PDE Models of Multilevel Selection: The Evolution of Cooperation and the Shadow of Individual-Level Selection

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Evolutionary Game Theory

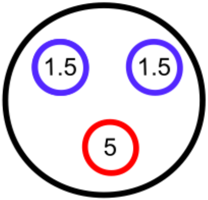
- Why cooperation?
- Two-player game with payoff matrix

$$\begin{array}{cc} & \begin{array}{cc} C & D \end{array} \\ \begin{array}{c} C \\ D \end{array} & \begin{pmatrix} R & S \\ T & P \end{pmatrix} \end{array}$$

- **R**eward, **S**ucker, **T**emptation, and **P**unishment
- Prisoners' Dilemma: $T > R > P > S$
  - Individuals receive higher payoff by defecting
  - Two cooperators outperform two defectors

Competition Between Individuals

$$\begin{array}{cc} & \begin{array}{cc} C & D \end{array} \\ \begin{array}{c} C \\ D \end{array} & \begin{pmatrix} 3 & 0 \\ 5 & 1 \end{pmatrix} \end{array}$$



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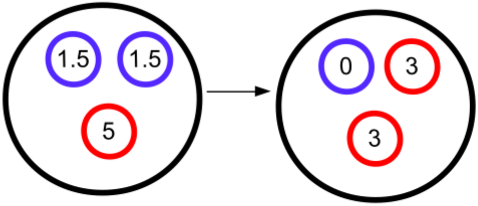

Competition Between Individuals

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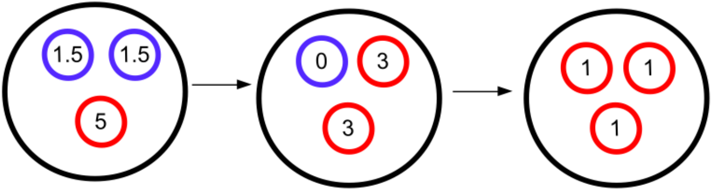
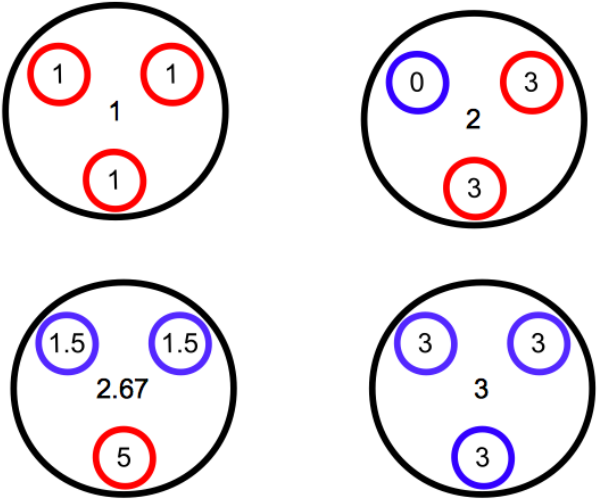


Competition Between Groups



Multilevel Selection

- Biological examples with competition at multiple levels.
  - Major Evolutionary Transitions (Origins of Life, Multicellularity, etc.)
  - Within-Host and Between-Host Disease Dynamics
  - Bottlenecks in Mitochondrial DNA (applications to aging)
  - Cancer: cell replication vs. host health
- Conflict between individual incentive to defect and collective incentive to cooperate

Prior Work on Two-Level Selection Models

- Evolutionary games in group-structured populations
  - Traulsen and Nowak ‘06, Traulsen et al ‘08, Böttcher and Nagler ‘16
  - Akdeniz and van Veelen ‘19
- Nested Birth-Death Models and PDE Limits
  - Luo ‘14, van Veelan et al ‘14, Luo and Mattingly ‘17
  - Dawson 18’, McLoone et al ‘18
  - Simon ‘10, Simon et al ‘13, Simon and Pilosov ‘16
- Population Genetics in Deme-Structured Populations
  - Kimura ‘55, Ogura and Shimakura ‘87a,b
- Evolution of Protocells and Chromosomes
  - Fontanari and Serva ‘13, 14’a,b
  - Maynard Smith and Szathmary ‘95

Ball and Urn Process (Luo-Mattingly): Individual Level

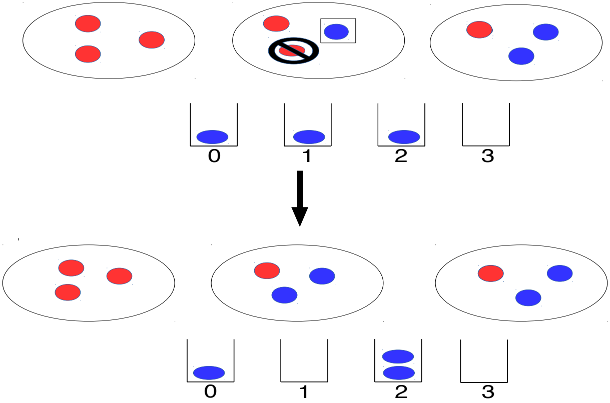


Figure: Schematic depiction of individual birth/death event in middle group

Ball and Urn Process (Luo-Mattingly): Group Level

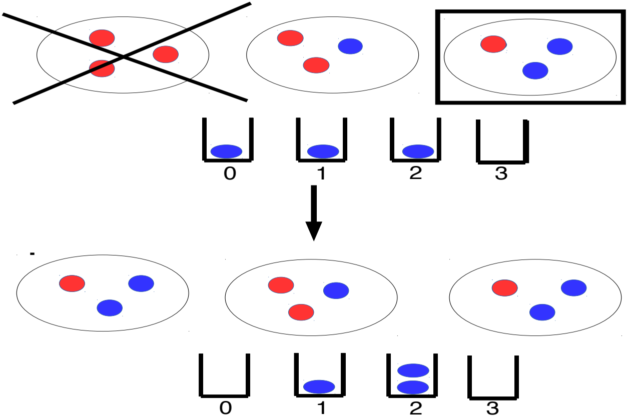


Figure: Schematic depiction of group-level birth/death event

Outline of Thesis

- Chapter 1: Introduction
- Chapter 2: The Replicator Dynamics for Multilevel Selection in Evolutionary Games
- Chapter 3: Analysis of Multilevel Replicator Dynamics for General Two-Strategy Social Dilemmas
- Chapter 4: Assortment and Reciprocity Mechanisms for Promotion of Cooperation in a Model of Multilevel Selection
- Chapter 5: Future Directions in Multilevel Selection Models: Finite Populations, Numerical Methods, and Migration Between Groups
- Chapter 6: Multilevel Selection Models for Protocell Evolution and the Evolution of Genomes

Payoff Functions

- Each individual plays a cooperative dilemma against every other member of its group
- For a group with i cooperators, cooperators and defectors obtain average payoffs of

$$\pi_i^C = \frac{1}{n-1}\left((i-1)R + (n-i)S\right)$$
$$\pi_i^D = \frac{1}{n-1}\left(iT + (n-i-1)P\right)$$

and the average payoff for group members is

$$G_i = \frac{1}{n}\left(i\pi_i^C + (N-i)\pi_i^D\right)$$
$$= \frac{1}{n(n-1)}\left(i^2(R-S-T+P) + ni(S+T-2P) + o(n^2)\right)$$

Individual-Level Events

- $f_i(t) :=$ fraction of groups with i cooperators
- $f_i(t)$ increases by $\frac{1}{m}$ due to within-group competition if
  - New cooperator replaces a defector in a group with $i-1$ cooperators, which happens with rate

$$m f_{i-1}(t)(i-1)\left(1 + w_I \pi^C_{i-1}\right)\left(1 - \frac{i-1}{n}\right)$$

  - New defector replaces a cooperator in a group with $i+1$ cooperators, which happens with rate

$$m f_{i+1}(t)(n-(i+1))\left(1 + w_I \pi^D_{i+1}\right)\left(\frac{i+1}{n}\right)$$

- Treat $f_i(t)$ decreasing by $\frac{1}{m}$ analogously

Group-Level Events

The between-group dynamics lead to an increase of $\frac{1}{m}$ of $f_i(t)$ with rate

$$\Lambda m f_i(t) \left(1 + w_G G_i\right) \left(1 - f_i(t)\right)$$

and lead to a decrease of $\frac{1}{m}$ with rate

$$\Lambda m f_i(t) \left(\sum_{j \neq i} f_j(t) \left(1 + w_G G_j\right) \right)$$

where Λ governs relative rate of within-group and between-group events, and w_G is the strength of selection for group-level events.

ODE Limit ($m \to \infty$)

Fixing group size n and sending number of groups $m \to \infty$ gives

$$
\begin{aligned}
\frac{df_i(t)}{dt} &= \frac{1}{n} D_2 \left(f_i(t) \frac{i}{n} (1 - \frac{i}{n}) \right) \\
&+ w_I \left(D_1^+ \left(f_i(t) \frac{i}{n} (1 - \frac{i}{n}) \pi_i^D \right) - D_1^- \left(f_i(t) \frac{i}{n} (1 - \frac{i}{n}) \pi_i^C \right) \right) \\
&+ \Lambda w_G f_i(t) \left((S + T - 2P) \left(\frac{i}{n} - \sum_{j=0}^{\infty} \frac{j}{n} f_j(t) \right) + \frac{R - S}{n} \right) \\
&+ \Lambda w_G f_i(t) \left((R - S - T + P) \left(\left(\frac{i}{n} \right)^2 - \sum_{j=0}^{n} \left(\frac{j}{n} \right)^2 f_j(t) \right) \right)
\end{aligned}
$$

where $D_1^{\pm}(\cdot)$ and $D_2(\cdot)$ are first and second order difference quotients.

PDE Limit ($m, n \to \infty$)

For large group size and many groups, we obtain the PDE

$$\frac{\partial f(t,x)}{\partial t} = -\frac{\partial}{\partial x}\left(x(1-x)(\beta+\alpha x)f(t,x)\right) + \lambda f(t,x)\left(\left(\gamma x + \alpha x^2\right) - \left(\gamma M_1^f + \alpha M_2^f\right)\right)$$

where

- $f(t,x)$ is probability density for x-cooperator groups
- $\alpha = R - S - T + P$, $\beta = P - S$, $\gamma = S + T - 2P$
- $M_j^f = \int_0^1 y^j f(t,y) dy$
- $\lambda := \frac{\Lambda w_G}{w_I}$ governs importance of between-group competition.

PDE Limit (Continued)

In terms of individual and group payoffs, the multilevel dynamics are given by

$$\frac{\partial f(t,x)}{\partial t} = -\overbrace{\frac{\partial}{\partial x}\left(x(1-x)(\pi_C(x)-\pi_D(x))f(t,x)\right)}^{\text{Within-Group Competition}}$$
$$+\lambda \underbrace{f(t,x)\left[G(x)-\int_0^1 G(y)f(t,y)dy\right]}_{\text{Between-Group Competition}}$$

What happens to long-time behavior of $f(t,x)$ as we vary relative impact of selection at the two levels (λ)?

Role of Individual Payoff

- Characteristic curves satisfy the (within-group) replicator dynamics

$$\begin{aligned}\frac{dx(t)}{dt} &= x(1-x)\left(\beta + \alpha x\right) \\ &= x(1-x)\left(\pi^C(x) - \pi^D(x)\right)\end{aligned}$$

- For $x(0) = x_0$, denote solution by $\phi_t(x_0) = x(t, x_0)$
- Backward trajectories $\phi_t^{-1}(x) = x_0(t, x)$
- Describes dynamics of individual-level birth/death dynamics
- Globally stable fixed point at $x^* = 0$ for PD

Role of Group Average Payoff

- The group-level fitness $G(x)$ for a group with x fraction of cooperators is given by

$$G(x) = P + (S + T - 2P)x + (R - S - T + P)x^2$$

- $G(x)$ is maximized by group composition

$$x^* = \begin{cases} \dfrac{S + T - 2P}{2(S + T - R - P)} & : 2R < S + T \\ 1 & : 2R \geq T + S \end{cases}$$

- **How does group average payoff affect dynamics of multilevel system?**

Density Steady States

- Steady state population satisfies

$$0 = -\frac{\partial}{\partial x}\left[x(1-x)(|\beta| - \alpha) f(x)\right] + \lambda f(x)\left[\gamma x + \alpha x^2 - \langle G \rangle_f\right]$$

- Steady state solutions are of the form

$$f(x) = Z_f^{-1} x^{\lambda |\beta|^{-1} \langle G \rangle_f - 1} (1-x)^{\lambda (|\beta| - \alpha)^{-1} (\gamma + \alpha - \langle G \rangle_f) - 1} (|\beta| - \alpha x)^{\mathrm{messy}}$$

- Infinitely many steady states (depends on $\langle G \rangle_f$)
- **Can't have steady state with** $G(1) = \gamma + \alpha < \langle G \rangle_f$
  - Average payoff limited by payoff of full-cooperator group

Measure-Valued Formulation

- To explore concentration of group types, incorporate possibility of delta-functions
- For C^1 test function $\psi(x)$, have equation for measure $\mu_t(dx)$

$$\frac{d}{dt}\int_0^1 \psi(x)\mu_t(dx) = \int_0^1 \psi'(x)x(1-x)(\beta+\alpha x)\mu_t(dx) + \lambda \int_0^1 \psi(x)\left[G(x) - \int_0^1 G(y)\mu_t(dy)\right]\mu_t(dx)$$

- Measures concentrated at equilibria of within-group dynamics ($\delta(x)$, $\delta(1-x)$, $\delta(\beta+\alpha x)$) are steady-states

Push-Forward Representation of $\mu_t(dx)$

- Within-group competition described by push-forward measure $P_t \mu_0(dx) = [\mu_0 \circ \phi_t^{-1}](dx)$ and in weak form

$$\int_0^1 \psi(x) P_t \mu_0(dx) = \int_0^1 \psi(\phi_t(x)) \mu_0(dx)$$

- Between-group competiton described along characteristics

$$w_t(\phi_t(x)) = \exp\left(\int_0^t \lambda \left[G(\phi_s(x)) - \langle G \rangle_{\mu_s(dx)} \right] ds \right)$$

- Can represent $\mu_t(dx)$ combining effects at each level

$$\int_0^1 \psi(x) \mu_t(dx) = \int_0^1 \psi(\phi_t(x)) w_t(\phi_t(x)) \mu_0(dx)$$

Solvable Special Case

- Consider special case of Prisoners' Dilemma with $S = P + 1$, $T = R + 2$ $(\beta = -1, \alpha = -1)$.
  - Replicator dynamics become $\dfrac{dx(t)}{dt} = -x(1-x)(1+x)$, which has exact solution

$$x(t, x_0) = \phi_t(x_0) = \frac{x_0}{\sqrt{x_0^2 + (1 - x_0^2)e^{-2t}}}$$

- For solvable individual dynamics, can use method of characteristics

Hölder Exponent of $\mu_t(dx)$ Near $x = 1$

- Asymptotic behavior depends on (tail of) initial population through the Hölder exponent near the endpoint $x = 1$
- Hölder exponent defined as

$$\theta_t := \inf_{\Theta > 0} \left\{ \lim_{x \to 0} \frac{\mu_0([1-x, 1])}{x^{\Theta}} > 0 \right\}$$

  - The densities $\theta(1-x)^{\theta - 1}$ have Hölder exponent of θ near $x = 1$.

$$\lim_{x \to 0} \frac{\displaystyle\int_{1-x}^{1} \theta(1-y)^{\theta-1} dy}{x^{\Theta}} = \lim_{x \to 0} x^{\theta - \Theta} = \begin{cases} 0 & : \Theta < \theta \\ 1 & : \Theta = \theta \\ \infty & : \Theta > \theta \end{cases}$$

Long-Time Behavior of Special PD

- With strong within-group selection, defectors take over the whole population.
- With strong between-group selection, some cooperation is supported in a density steady state.

Proposition

Suppose $\mu_0(dx)$ has Hölder exponent θ near $x = 1$. If $\lambda(\gamma - 1) < 2\theta$, then $\mu_t(dx) \rightharpoonup \delta(x)$. If $\lambda(\gamma - 1) > 2\theta$, then

$$\mu_t(dx) \rightharpoonup \frac{1}{Z_f} x^{\lambda(\gamma-1)-2\theta-1}(1-x)^{\theta-1}(1+x)^{-\lambda\gamma+\theta-1}dx.$$

Steady State Densities

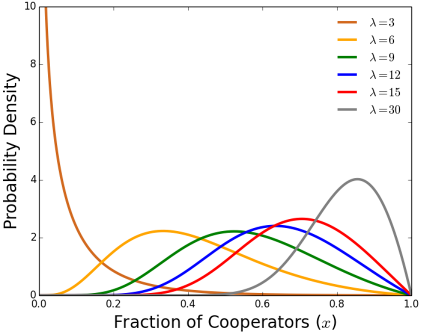


Figure: Steady state densities for various relative selection strengths λ (when $\gamma = 2.5$)

When groups are best off with full cooperation, we can achieve as much cooperation as possible by increasing λ.

Steady State Densities

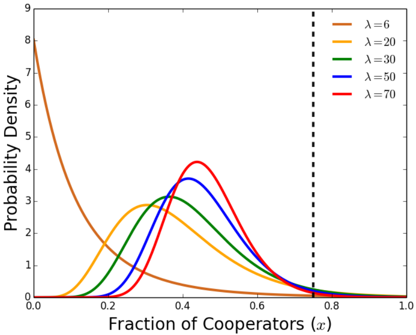


Figure: Steady state densities for various relative selection strengths λ (when $\gamma = 1.5$)

When group is best off with 75 percent cooperators, most groups appear to only achieve 50 percent cooperation for large values of λ.

Peak Abundance at Steady State

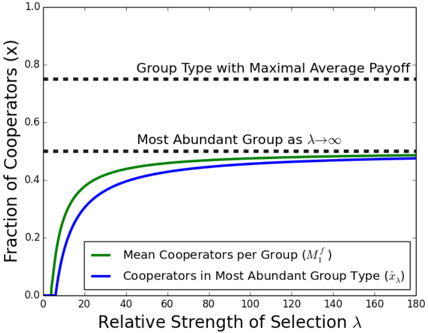


Figure: Mean fraction of cooperators and most abundant group type for various relative selection strengths λ.

When group is best off with intermediate level of cooperators, mean and modal cooperation levels are limited to 50 percent.

Limit of Strong Between-Group Competition ($\lambda \to \infty$)

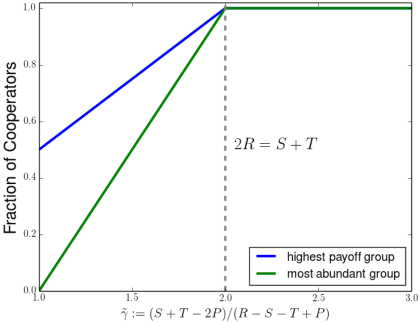


Figure: Group compositions with maximal average payoff and with greatest abundance in limit as $\lambda \to \infty$

When group is best off with intermediate level of cooperators, we cannot achieve optimal levels of cooperation even as between-group selection becomes infinitely strong.

General Case: Comparison Principle Approach

- What if we don't have explicit solution to within-group dynamics?
- We know how to find $\Psi_t(k; x_0)$ solving logistic ODE

$$\frac{dx}{dt} = -kx(1-x) \;\; ; \;\; x(0) = x_0$$

- For PD with $\alpha < 0$, see that

$$-\left(|\beta|+|\alpha|\right) x(1-x) \leq -x(1-x)\left(|\beta|+|\alpha|x\right) \leq -|\beta|x(1-x) \leq 0$$

- This produces ranking of forward and backward characteristics

$$\Psi_t(|\beta|+|\alpha|; x_0) \leq \phi_t(x_0) \leq \Psi_t(|\beta|; x_0)$$

$$\Psi_t^{-1}(|\beta|; x) \leq \phi_t^{-1}(x) \leq \Psi_t^{-1}(|\beta|+|\alpha|; x)$$

Loss of Cooperators in General PD (low λ)

Defectors take over when between-group selection is relatively weak.

Proposition

Suppose $\gamma > 0$, $\alpha < 0$, and we have initial condition $\mu_0(dx)$ with Hölder coefficient θ near $x = 1$. If $\lambda(\gamma + \alpha) < (|\beta| - \alpha)\,\theta$, then $\mu_t(dx) \rightharpoonup \delta(x)$.

- Idea of proof: want to show that $\int_0^1 \psi(x)\mu_t(dx) \to \psi(0)$
- Use comparison principle to estimate characteristic curves and solution along characteristics

Preservation of Hölder Exponent

For PD, Hölder exponent near full-cooperation is preserved in time.

Proposition

If initial measure $\mu_0(dx)$ has Hölder exponent θ near $x = 1$, then so does the solution $\mu_t(dx)$ for $t > 0$.

- Idea: Using push-forward representation, find C_1 and C_2 such that

$$\lim_{x \to 0} x^{-\Theta} \mu_t \left([1 - x, 1] \right) \leq C_1 \lim_{x \to 0} x^{-\Theta} \mu_0 \left([1 - x, 1] \right) \text{ so } \theta_t \geq \theta$$

$$\lim_{x \to 0} x^{-\Theta} \mu_t \left([1 - x, 1] \right) \geq C_2 \lim_{x \to 0} x^{-\Theta} \mu_0 \left([1 - x, 1] \right) \text{ so } \theta_t \leq \theta$$

Threshold for Steady-State Cooperation

- Two expressions for steady state density

$$f(x) = Z_f^{-1} x^{\lambda|\beta|^{-1}\langle G\rangle_f - 1} (1-x)^{\lambda(|\beta|-\alpha)^{-1}(\gamma+\alpha-\langle G\rangle_f)-1} (|\beta|-\alpha x)^{\text{messy}}$$

$$f(x) = Z_f^{-1} x^{\lambda|\beta|^{-1}(\gamma+\alpha)-(|\beta|-\alpha)\theta-1} (1-x)^{\theta-1} (|\beta|-\alpha x)^{\text{messy}}$$

- Threshold λ to achieve density steady state supporting cooperation is

$$\lambda^* = \frac{(|\beta|-\alpha)\,\theta}{\gamma+\alpha} = \frac{(\overbrace{\pi_D(1)-\pi_C(1)}^{\text{Individual Incentive to Defect}})\theta}{\underbrace{G(1)-G(0)}_{\text{Group Incentive to Cooperate}}}$$

- Tug-of-war between individual and group incentives

Average Payoff at Steady State

- Can use steady state expressions to find that average fitness of population is

$$\langle G(\cdot) \rangle_f = \gamma + \alpha - \frac{(|\beta| - \alpha)\,\theta}{\lambda} = G(1)\left(1 - \frac{\lambda^*}{\lambda}\right)$$

- $\langle G(\cdot) \rangle_f = 0$ for $\lambda = \lambda^*$ and $\lim_{\lambda \to \infty} \langle G(\cdot) \rangle_f = G(1)$
- Population limited by fitness of full-cooperator group
- Long-time behavior doesn't necessarily interpolate between individual and group interest

Conjectured Long-Time Behavior

- What do we know about long-time behavior of general case of multilevel PD?
  - Hölder exponent near $x = 1$ is preserved by dynamics
  - If $\lambda < \lambda^*$, $\mu_t(dx) \rightharpoonup \delta(x)$
  - When $\lambda > \lambda^*$, there is a unique steady state with Hölder given exponent θ near 1
  - Convergence to this steady state holds in solvable special case

Conjecture

Suppose the initial distribution $\mu_0(dx)$ has a Hölder exponent of θ near $x = 1$. If $\lambda(\gamma + \alpha) > (|\beta| - \alpha)\theta$, then

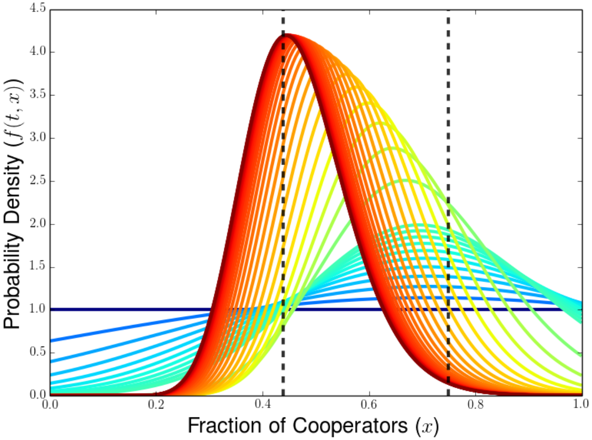
$$\mu_t(dx) \rightharpoonup Z_f^{-1} x^{|\beta|^{-1}(\lambda(\gamma+\alpha)-(|\beta|-\alpha)\theta)-1} (1-x)^{\theta-1} (|\beta|-\alpha x)^{-\frac{\lambda}{|\beta|}(\gamma+|\beta|+\alpha)-\frac{\alpha}{|\beta|}\theta-1} \, dx.$$

Finite Population and Numerical Results

- Can consider underlying stochastic model for finite population
  - Shadow of lower-level selection can be seen in relative fixation properties of cooperators and defectors
- For games with collective optimum of full-cooperation, initial partial concentration at full-cooperation group results in covergence to $\delta(1-x)$
  - Finite differences solutions by sums of deltas
  - Finite difference solutions can qualitatively disagree with behavior of PDE limit
- Instead turn to finite volume discretization

Numerical Tests for Long-Time Behavior

Finite volume scheme can be used to test long-time behavior with initial densities with Hölder exponent $\theta = 1$.



Comparison of Numerics with Conjecture (when $x^* = 1$)

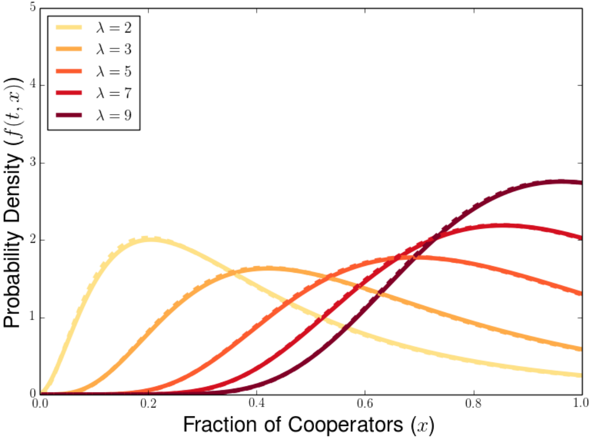


Figure: Comparison of numerics to predicted steady state

Comparison of Numerics with Conjecture (when $x^* = 0.8$)

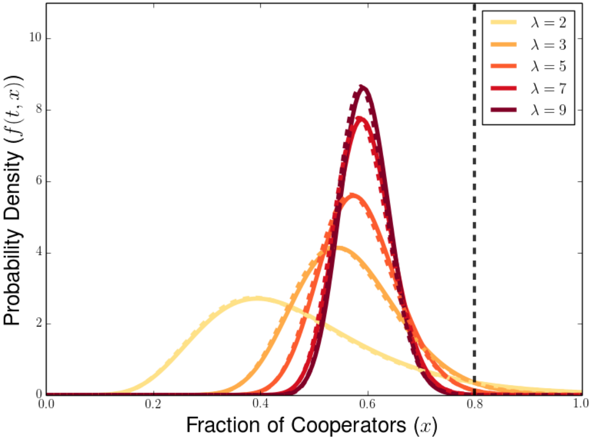
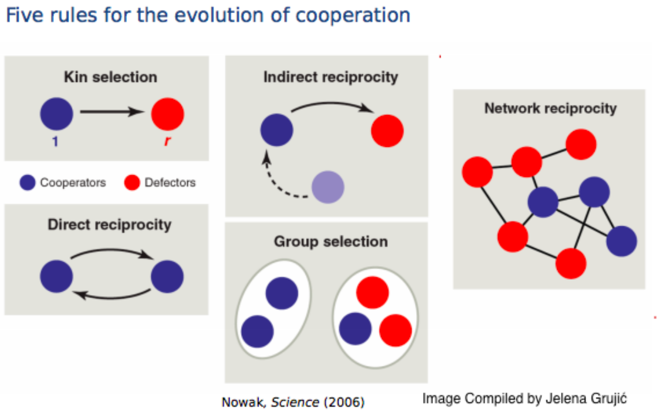


Figure: Comparison of numerics to predicted steady state

Reciprocity & Assortment Mechanisms



- **Are there synergies between multilevel selection and assortment or reciprocity?**

Assortment or Kin Selection

- Assortment/Relatedness parameter r
- Payoffs given by

$$\pi_C^r(x) = rR + (1-r)\left[xR + (1-x)S\right]$$
$$\pi_D^r(x) = rP + (1-r)\left[xT + (1-x)P\right]$$

- Average payoff given by $G^r(x) = [\gamma + r\alpha]\, x + (1-r)\alpha x^2$
- Average payoff at steady state is

$$\langle G^r(\cdot)\rangle_{f(x)} = \gamma + \alpha + \frac{(\alpha + \beta + r(\gamma - \beta))\,\theta}{\lambda}$$

and we have $\dfrac{\partial \langle G^r(\cdot)\rangle_{f(x)}}{\partial r} = \dfrac{\theta}{\lambda} \underbrace{(\gamma - \beta)}_{T-P} > 0$

Density Steady States for Various r (Fixed λ)

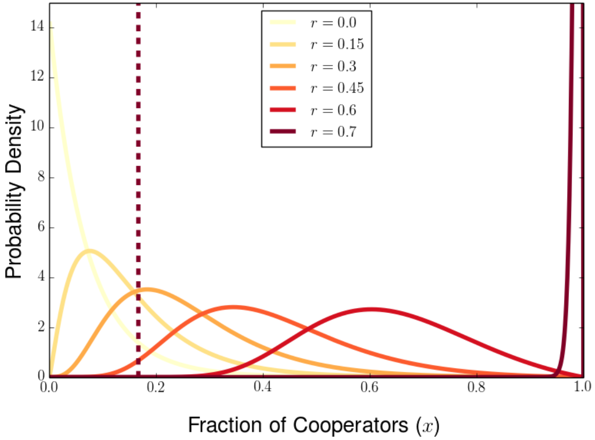
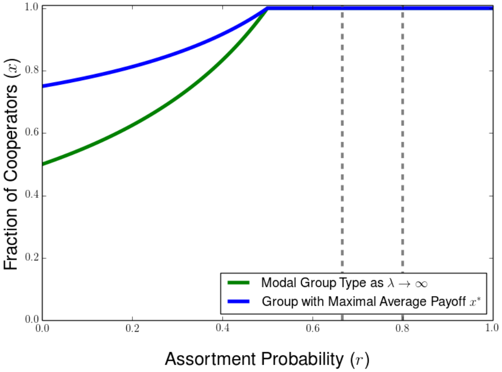


Figure: Steady state density $f_\infty(x)$ for $\lambda = 10$ and various values of r

Limit of Strong Between-Group Competition ($\lambda \to \infty$)



With high assortment probability r, we can achieve arbitrary levels of cooperation (given sufficient group competition λ).

Reciprocity / Punishment

- Detection parameter q
- Payoffs given by

$$\pi_C^q(x) = xR + (1-x)\left[qP + (1-q)S\right]$$
$$\pi_D^q(x) = x\left[qP + (1-q)T\right] + (1-x)P$$

- Average payoff given by $G^q(x) = (1-q)\gamma x + (\alpha + q\gamma)x^2$
- Average payoff at steady state is

$$\langle G^q(\cdot)\rangle_{f(x)} = \gamma + \alpha + \frac{(\alpha + \beta + q(\gamma - \beta))\theta}{\lambda}$$

and we have $\dfrac{\partial \langle G^q(\cdot)\rangle_{f(x)}}{\partial q} = \dfrac{\theta}{\lambda}\underbrace{(\gamma - \beta)}_{T-P} > 0$

Density Steady States for Various q (Fixed λ)

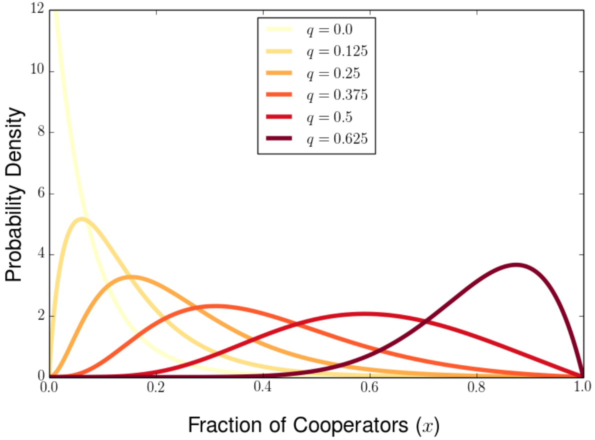
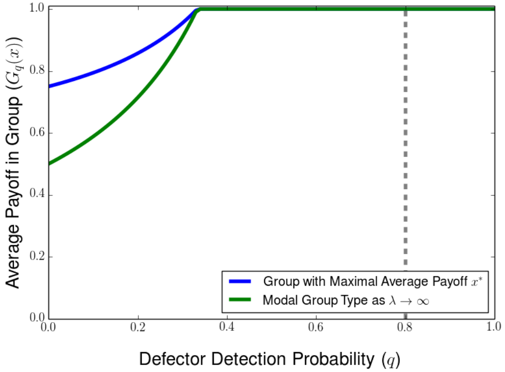


Figure: Steady state density $f_\infty(x)$ for $\lambda = 10$ and various values of q

Limit of Strong Between-Group Competition ($\lambda \to \infty$)



With high detection probability q, we can achieve arbitrary levels of cooperation (given sufficient group competition λ).

Protocell Model[1]

Key Questions:

1. How did coexistence between complementary genes evolve in (proto)cells?
2. Why are our genes linked in chromosomes?

- Two types of genes in protocells: fast replicators (F) which reproduce at rate $1+s$ and slow replicators which reproduce at rate 1
- Describe cell by fraction x of type S replicators
- Protocells reproduce with rate $\lambda_{FS} G(x) = \lambda_{FS} x(1-\eta x)$
  - For $\eta = 0$, $G_{FS}(x) = x$ (linear benefit of slow replicators)
  - For $\eta = 1$, $G_{FS}(x) = x(1-x)$, fast and slow replicators are perfect complements

[1] Part of collaboration with Fernando Rossine and Dylan Morris

PDE Multilevel Selection Model

For many protocells with many genes per protocell, obtain PDE

$$\frac{\partial f(t,x)}{\partial t} = \frac{\partial}{\partial x}\left(sx(1-x)f(t,x)\right) + \lambda_{FS} f(t,x)\left(\left(x - \eta x^2\right) - \left(M_1^f - \eta M_2^f\right)\right)$$

- Threshold λ_{FS} to maintain any coexistence at steady state

$$\lambda_{FS}^* = \frac{s\theta}{1-\eta}$$

- Average group reproduction function at steady state

$$\langle G_{FS}(\cdot)\rangle_{f^\infty} = (1-\eta)\left(1 - \frac{\lambda_{FS}^*}{\lambda_{FS}}\right)$$

Dimerization: Linking Genes Together

- Introduce dimers D, a slow and fast gene linked together
- S, F, and D replicate within cells at rates satisfying $b_D < b_S < b_F$
  - For example, can pick $b_D = \frac{1+s}{2+s} = 1 - \frac{1}{2+s}$
- Denote fractions of S, F, and D by x, y, and z
- Fraction of slow genes is $x + \frac{z}{2}$, fast genes is $y + \frac{z}{2}$
- Have cell reproduction function given by

$$G(x,y,z) = \left(x + \frac{z}{2}\right)\left((1-\eta)x + y + \left(1 - \frac{\eta}{2}\right)z\right)$$

  - Generalizes cell reproduction function from fast-slow competition

PDE for Fast-Dimer Competition

On the fast-dimer edge of the simplex, density of dimers z follows

$$\frac{\partial g(t,z)}{\partial t} = \frac{\partial}{\partial x}\left(sx(1-x)f(t,x)\right) + \lambda_{FS} f(t,x)\left(\left(x - \eta x^2\right) - \left(M_1^f - \eta M_2^f\right)\right)$$

- Threshold λ_{FD} to maintain any coexistence at steady state

$$\lambda_{FD}^* = \left(s + \frac{1}{2+s}\right)\left(\frac{2\theta}{1-\frac{\eta}{2}}\right)$$

- Average group reproduction function at steady state

$$\langle G_{FD}(\cdot)\rangle_{h^\infty} = \frac{1}{2}\left(1 - \frac{\eta}{2}\right)\left(1 - \frac{\lambda_{FD}^*}{\lambda_{FD}}\right)$$

Comparison of Fast-Slow and Fast-Dimer Competition

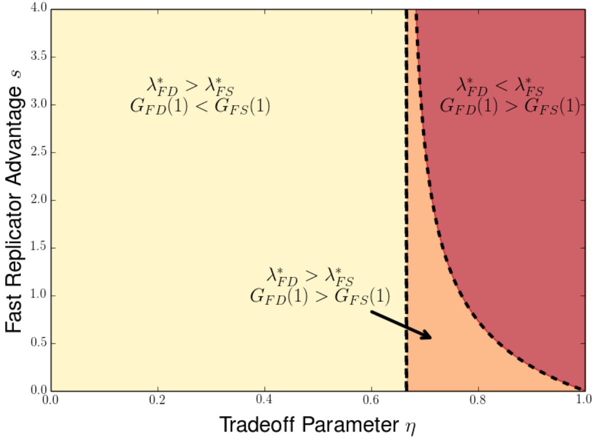


Figure: Ranges of η and s for which dimerization helps or hurts in establishing coexistence

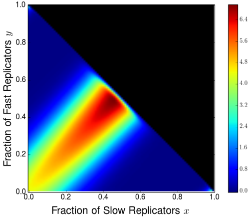
Fast-Slow-Dimer Competition

For relative birth rates $\alpha = b_S - b_{FS}$ and $\beta = b_F - b_{FS}$, and b_{FS}, we get multilevel dynamics governed by

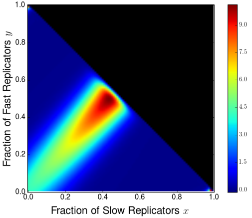
$$\begin{aligned}\frac{\partial f(x,y,t)}{\partial t} &+ \frac{\partial}{\partial x}\left[x\left(\alpha(1-x) - \beta y\right)\right] + \frac{\partial}{\partial y}\left[y\left(\beta(1-y) - \alpha x\right)\right] \\ &= \lambda f(x,y,t) G(x,y,1-x-y) \\ &- \lambda f(x,y,t)\left[\int_0^1 \int_0^{1-\chi} G(\xi,\chi,1-\xi-\chi) d\xi d\chi\right]\end{aligned}$$

We extend our finite volume scheme to the three-type simplex to study time dynamics on the fast-slow-dimer simplex.

Numerics for Trimorphic Competition ($s = 0.4$, $\eta = 1$)



(10 steps)



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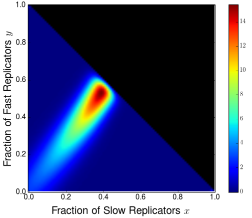

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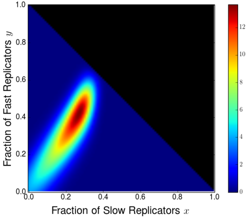
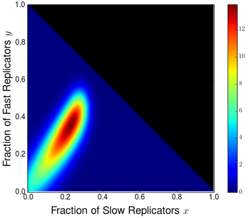
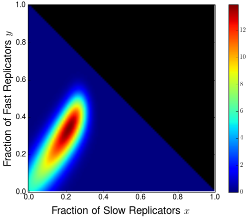


(100 steps)

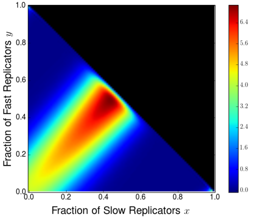


(150 steps)

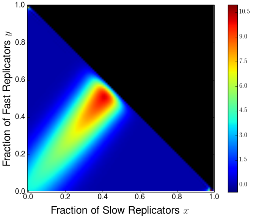


(200 steps)

Numerics for Trimorphic Competition ($s = 0.7$, $\eta = 1$)



(10 steps)



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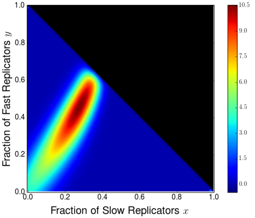
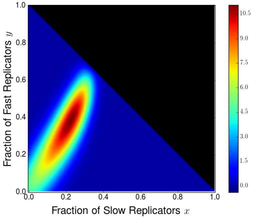
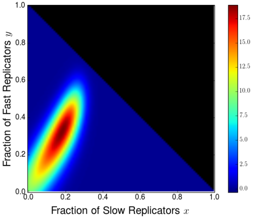


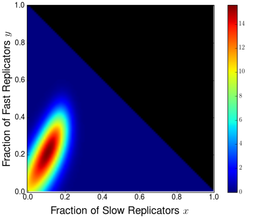
(50 steps)



(60 steps)



(75 steps)



(200 steps)

Future Directions

- Characterization of convergence to steady state (conjecture)
- Mathematical Extensions of Multilevel Framework
  - Long-time behavior and numerical schemes in higher dimension
  - Incorporating effects of noise and migration
- Multilevel Selection in Cellular Evolution
  - Evolution of Protocells / Origin of Chromosomes
  - Copy number regulation in plasmids
- The role of space in hierarchical biological competition
  - Interacting Particle System approach
- I hope this thesis can be seen as an invitation to learn more about multilevel selection!

On The Method of Characteristics...

"In mathematics, you don't understand things. You just get used to them."

— John von Neumann

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Further Reading

- DC (2019). The replicator dynamics for multilevel selection in evolutionary games. *Journal of Mathematical Biology*, *79(1)*, 101-154.
- DC (2019). Assortment and Reciprocity Mechanisms for Promotion of Cooperation in a Model of Multilevel Selection. *arXiv preprint arXiv:1910.06933*.
- DC (2020). Analysis of Multilevel Replicator Dynamics for General Two-Strategy Social Dilemmas. *Bulletin of Mathematical Biology*, in press.
- Luo, S., & Mattingly, J. C. (2017). Scaling limits of a model for selection at two scales. *Nonlinearity*, 30(4), 1682.
- Luo, S. (2014). A unifying framework reveals key properties of multilevel selection. *Journal of Theoretical Biology*, 341, 41-52.
- Simon, B., & Pilosov, M. (2016). Group-level events are catalysts in the evolution of cooperation. *Journal of Theoretical Biology*, 410, 125-136.