Mathematical model of evolution of chemical production and sensitivity in social amoeba

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Evolutionary theory based on molecular basis is hopeful.
The process of forming a mature fruiting body takes 24 hours. The mature, or maturing, organism undergoes culmination, the formation of a fruiting body, which contains a sorus of spore cells on top of a stalk that is composed of vacuolated cells. Spore and stalk cells — prestalk and prespore cells — differentiate and sort, forming a tipped fruiting body, which contains a sorus of spore cells on top of a stalk that is composed of vacuolated cells. One important transition occurs between growth and aggregation, which is mediated by signals from the environment, and follow a developmental pathway that is defined by a genetic response to those signals. The formation of a multicellular organism, known as a mound, in which the precursors of the mature organism are found at the front end, whereas the stalk cells contain cytoplasmic granules to one side of the fertilized oocyte. The initial asymmetry is established before the first cell division and is defined by a genetic response to those signals. Therefore, the initial asymmetry in the developing embryo to segregate these biochemical signals is established in the oocyte and the developmental process is initiated by fertilization. The cells of the organism and are found at the front end, whereas the stalk cells. The entire organism then sort within the mound to form a newly patterned multicellular aggregate (known as a mound; FIG. 1). The entire organism is initiated by fertilization. The cells of the organism undergo differential chemotaxis of the pstA O cells, which undergoes differentiation to prespore and prestalk cell, which are sorted along the anterior–posterior axis: the pstA, pstO and pstAB cells combined comprise about 25% of the total cell number, whereas cyclic AMP, which functions both extracellularly in slugs, the cell types are arranged along the anterior–posterior axis, which is composed of a ball of spores (called the sorus) resting on top of a stalk containing vacuolated cells (called the sorus) resting on top of a stalk containing vacuolated cells. One important transition occurs between growth and aggregation, which is mediated by signals from the environment, and follow a developmental pathway that is defined by a genetic response to those signals. Therefore, the initial asymmetry in the developing embryo to segregate these biochemical signals is established in the oocyte and the developmental process is initiated by fertilization.
Altruistic behavior of amoeba

**Motility**
- **Amoebae**, unicellular organisms, exhibit amoeboid motility.
- This involves the formation of a **pseudopodium**, a branching meshwork of actin filaments. The movement of a pseudopodium and retraction of the tail result in locomotion.

**Chemotaxis**
- The movement of a cell towards a chemoattractant gradient is known as chemotaxis. F-actin polymerization and retraction of the tail are key processes.

**PI3K and Akt**
- **Phosphatidylinositol 3-kinase (PI3K)** and its downstream effector, **Akt/protein kinase B (PKB)**, play crucial roles in chemotaxis.
- PI3K is activated by chemoattractants in mammalian cells, and its activation leads to the amplification of the intracellular anterior–posterior gradient.

**Regulation**
- **Regulation of PI3K and Akt** is essential for maintaining the directional movement of many cell types, including amoebae.

**Cell Fate**
- **Prespore cells** differentiate and undergo cell death, while **prestalk cells** contribute to the stalk and spore formation.

**Patterns**
- **Pattern formation** in fingers, slugs, and early culminants is a hallmark of amoeboid behavior.
- DIF-1 is produced by prespore cells
- DIF-1 makes prespore cells become prestalk cells
- DIF-1 is inactivated by prestalk cells

DIF-1

\[
\text{Cl} \quad \text{OH} \quad \text{O} \\
\text{H}_3\text{CO} \quad \text{Cl} \quad \text{OH}
\]

Prespore cells

Prestalk cells
DIF-1 increases prestalk calls

Control

DIF-1

Adding DIF-1

Prespore cells

Prestalk cells

Kay et al. 1999
Cell differentiation by DIF-1

\[ f(C) = f_0 C \]

\[ g(C) = \frac{g_0}{C} \]

Prespore cells

DIF-1

Prestalk cells

C

\( a \)

\( b \)
Kinetics of cells and DIF-1

\[ \frac{dT}{dt} = f(C)P - g(C)T \]  
(Pre-stalk cells)

\[ \frac{dC}{dt} = aP - bCT \]  
(DIF-1)

\[ N = P + T \]  
(Total cell number)
Stalk/Spore (T/P) ratio converges on a constant

\[
\frac{\hat{T}}{\hat{P}} = \left( \frac{f_0}{g_0} \right)^{1/3} \left( \frac{a}{b} \right)^{2/3}
\]
The stalk/spore ratio is **NOT always fixed**.
Cheater becomes more spores than normal cells in mixed fruiting body

Normal (wild type) + Labeled normal

Prespore cells

Normal + Labeled Cheater

Prespore cells

Santorelli et al. 2008
Stalk/spore ratio is not always fixed

Mechanism of cell differentiation can explain the behavior of cheater

- Only normal
- Only Cheater
- Normal + Cheater

Cheater looks like normal
Cheater makes more spores

Mixing two strains
Mixed two strains share DIF-1

**Production & Inactivation**

**Strain 1**
\[ a_1, b_1, f_1(C), g_1(C) \]

**Strain 2**
\[ a_2, b_2, f_2(C), g_2(C) \]

**Regulation of differentiation**

- DIF-1

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In a mixture of multiple strains

\[
\frac{dT_1}{dt} = f_1(C)P_1 - g_1(C)T_1 \quad \text{(Pre-stalk cells of st.1)}
\]

\[
\frac{dT_2}{dt} = f_2(C)P_2 - g_2(C)T_2 \quad \text{(Pre-stalk cells of st.2)}
\]

\[
\frac{dC}{dt} = a_1P_1 + a_2P_2 - C(b_1T_1 + b_2T_2) \quad \text{(DIF-1)}
\]

\[
N_i = P_i + T_i \quad (i = 1, 2) \quad \text{(Total cell number)}
\]
A strain has lower sensitivity becomes more spore

- **a single strain**
  - Prespore cells $P$
  - Prestalk cells $T$

- **a mixture of two strains**
  - Red strain becomes more spore
    - High production, Low sensitivity
    - = Red strain is cheater

Low production, High sensitivity

High production, Low sensitivity
Kinetics models show...

- Stalk/Spore ratio is independent of initial stalk/spore ratio.
- Cheater has lower sensitivity than normal.
How do the **Stalk/Spore ratio**, production of DIF-1 and **sensitivity for DIF-1** evolve?

Evolution

- **Cell division**
- **Make fruiting body**
- **Starvation**
- **Dispersal**
A single spore makes fruiting body

Cell division → Aggregation → Only strain 1
N cells

spore of strain 1

spore of strain 2

Only strain 2
Dispersal and settlement success of spores $S(\hat{T})$

$$S(\hat{T}) = \frac{S_0 \hat{T}^l}{\alpha^l + \hat{T}^l}$$

$\alpha=10000$, $l=2$, $S_0=1.0$
Fitness

\[ W_i = S(\hat{T}_i) \hat{P}_i e^{-k a_i} \]

Dispersal success

Number of prespores

Cost of DIF-1 production

\[ i \] indicates a strain

A strain has lower fitness is replaced by the other strain which has higher fitness.
Two strain do NOT mix

Sensitivity

DIF-1 Production

Optimal T/P ratio
Two strain do NOT mix

Keeping optimal T/P ratio

Reducing production cost

Optimal T/P ratio

Sensitivity

DIF-1 Production
If two strains do NOT mix

Keeping optimal Stalk/Spore (T/P) ratio, amoeba evolve to produce less DIF-1 and to have high sensitivity.
Two spores make fruiting body (prob. $m$)

- Cell division
- Aggregation

- Mixed
- Only stain1
- Only strain2
Two spores make fruiting body (prob. $m$)

\[ W_i^{\text{mix}} = S \left( \hat{T}_1^* + \hat{T}_2^* \right) \hat{P}_i^{\text{mix}} e^{-k_a i} \]

- Summation of prestalk cells

※ $i$ indicates a strain
Mixing change the outcome

Sensitivity

Optimal T/P ratio

DIF-1 Production
Mixing change the outcome

Sensitivity

Keeping optimal T/P ratio

Reducing production cost

DIF-1 Production
Mixing change the outcome

Reducing the risk of cheating

Keeping optimal T/P ratio

DIF-1 Production
Mixing change the outcome

Sensitivity

DIF-1 Production
If two strain can mix

Amoeba evolve to make more DIF-1 and to have lower sensitivity than the case two strain do not mix.
• *LsrA* mutant
  - produces lower stalk inducing factor
  - has higher sensitivity
  - becomes more stalk when mixed with normal


LsrA mutant become more stalk = LsrA mutant is “Loser”
Summary

Even if stalk/spore ratio is not different much, DIF-1 production & sensitivity may be different.

Evolution when two strains do not mix

→ DIF-1 production is little & Sensitivity is high

Evolution when two strains can mix

→ DIF-1 production is higher & Sensitivity is lower