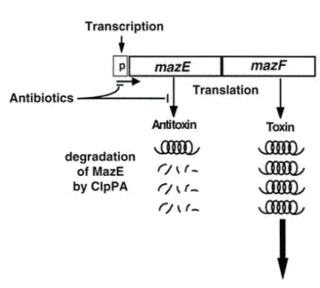
- Evolutionary drift takes regulatory sequences far from consensus, subject to some binding constraints.
- Model indicates that more pleiotropic ->less specific (Sengupta, Djordjevic, Shraiman, PNAS, 2002).

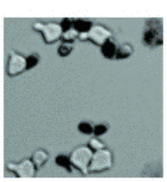
"Altruistic suicide" in unicellular organisms

- Dicty stalks
- Bacteria
- Yeast









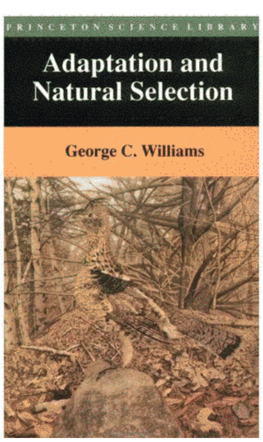
But, why?

Usual argument: "It is good for the species! Provides nutrients for a few which could grow!"

Rebuttal from evolutionary biologists:
"Group selection!"

Group Selection

Individual animals often expose themselves to danger or forego reproduction for the greater good of the group as a whole. Groups containing altruistic individuals would have some selective advantage over groups lacking such members.: Vero C. Wynne-Edwards



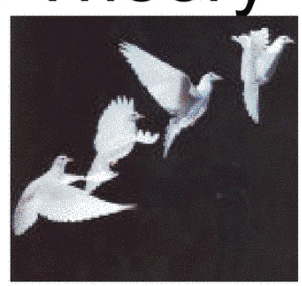
"Group selection was not strong enough to produce …*biotic adaptation*…organisms' playing roles that would subordinate individual interest for some higher value as in the often proposed benefit to the species"
-George C. Williams

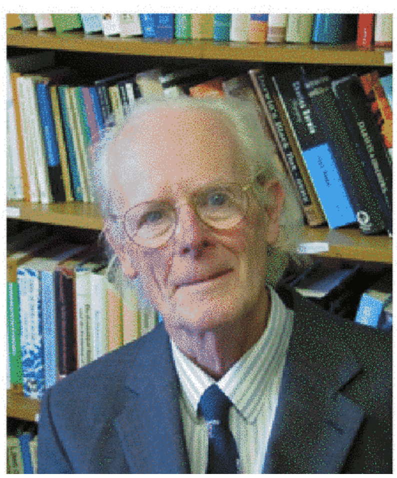
The problem of mixed populations

What if a “selfish” cell invades
(or gets generated by mutation)
the altruistic population?

Would it take over the population?

Hawks and Doves: Evolutionary Game Theory





John Maynard-Smith

Evolutionarily Stable Strategy

	If it meets a Hawk	If it meets a Dove
Hawk gets	(G-C)/2	G
Dove gets	0	G/2

Optimal fraction of hawks, x, determined by
x(G-C)/2+(1-x)G=(1-x)G/2
Or x=G/C

Replicator Dynamics

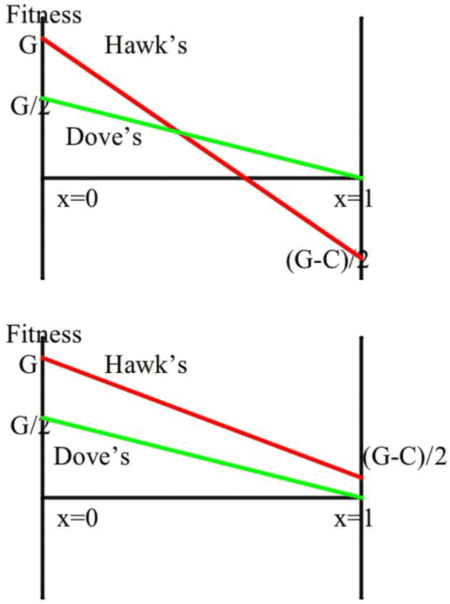
$$dx_i / dt = x_i((Ax)_i - x \bullet Ax)$$

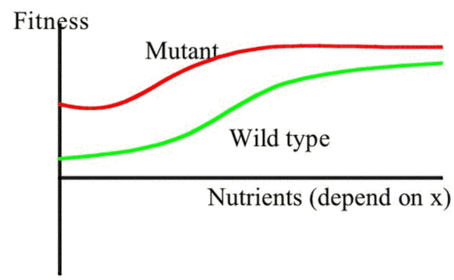
$$x_1 = \text{fraction of hawks} = x$$

$$x_2 = \text{fraction of doves} = 1 - x$$

$$A = \begin{pmatrix} (G-C)/2 & G \\ 0 & G/2 \end{pmatrix}$$

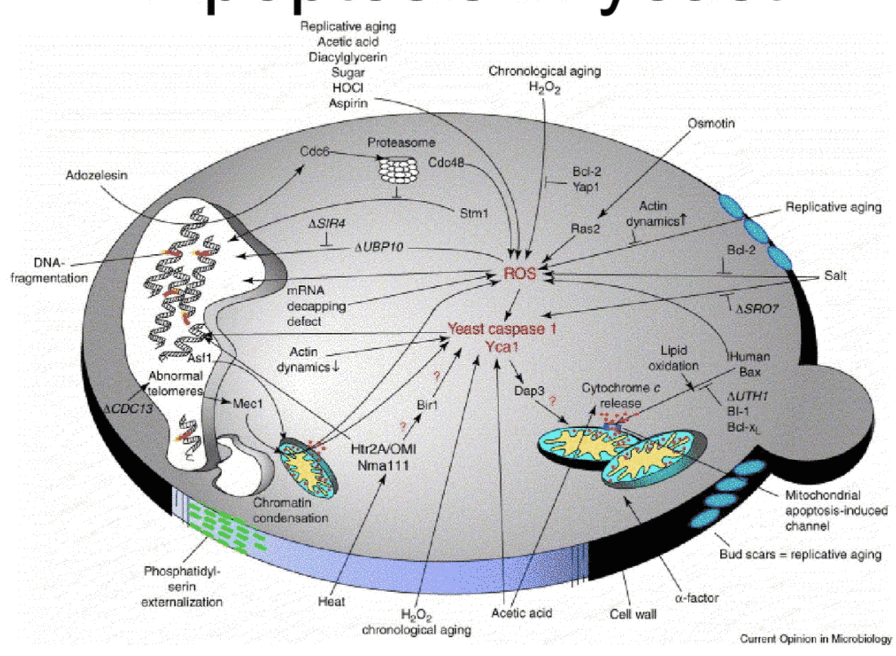
Similarities and Differences





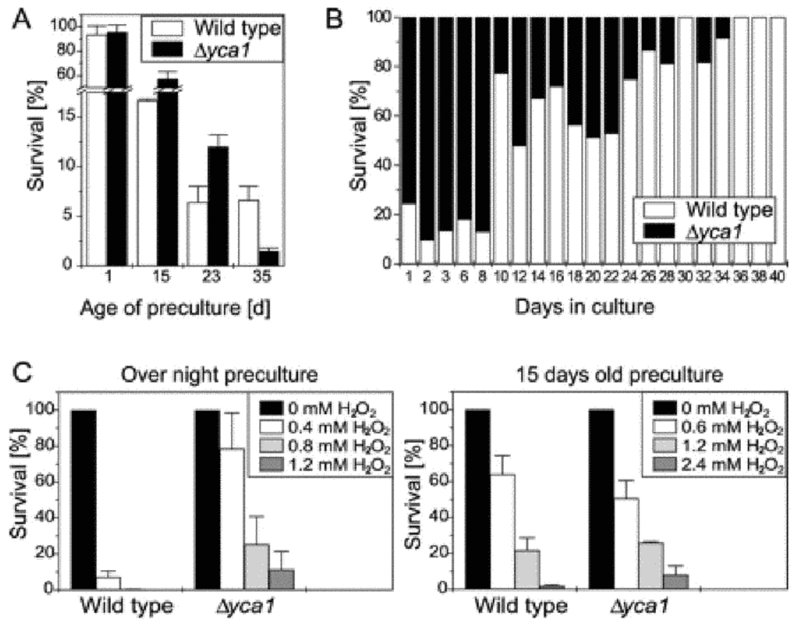
In the hawk-dove problem, we have two player conflicts.
Ours is more like a n-player game, with n tending to infinity.
As a result, everyone is exposed to the same medium.

Apoptosis in yeast



From Madeo et al., Curr. Opin. Microbiol., 2004

Is this what is happening?

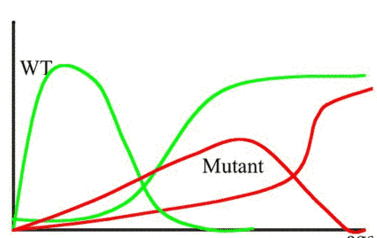


Herker et al.
JCB vol 164,
p 501-7, 2004

Could additional structure in the population help?

- Aging
- Damage

Plausible argument: Mutants with less death rate would have a higher proportion of aged/damaged cell. If dying cells secrete something in the medium that helps younger cells more than the older cells then may be this will help the wild type to recover.



Simple Model

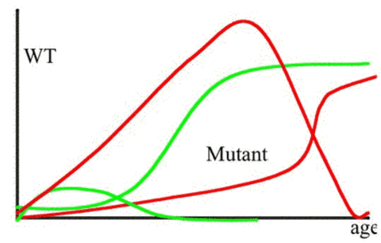
Wild type abundances: $\{x_i | i=1,\ldots,N\}$
Mutant abundances: $\{y_i | i=1,\ldots,N\}$

$$dx_i/dt = \sum_j q_{ij}(\vec{s})x_j - x_i/\tau_i(\vec{s})$$

$$dy_i/dt = \sum_j q_{ij}(\vec{s})y_j - y_i/\tau'_i(\vec{s})$$

$$d\vec{s}/dt = \vec{f}(\vec{x},\vec{y})$$

$$\tau'_i(\vec{s}) > \tau_i(\vec{s}), \text{ for each } i$$



Impossibility of Altruism?

If we have two well mixed populations, the wild type and a mutant with the same (ageing or damage) substructure with the following properties:

(a) the only way they interact with each other is via secretions in the medium;

(b) the only difference between them is the higher death rates for each subcategory of the mutant compared to the wild type;

(c) the secretions affect both populations similarly;

then the wild type would be susceptible to being overtaken by the mutant.

What are the alternatives?

- All mutants have fitness deficits
- Mutant specific poisons
- Cells of the same kind are bunched together. Locality helps. Similar to kin selection.
- Maybe nothing is stable: One always gets new mutants as a result of such contests.

Each of these possibilities is could be subjected to experimental tests!

Conclusion

- Evolutionary game theory and population dynamics is well-studied, saturated subjects.
- Recent developments in programmed cell death could resurrect the subject put some of these ideas to test.
- Hopefully the gap between evolutionary theory and biological mechanism narrow at some point.