Exercise sheet 9
Systems Biology class 2014

June 2, 2014

Print and return to Pablo Szekely during classes, tutorials, office hours or to the envelope outside of room 612 until June 8th 2014.

1 Calcium control

Consider the system that controls calcium blood levels in mammals. Mammals maintain tight control over the concentration of calcium in their blood, aiming to keep it at a baseline level of several grams per liter. Data from dairy cows shows that after giving birth, calcium levels drop primarily due to milk production. In response, the hormones PTH and 1, 25-DHCC rise, leading to release of calcium from body stores. Calcium blood levels return to baseline exponentially, reaching halfway to steady-state after about 1 day. In some cases, failure to recover baseline calcium levels leads to sickness (parturient paresis), which can be prevented by injecting calcium into the bloodstream.

Reminder: In class we saw the heat shock system where u was temperature, x represented heat-shock proteins and y was the level of unfolded proteins. The equations we used were:

$$\frac{dx}{dt} = k\,(y - y_0) \quad (1)$$

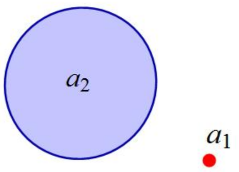
$$y = u - x \quad (2)$$

1. In the Calcium system, let u be the rate of milk production, y be the blood calcium level and x be the flux from the calcium stores in the body to the blood. Draw a schematic arrow diagram of the circuit.
2. Schematically plot the dynamics of x and y after birth, assuming a step increase in milk production.
3. Schematically plot the response of x and y to injecting calcium into a healthy cow that is not producing milk.
4. Write integral feedback equations to describe the homeostasis circuit.
5. Are the equations exactly the same or slightly different from the equations (1) and (2) for the heat shock system?
6. In the heat shock system that we saw in class, we found two archetypes: effectiveness which minimizes the amount of unfolded proteins, and economy which minimizes the amount of chaperones.
   In the calcium homeostatis model, consider the trait space k vs Δy_0, where Δy_0 is the deviation from the target calcium in the blood that is tolerated before integral feedback kicks in.

   Can the two systems (Heat Shock and Calcium homeostasis) be compared on the Pareto front we saw in class? If so, what could be the archetypes in the calcium homeostatis model?
7. Estimate the integral feedback constant k.

2 Optimal region for a task

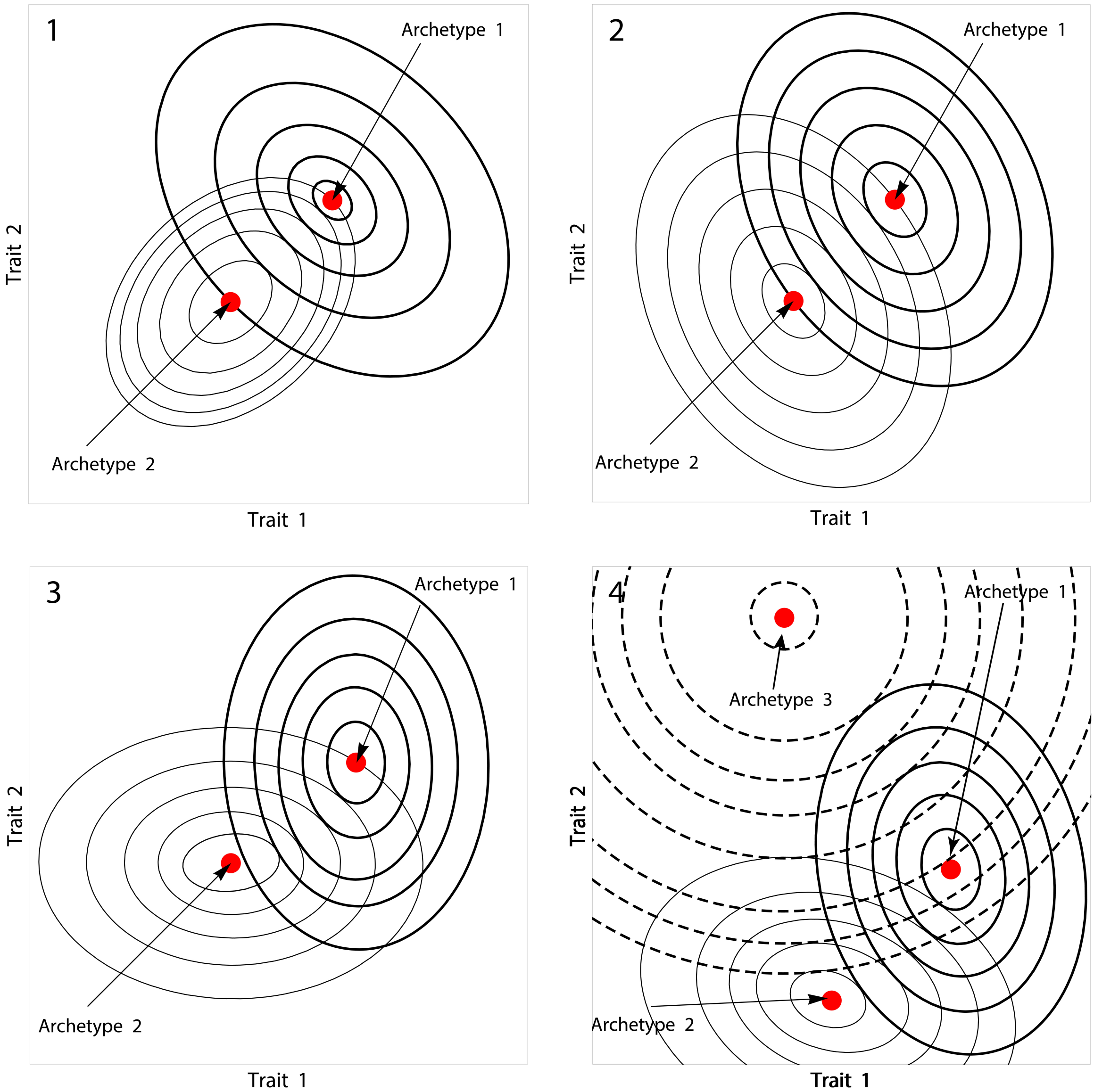
Suppose that a system has a trade-off between two tasks. One task is optimal at a single point in trait space, called archetype 1. The other task, however, is optimal in an entire region (e.g a blob-like area of trait space). Archetype 2 is therefore a region of trait space, and not a single point. Performance decreases with the distance from the archetypes. (In the case of a region-archetype, performance at a point in trait space is determined by its distance to the closest point in the archetype region).



What is the Pareto front in this case? Sketch an example.

3 Curved Pareto fronts

The Pareto front can be found by the set of points at which the performance contours for different tasks are tangent. Consider the following figures, in which the performance contours are concentric ellipses. Sketch the corresponding Pareto front in each case. In which case/s is the Pareto front curved?



4 The game of the Calvin cycle

Plants use carbon from CO_2 in the air and the energy of light to make their biomass. An important part of this process is called the Calvin cycle. A simplified version of this cycle was described by Melendez-Hevia and Isidoro (The Game of the Pentose Phosphate Cycle, E. Melendez-Hevia and A. Isidoro, J. theor. Biol. 1985) as a game: convert five 3-carbon molecules to three 5-carbon molecules. Use the same rules as in the game discussed in class:

1) transfer two or three carbons at each step.
2) Molecules of 1 or 2 carbons are not allowed.

1. Find the solution with the minimal number of steps.
2. How many kinds fo enzymes are used?
3. Why does it make sense to assume that natural selection would tend to find a solution with minimal number of steps (limit your answer to 200 words).
4. *Optional:* read about the plant Calvin cycle and compare your solution to the real cycle found in plants. Which enzymes corresponds to which step in the solution?