

Chapter 2

A. coli: Complexity in the Environment

Introduction and review of certain basic notions from the calculus: functions, directional derivatives, gradients; vector fields, gradient ascent. It is done in the context of understanding a simple creature modeled on the behaviour of Euglena and E-coli. Run and Tumble behavior. Tangent is the best "linear" approximation to curve near a point. For surfaces, the gradient points in the direction of maximum increase. Gradient Ascent (Hill Climbing) algorithm. First view of the tangent and normal local frame attached to curves. Tumble frees A. coli from local maxima.

Organisms exhibit behaviours in an environment. We begin with very simple characterizations of the environment, the organism, and their interaction. Our goal is to find an abstraction of the animal's behavioral function so that we can analyze it.

We start with an emphasis on modeling the environment, and assume that the organism is an extremely simple one. The resulting complexity in behaviour is therefore from the environment – see H. A. Simon, *The Sciences of the Artificial*, for a discussion of this.

2.1 Introduction

The purpose of vision is clearly to enable organisms to interact more effectively with their environment. This is reflected in the “principle of structure into function,” and suggests that one source of insight into understanding complex behaviour is understanding which aspects of the environment are most important to the organism, and why. Three basic types of behavioural interaction derive from:

1. finding food (prey);
2. avoiding becoming food (fleeing/avoiding predators and other dangers);

2.2. SINGLE-CELL ORGANISMS: “COMPLEXITY IN THE ENVIRONMENT”

3. reproduction.

In general, we have the following constraints:

- C1. The physical environment must be capable of conveying relevant “signals” [or physical encodings of information].
- C2. The organism must be capable of perceiving (i.e., receiving and analyzing these signals).
- C3. the organism must be capable of reacting differentially on the outcome of the analysis.

This is the *perception—action cycle* that couples the organism to its environment.

But all of this is very vague; how might it be developed into the context of a specific creature? To build intuition about this, we begin our computational analysis of vision from a very primitive structure modeled on the tropic behaviours illustrated by simple, single-celled organisms. Our goal is not to be biologically exact but rather to show how an simplified abstraction can be used to understand a class of behaviours and what they imply about an organism. Philosophically the cartoon creatures we shall develop are in the spirit of Braitenberg’s *vehicles*¹. They are introduced in a series of vignettes. Remember, the purpose here is to illustrate the style of analysis, and to develop a basic common background. The cost is biological accuracy.

2.2 Single-Celled Organisms “Find Food.”

We begin with a very simple model system that couples sensory data with behaviour. There are a number of single-cell organisms that suffice to illustrate the above constraints, so we build an artificial one that is a combination of them. It is based on several real organisms, but we have two in mind. We only discussed the second one in class.

The first creature, *Euglena*, exhibits phototropic behaviour or the tendency to move toward a light source. This is necessary because *Euglena* is a complex that contains chloroplasts so it achieves photosynthesis. (It can also consume food, but we shall ignore that aspect of its biology.) Movement is provided by a single flagellum, which “pulls” it along. The flagellum is part of a paraflagellar body that also contains the “eyespot” which contains a rhodopsin-like photopigment² (We shall consider such primitive light-sensitive organs in the next lecture.) The flagellum is helical, and a corkscrew motion accounts for the propulsion. Although the mechanism behind

¹V. Braitenberg, MIT Press

²James T.W., Crescitelli F., Loew E.R., McFarland W.N. The eyespot of *Euglena gracilis*: A microspectrophotometric study (1992) Vision Research, 32 (9), pp. 1583-1591.

the movement is still not completely understood,³ it is clear that it moves toward certain intensities. This phototactic movement is by flexing the flagellum, and consists either of moving forward or rotating sideways. Since *Euglena* rotates as it swims, the eyespot is alternately oriented toward or away from the source. While this provides a sequence of signals about the intensity of light, in general *Euglena* tends to move toward brighter places so photosynthesis improves. For our current purposes, such phototropic behaviour can thus be seen as “seeking food.”

Bacteria, such as *E. Coli*, also seek food from their environment, and the manner in which they do this will inspire the second (artificial) organism for this lecture. In particular, their behaviour consists of periods of movement in a straight direction, during which a collection of several flagella rotate together in a screw-type motion to propel the animal forward, but punctuated by occasional periods in which the flagella whip chaotically in the other direction causing *E. Coli* to rotate. The phases of this two-stage motion are described as RUN AND TUMBLE; (a tumble used to be called a ‘twiddle’). For a beautiful mathematical description, see⁴ It seems a reasonable hypothesis that this behaviour is part of how the animal searches for food, as it was for *Euglena*, so the chloroplasts are properly illuminated.

The basics of run-and-tumble are shown in Fig. 2.1

Examining a variety of such trajectories, while each differs in detail we notice an overall organizational tendency: the bacteria seem to be going somewhere. Let’s take a more detailed look at how they ‘work’.

2.2.1 Run and Tumble in *Artificial coli*

For this lecture we will cartoon the above biological organisms with an artificial one that we’ll call *Artificial coli* or *A. coli* to concentrate on certain of its properties. From a computer science perspective, one can think of *A. coli* as a random agent with two states:

$$\text{STATES} = \{\text{RUN}, \text{TUMBLE}\}.$$

The animal switches between these states in a stochastic manner. Since the signal driving *A. coli* through its environment is the attraction of food, this should affect the switching probabilities. We endow *A. coli* with a sensor capable of “measuring” the number of food particles per unit volume of fluid (at a particular time and location) and seek a simple computation that will keep its nutrient requirements satisfied.

Perhaps the simplest such computation is to compute the difference between the concentration at its current location and the concentration at its previous location. If this difference is positive, then it would seem to be moving toward the source of food and life would seem to be going well for the creature; if this difference is negative

³Rhodopsin: A photopigment for phototaxis in *Euglena gracilis* Walne, P.L., Passarelli, V., Barsanti, L., Gualtieri, P. 1998, *Critical Reviews in Plant Sciences* 17 (5), pp. 559-574

⁴Flagellar Hydrodynamics: The John von Neumann Lecture, 1975 James Lighthill, *SIAM Review*, Vol. 18, No. 2. (Apr., 1976), pp. 161-230.

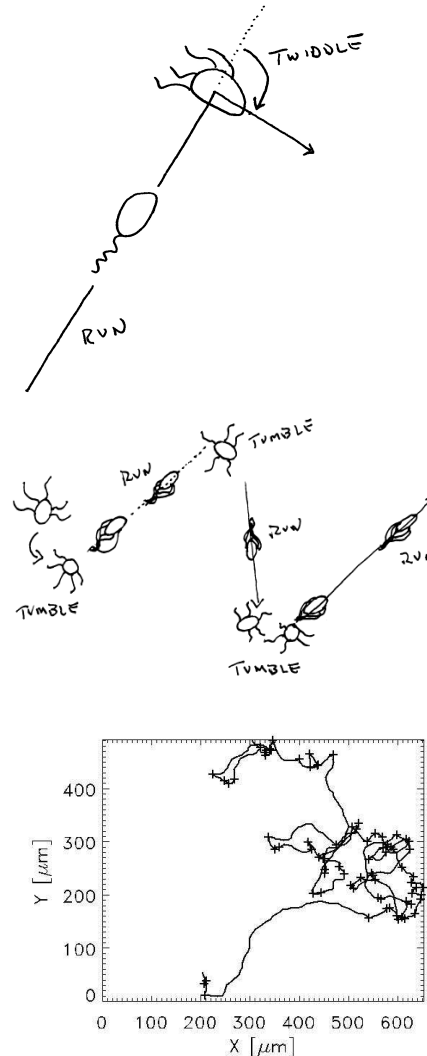


Figure 2.1: Illustration of the run and tumble. (TOP) The basics of run (move along a direction) and tumble (rotate by a random amount. (MIDDLE) In *E. coli* this is accomplished by a number of flagella which organize into a screw-type “motor” for the run portion and disentangle randomly to effect the tumble. For the latter reason a tumble is a rotation to the right by an angle that is in part random and in part dependent on a number of parameters such as the food gradient. (BOTTOM) Illustration of the path followed by a wild type *E. coli* (strain aw405) searching for food in a 2D uniform (no attractant) medium. The X’s indicate tumbles. Shown are about 100 frames each 3 second long. This long exposure time means that the cell will move (speed 13 micrometer/sec) on average 40 micrometer per frame (20 times their size).

Statistics: Tumble Freq = 0.300450 (sec^{-1}).

(i.e. it seems to be going away from the peak), then it would seem that it could be moving away from the food and its direction should change.

Suppose *A. coli* is pointing in DIRECTION; (this is an internal variable that has been set). The motile behavior of *A. coli* then alternates between the two STATES:

- RUN: advance 2 units in DIRECTION.
- TUMBLE: rotate (update) DIRECTION by an chosen angle chosen randomly and uniformly between 20 and 90 degrees. This models the fact that *E. coli* can only rotate clockwise.

The switch between STATES happens according to the following probabilities:

$$\begin{aligned}\text{RUN-to-TUMBLE} &= 0.1 \\ \text{TUMBLE-to-RUN} &= 0.3\end{aligned}$$

For *E. coli*, the length of a run is in proportion to nutrient and is limited by rotational diffusion (think of pushing a cigar through fluid). Following this loosely, when *A. coli* measures a positive difference, indicating that the concentration of food is increasing, the tumble should be less so the animal stays on about the same path. (Note: it doesn't really know the correct direction in which to go, only that it's projection on the current direction is reasonable.) In this case we simply divide the angle range for TUMBLE in half. When the concentration decreases, the tumble angle is chosen as above, uniformly between 20 and 90 degrees.

Will this stochastic behaviour actually work for *A. coli*? If so, why? We now start to build different abstractions of it, to answer those questions. Implicitly we shall have to consider:

- Should we focus on an individual organism or a group of organisms?
- Should we focus on the “jerky” paths implied by run-and-tumble, or should we consider some approximation to it? If the latter, which approximation?
- What is special about the environment?
- What are the consequences of taking discrete samples, rather than sampling the environment continuously? (We won't get to this question for a few lectures.)

2.3 Analysis of *A. coli*

We'll look at three different ways of approaching *A. coli*: statistical, geometrical, and via calculus.

2.3.1 Histograms over position

The natural place to start is in the lab, where we run zillions of experiments with *A. coli*. (Suppose, for now, that you don't actually know the internal dynamics of *A. coli*.) This results in zillions of different trajectories. The first thing to do is to summarize the data statistically, an approach that is reinforced by the fact that the agent appears (is) random.

How might we summarize the experimental data? HISTOGRAMS, made by breaking up the domain into little "boxes" and counting the fraction of time that an *A. coli* spends in it (normalized so the percent adds to 1!) (see Fig. 2.2) provides a first-order statistic that contains lobes and peaks. These indicate that the different organisms *tend* to move in a common direction. See Fig. 2.3.

2.3.2 Vector Geometry of Paths

Now, let's zoom in on the details of a path for an individual animal and ask how this might be described. Since it moves in a direction, of course vectors are used. Let the animal swim in a rectangular domain spanned by (x,y) coordinates (Fig. 2.4) and let's describe the positions of *A. coli* as functions of time:

$$\vec{P}(t) = \begin{pmatrix} x(t) \\ y(t) \end{pmatrix} \quad (2.1)$$

and

$$\vec{P}(t + \Delta t) = \begin{pmatrix} x(t + \Delta t) \\ y(t + \Delta t) \end{pmatrix}. \quad (2.2)$$

In VECTOR notation, think of the point P as the position of the *A. coli*; i.e., as the "head" of a vector whose "tail" is at the origin.

Vectors are mathematical objects in their own right, and enjoy a number of basic properties. Each one can be expressed in terms of COORDINATES, which indicates how far one extends in a given direction. The vector $P(t)$ extends $x(t)$ units in the x -direction and $y(t)$ units in the y -direction at time instant t . $x(t)|_{t=t_0}$, read the x -position coordinate evaluated at time $t = t_0$, emphasizes that the position coordinate is a number. Defining a unit coordinate FRAME by a unit step in the x -direction as \hat{i} and a unit step in the y -direction as \hat{j} , we can express one vector in terms of others:

$$\vec{P}(t) = x(t)\hat{i} + y(t)\hat{j}$$

where the process of VECTOR ADDITION is introduced. (It's convenient to think of these unit coordinates as being ORTHONORMAL.

Think of the coordinate functions, $x(t)$ and $y(t)$ as numerically-valued: For a fixed value of t they are just numbers, or SCALARS, that signify the length of the PROJECTION of a vector onto one of the coordinate axes. For a unit-length vector

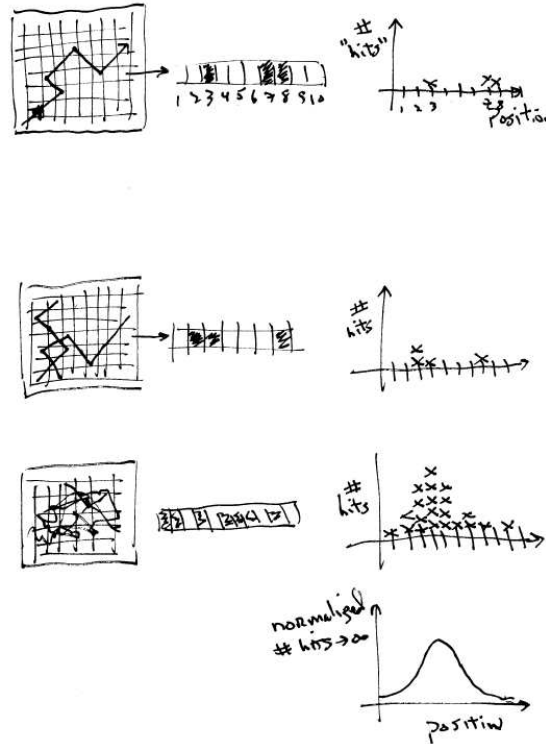


Figure 2.2: Building up a statistic to understand the pathways traveled by *A. coli*. (top) We begin by quantizing the domain over which it can swim into little boxes (left) and then focus on one row of boxes (middle). When a box is crossed, it is blackened, and a count of these crossing is begun (right). (middle) For several superimposed trajectories, some positions are crossed more than once. (bottom) For a large number of positions, the counts start to resemble a frequency distribution (number of times a position might be visited by many animals). Finally if the number of animals gets large, and the counts are normalized, a function approximating the probability that an animal will encounter a position is obtained.

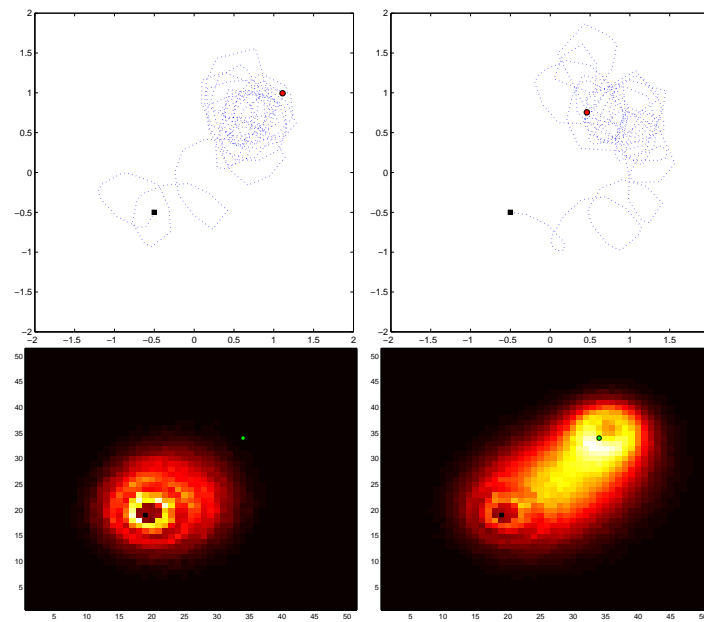


Figure 2.3: Run and tumble for an artificial creature *A. coli*. In each case an *A. coli* starts at a point toward the lower left and proceeds toward a food source. Can you guess where the food source is from these examples? (TOP) Two trajectories followed by *A. coli* (different realizations of the random number generator). (BOTTOM) Summary statistics for 10,000 runs of length 15 steps (LEFT) and 75 steps (RIGHT). To compute this statistic, the domain was partitioned into small regions (30 x 30), and every time the creature passed through the region a counter was incremented. Normalized counts were then mapped into the color scale. Thus color indicates an empirical approximation to the probability that *A. coli* entered a given region.

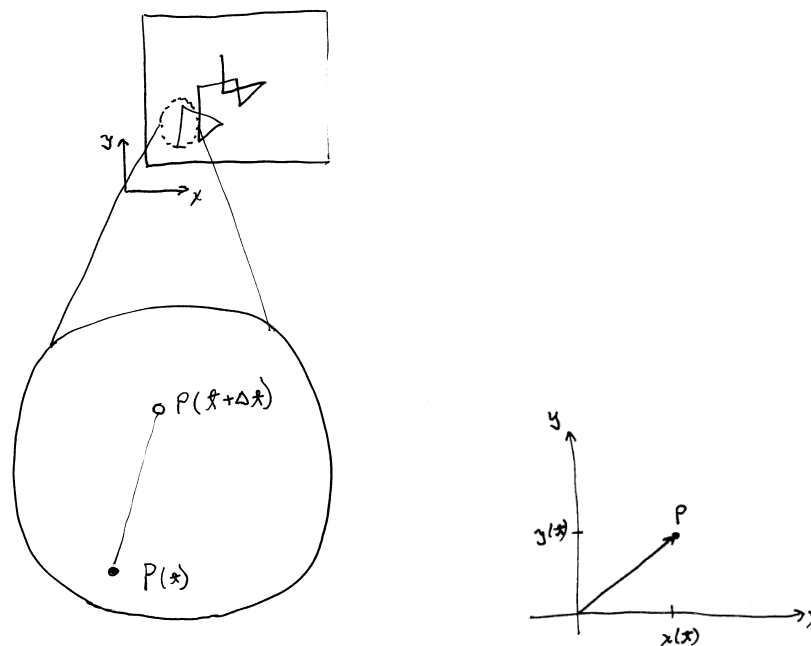


Figure 2.4: Analysis of *A. coli*'s trajectory. (left) Zoom onto a portion of the run and tumble path illustrating two points along this path in time. (right) Establishing coordinates for the position P of *A. Coli* at some instant of time. Notice that these coordinates will change as the animal swims; thus the coordinates should be thought of as functions of time. The position vector, as well, is a function of time. (Think of it's "head" moving around in time, always pointing to the position of the animal.

$\|\vec{P}\| = 1$, where the bars designate LENGTH defined as:

$$\|\vec{P}(t)\| = \sqrt{x^2(t) + y^2(t)}$$

. It follows that the x -coordinate lies in the range $[0, 1]$, where the square brackets indicate that 0 and 1 are included in the interval:

$$0 \leq x \leq 1.$$

Thinking discretely, the position after two time steps can be modeled as a sum of vectors. Let $\vec{P}(t_i)$ designate the position of *A. coli* at the i -th time instant, and $\Delta\vec{P}(t_i, t_j)$ denote the change in position from t_i to t_j . Here are some: Questions to review:

- What does $\vec{P}(t_3) = \vec{P}(t_1) - \vec{P}(t_2)$ represent?
- What does $\vec{P}(t_3) = \vec{P}(t_1) + \vec{P}(t_2)$ represent?
- Express *A. coli*'s current position in terms of previous positions. Should one use $\vec{P}(t_i)$, $\vec{P}(t_j)$, $\Delta\vec{P}(t_i, t_j)$, or some combination of them? Why?
- Pythagoras' Theorem. If we think about how far the animal has moved from the origin, then we obtain an inequality which states that the length from the origin is bounded by the lengths of the previous steps. How would you express this?

2.3.3 Sampling Changes in the Nutrient Distribution

Now, suppose that *A. coli* has receptors on its cell membrane that are selective for particles of food and that it can take such a measurement at discrete points along its trajectory (for example, just before a tumble). This gives us a discrete set of samples of food (or, more accurately, the number of food particles detected). We'll be working toward denser and denser samplings. How should we think about these discrete samples?

Now, the position of the animal follows a trajectory given by the run-and-tumble mechanism through its environment. (The environment is two-dimensional; position along the trajectory is one-dimensional.) We plot the value of the food sampled along this 1-D section of the trajectory, but wonder what the actual food distribution is. That is, given a sequence of discrete samples of the concentration of food particles, we might ask what distribution they come from, so that, if the sampling were twice as dense, or along a different trajectory, we could have those samples as well. (In a few weeks we'll return to this question of sampling distributions with some care.)

One might be tempted to think food follows a crazy distribution because of turbulence and the mixing properties of the environment, and there's some truth to this.

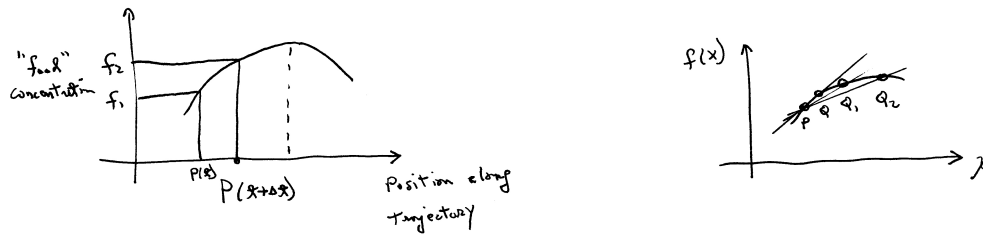


Figure 2.5: (LEFT) The distribution of food particles per unit volume along the trajectory. At position $P(t)$ the concentration is f_1 . Although unrealistic, the food distribution is shown as a very nice, smooth function. This is an idealization that lets us think about some continuous methods for understanding how it is changing. From the perspective of *A. coli*, we can think of the probability that a particle of food is detected (i.e., binds with a receptor is monotonic) with the density of food. The peak on the curve can be viewed as the location of the food source. It begins to suggest that the behaviour of *A. coli* could be related to finding this peak. (RIGHT) The notion of tangent and derivative as a limiting process.

But for now let's pretend it's from a well-behaved distribution; see Fig. 2.5. Formally this means that we switch perspectives and assume the food distribution is a SMOOTH FUNCTION, so that we can review ideas from calculus.

Immediately we think of evaluating the change in food concentration with respect to nearby positions, and this in turn suggests two possibilities: (i) that the concentration is increasing (good news) or (ii) the concentration is decreasing (bad news). Normally the animal would prefer (i), which suggests seeking a maximum. (It's also possible for the concentration not to change – what would this imply that the animal should do?)

At the least, this (very artificial) assumption provides an opportunity for review. The difference between nearby values along a function approximates one of the fundamental constructs of the differential calculus: the DERIVATIVE⁵. To review: consider a smooth function (see Fig. 2.5, right.):

$$y = f(x)$$

that maps points x (in the DOMAIN SET $x \in X$) into points $y \in Y$, the RANGE. Now, consider a point of the function denoted by $P = (x, y)$, and two other points in its neighborhood, denoted $Q_1 = (x_1, y_1)$ and $Q_2 = (x_2, y_2)$. When Q_1 and Q_2 are near P , the straight line connecting them approximates the slope of $f(x)$ at P ; that is,

⁵Please consult your favorite calculus text, to remind yourself of these basic ideas. I used: Thomas, G. B., Calculus and Analytic Geometry, Addison-Wesley, Reading, MA, 1962.

for a small change in x , denoted $\Delta x = x_2 - x_1$ there is a comparable change in y , $\Delta y = y_2 - y_1$ such that

$$\text{slope of } PQ = \frac{y_2 - y_1}{x_2 - x_1} = \frac{\Delta y}{\Delta x}.$$

Now, in this example with P fixed, move the point Q along $f(x)$. Observe that the slope of the line PQ will most likely change its angle, and in the limit as Q approaches P that slope will approach a constant or limiting value: the TANGENT to f at x_1 .

To repeat the above procedure at an arbitrary point, hold P constant and write $Q = (x + \Delta x, y + \Delta y)$ from which we obtain

$$\Delta y = f(x + \Delta x) - f(x).$$

Now, letting Q approach P along the curve becomes analogous to taking the limit $\Delta x \rightarrow 0$, yielding the derivative $f'(x)$ of the function $f(x)$:

$$f'(x) = \lim_{\Delta x \rightarrow 0} \frac{\Delta y}{\Delta x} = \lim_{\Delta x \rightarrow 0} \frac{[f(x) + \Delta x] - f(x)}{\Delta x}.$$

The abstract notion of a derivative takes on a nice physical intuition when the function denotes position (s) as a function of time ($s = f(t)$). Then a body at position $s = f(t)$ at time t undergoes a displacement Δs in time Δt , and the velocity

$$v(t) = \lim_{\Delta t \rightarrow 0} \frac{\Delta s}{\Delta t} = f'(s).$$

Questions:

- Is this a definition of the derivative? (Think about connectedness and continuity)
- Does it always make sense? (Is the function shown in the figure truly general)
- Does it always exist? (Think about snowflakes and fractals and curves with jumps. How might these be relevant to the study of vision?)

Remember: The limiting process simply cannot be done by *plugging-in*, or $\frac{0}{0}$ arises.

Time is a special variable because it always moves forward. The notion of limit requires that it makes sense no matter how the increment is taken. The limit must be the same as we approach from the right as from the left. See Fig. 2.6.

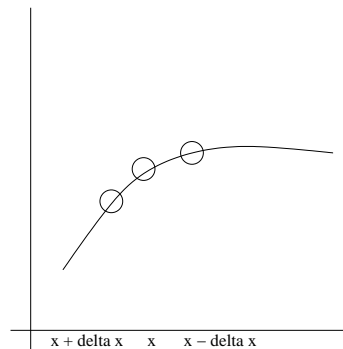


Figure 2.6: To define the limiting operation, we must be able to approach the point from *all* directions. In 1-D this simply means from the right and from the left. Clearly, the domain must be connected and the function smooth. For an interesting example, think of a sheet of white paper on a dark table. Now how does the brightness vary along a path from the table onto the paper? Is this smooth? Piecewise smooth?

2.3.4 Errors Bound the Limit Operation

The derivative is defined as the limit of the ratio of two small quantities, rather than the ratio of the limits of the numerator and denominator. In addition, actually carrying out a limiting process is a mathematical idealization; it is not a process that can be accomplished by physical measurements. We interpret the limit:

$$f'(x) = \lim_{h \rightarrow 0} \frac{f(x+h) - f(x)}{h} \quad (2.3)$$

in terms of the expression:

$$f(x+h) - f(x) = hf'(x) + \epsilon h \quad (2.4)$$

where ϵ is a quantity that approaches 0 with the increment $h = \Delta x$ approaching 0. Thus we can think of ϵh as a kind of “error term”, and we must physically/numerically choose the step Δx so that it is sufficiently small. This will turn out to be a very tricky process in vision, and much care will be required to do it appropriately. See Fig. 2.7.

2.3.5 Aside: what is a limit?

The notion of a LIMIT lies at the very foundation of mathematical analysis. Since some students might not have seen this, I include an aside on how mathematicians think about it; discussion from R. Courant’s classic text on calculus⁶. Compare this

⁶R. Courant, Differential and Integral Calculus, vol. I, Wiley-Interscience.

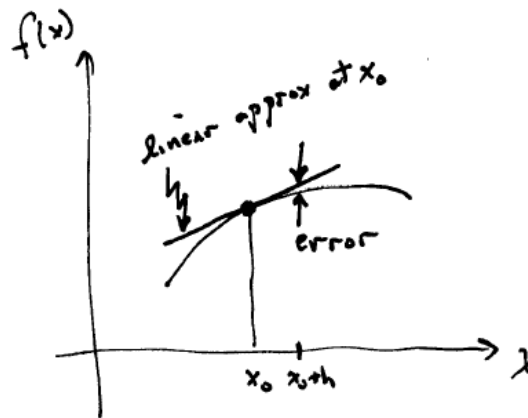


Figure 2.7: The derivative as a linear approximation. Consider a function $y = f(x)$ and take its derivative at the point x_0 ; in the neighborhood of x_0 the function is approximated by a line through the point $(x_0, f(x_0))$ whose slope is given by the value of the derivative at that point. However, as we move along $f(x)$ a distance h the function deviates from it's linear approximation by an error that is expected to grow with h .

to the limiting questions that A. coli might have to consider: when should it stop for food?

To illustrate the notion of limit, consider the sequence:

$$\alpha_1 = 1, \alpha_2 = \frac{1}{2}, \alpha_3 = \frac{1}{3}, \dots$$

with general member $\alpha_n = \frac{1}{n}$. Intuitively, as n gets larger and larger, the ratio $\frac{1}{n}$ gets closer and closer to 0. We thus say that the sequence CONVERGES to 0, or that in the LIMIT as $n \rightarrow \infty$ the numbers α_n tend to 0.

It is important to note, however, that for no number in this sequence is the limit of 0 actually attained; rather, if we were to define an interval around 0 then, from some number α_N onward, each successive number would remain in the interval. Mathematically, let us denote the limit point of the sequence by Ω , and the “size” of this interval by ϵ . Then, no matter how small we choose ϵ , there will be an integer $N = N(\epsilon)$ such that $|\alpha_n - \Omega| < \epsilon$ for $n > N(\epsilon)$; i.e., for each element in the sequence after N .

For this example, we would write $\lim_{n \rightarrow \infty} \alpha_n = 0$. Of course, not every sequence converges to a limit; one test (Cauchy's convergence test) can be defined as follows: A sequence is intrinsically convergent if there exists a number $N = N(\epsilon)$ for every (arbitrary small) positive number ϵ for which the difference between any two members in the sequence after N , $|\alpha_n - \alpha_m| < \epsilon, n, m \geq N(\epsilon)$. All intrinsically convergent

sequences possess a limit.

2.3.6 Partial and Directional Derivatives

The food distribution function along the path that we have been considering will vary for different paths because it is really a two-dimensional distribution. For visualization purposes you can think of this distribution as a surface. This makes life a little more complicated; Fig. 2.8. Of course, the existence of such surfaces requires a generalization of the conditions we discussed in 1D for the derivative. But for now just imagine that it has no kinks, or jumps, or discontinuities, or holes.

To be concrete, we previously drew the graph of the function $y = f(x)$ by plotting the points $(x, f(x))$; now we draw the graph of the surface as $(x, y, f(x, y))$.

In which direction should we move?

One natural choice is to take x and y , the coordinates with which we're already familiar, as special coordinates, and to consider what it would mean to take a derivative in those directions; this is the PARTIAL DERIVATIVE. To develop it, suppose we have a surface as above but now take a step parallel to the x -direction; what happens to the value of the function? Looking "straight up", imagine that your gaze cuts the surface with a knife. The locus of this cut traces out a curve along the surface as you take the step. Starting from the origin, movement along x gives a function of a single variable $f(x, 0)$ and, for movement along y , we obtain another function of a single variable $f(0, y)$; see Fig. 2.8, bottom. Mathematically, we're building up a more complicated object in terms of simpler ones (that we already 'understand.')

Operationally, then, to take a PARTIAL DERIVATIVE in the x -direction we treat that as one variable and the other as constant. Importantly, *the partial derivative can be taken in any direction u in the circle surrounding the point P* , provided P is not on the boundary. This DIRECTIONAL DERIVATIVE can be sensed by a family of *A. coli*, all starting from the point P and moving in random directions. Of course we shall require a large enough number of them to cover, in some sense, all of the relevant directions.

2.3.7 Gradients and Vector Fields

Given the two directional derivatives above, it's tempting to try to combine them, and their linear sum is an extremely important object; this is the generalization of the derivative of a function of one variable to a function of several variables.

It helps to build conceptually upon what we already have. For derivatives of functions of one variable, the tangent line is the best linear approximation to the function in the neighborhood of a point; as we move away, the error grows between the function and this linear approximation (Fig. 2.7). In two dimensions the story is basically the same; see Fig. 2.9.

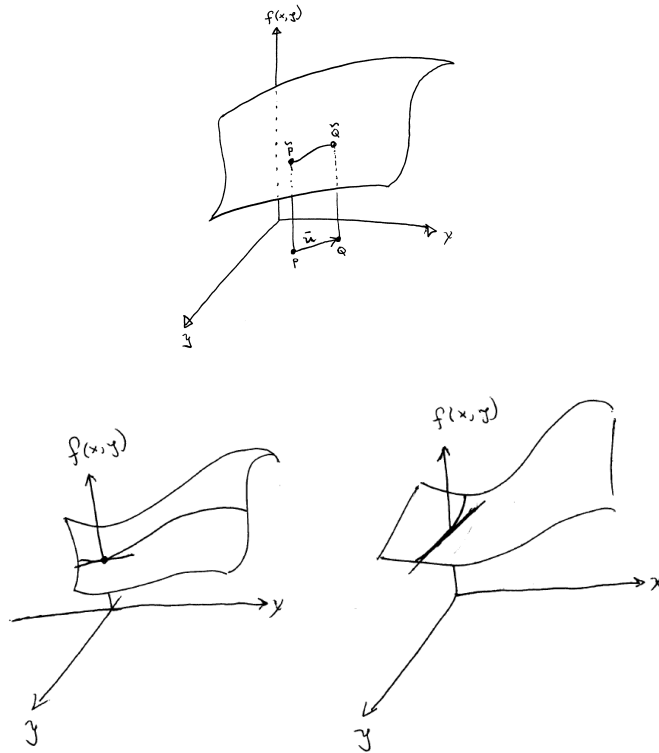


Figure 2.8: The “food function” $f(x, y)$ can be pictured as a surface over the domain through which *A. coli* can swim. The graph of this surface is given by $(x, y, f(x, y))$. To build up the notion of the directional derivative for a function of two variables, start at a point P ; in which direction should the increment be taken? Note that it is possible to take a unit step \vec{u} in a circle of directions in the (x, y) domain, each of which will, in general, offer a new derivative. Thus the derivative depends on the direction. In the bottom figures we show the two canonical directions. Movement along x yields a curve on the surface, $f(x, 0)$ and movement along y yields a different curve, $f(0, y)$. Evaluating the derivative of these curves at the origin yields the tangent lines shown.

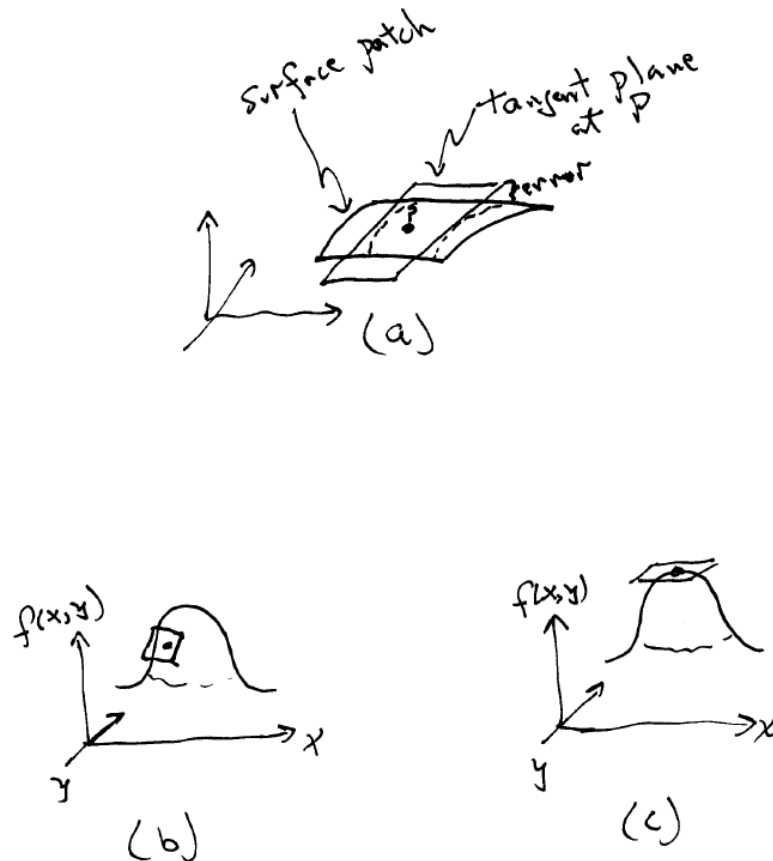


Figure 2.9: The derivative as a linear approximation in two dimensions. Consider a function $z = f(x, y)$ and take its derivative at the point $P = (x_0, y_0)$; in the neighborhood of P the function is approximated by a plane – the TANGENT PLANE – through the point P that best approximates $f(x, y)$ near P . (a) The tangent plane to the surface is shown, with the error increasing as we move away from P . Because it’s a 2-D function, this error grows as we move along the x-axis and along the y-axis. (b) The tangent plane varies from point to point along the surface. It exists when the partial derivatives exist, and is “flat” at the peak.

Now let's think about this linear approximation directly. Since the tangent plane is the best linear (in 2D, planar) approximation to the function near $P = (x, y)$, we can think of $f(x + h, y + k)$ as $f(x, y)$ plus the error term (which now is a function of both h and k). In fact, this error function adds a deviation of “a” units in the h direction and “b” units in the k direction. In symbols we denote this:

$$(h, k) \mapsto ah + bk \quad (2.5)$$

That is, near P we just have to add a linear function to $f(x, y)|_P$. This linear map can be represented by the numbers (a, b) and formally serves as a definition of the derivative.

Now, if we follow the convention from the beginning of this lecture and denote a unit step in the x -direction as \hat{i} and a unit step in the y -direction as \hat{j} , we can combine them to get the derivative in a certain direction. It is important to note that the partial's are like functions that multiply the unit vectors; these partials are the a and b .

The linear combination gives us:

$$\left(\frac{\partial f}{\partial x}\hat{i} + \frac{\partial f}{\partial y}\hat{j}\right) = \nabla f$$

This is the GRADIENT of f . It is a very special object, indicating important properties of the function $f(x, y)$ by its magnitude and its direction.

Writing this generalized case, as in Eq. 2.4 we have (using notation: $\vec{P} = (x, y)^T$; $\vec{h} = (h, k)^T$):

$$f(\vec{P} + \vec{h}) \approx f(\vec{P}) + \vec{h} \cdot \nabla f. \quad (2.6)$$

The gradient of a scalar function $f(x, y)$ is a vector pointing in the direction of the greatest rate of increase; it's magnitude is the rate of increase.

If we assign the above vector $\nabla f(x, y)$ at each position (x, y) in the domain through which *A. coli* could swim, it forms a VECTOR FIELD. Each such vector points in the direction an animal would be going, if it were to swim through that point and were perfect in following the gradient.

(A mental picture to keep in mind: Notice that the set of all possible vectors at a point gives all directions that different animals could swim in, provided they passed through the point. Notice further that this is like the set of all directions that we could take a directional derivative in. This mental picture will recur when we study the visual cortex of primates in an important way.)

Such vector fields can be thought of as a map: $\nabla f : \mathbb{R}^2 \rightarrow \text{vectors}$, that is, vectors with a direction and a magnitude.

Examples in Fig. 2.10

⁷The superscript T denotes the TRANSPOSE of a vector.

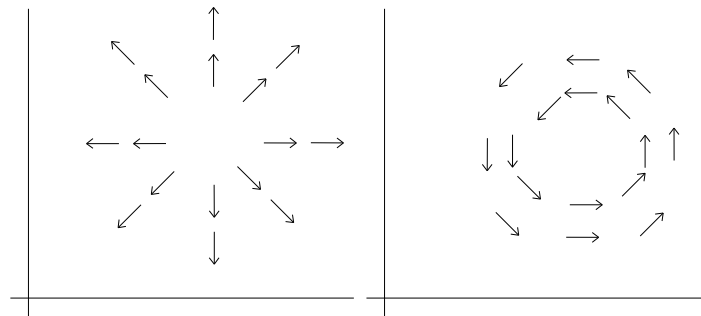


Figure 2.10: Examples of common vector fields (LEFT) $f(x, y) = x\hat{i}, y\hat{j}$; (RIGHT) $f(x, y) = \frac{-y\hat{i} + x\hat{j}}{\sqrt{x^2 + y^2}}$

Remark: Now consider different paths: Height $PQ \rightarrow P'Q'$. Path does not matter for this type of surface, which is important. Such surfaces are

- Smooth
- Continuous
- Connected

One of the most important mathematical points about the gradient is the way it connects to the earlier notion of directional derivative. Recalling equation 2.3, we start by putting vector-valued positions into it. Let $\vec{x} = (x, y)$ from our previous notation, and think of the directional derivative (in direction \vec{u}) as

$$D_{\vec{u}}f(\vec{x}) = \lim_{h \rightarrow 0} \frac{f(\vec{x} + h\vec{u}) - f(\vec{x})}{h} \quad (2.7)$$

provided it exists.

$D_{\vec{u}}$ = partial derivative in direction $\vec{u} = \vec{u} \cdot \nabla f$.

This gives us a nice way to define the directional derivative; it is, in effect, another of the key reasons why the gradient is so important; and why the gradient is, essentially, the generalization of the derivative to higher dimensions.

need to introduce dot products better

2.3.8 Level Sets

There are very different ways to represent the function $f(x, y)$; see Fig. 2.11. One way, which we have been following up to now in this lecture, is to think of $f(x, y)$ as the *height* of a surface (or mountain range) above the point (x, y) . This plots it as a graph of function. Another is to imagine slicing through this mountain range

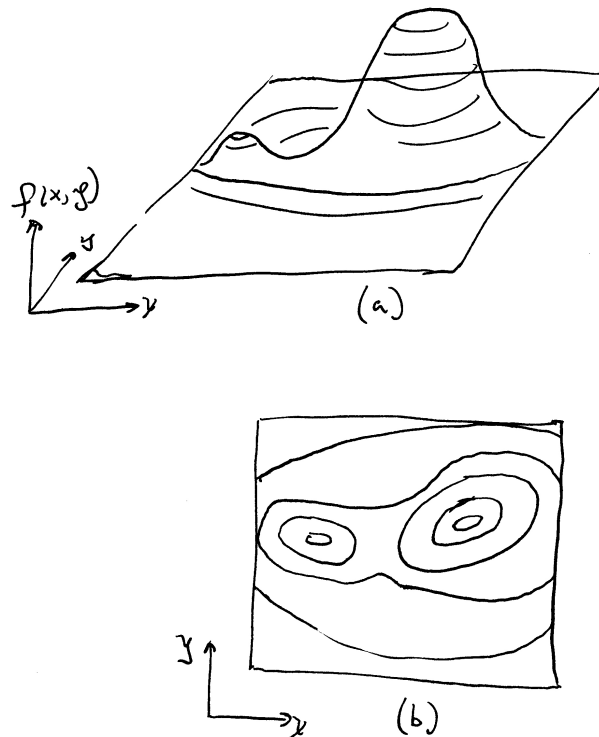


Figure 2.11: Two ways of representing the function $f(x, y)$ (a) height function. (b) level sets. Think of a hiker's topographic map to develop some intuition about level sets; or more generally, think about isothermal or atmospheric pressure maps. Note in particular how the level sets are nested inside of one another. What other properties do you think level sets might enjoy? How do they differ from the paths followed by *A. coli*?

with sharp planes held parallel to the (x, y) -plane but at different heights; the locus of positions at which each of these planes slices through the mountain range is a (collection of) curves, called *level sets*. Each level set is a collection of points at which $f(x, y) = c$; different values of the constant c yield different level sets.

(You probably saw level sets in topographic maps, or in isothermal plots. Later in the class they'll be important to us as level sets of image brightness, or isophotes.)

Certain properties of the gradient become more clear given this different way of thinking about surfaces, if we do a little work to adapt constructions that have been going through this lecture. In particular, the Cartesian coordinates (x, y) provided a natural way to locate and index different points on the plane. To specify the gradient we used a function defined over (x, y) .

Changing our focus of attention from the plane to one of these curves, however, suggests another way to think about coordinate systems. Now let’s zoom in to one of the level sets, and ask *in which direction does the gradient point?*

The answer is immediate if we adapt the notion of coordinate systems by attaching them directly to objects such as level set curves; see Fig. 2.12. Such coordinate systems are called *frames*. Remember that the tangent to a curve was in the direction of the derivative; well, let’s use this tangent direction as one of the frame coordinates. Given this tangent direction, it’s then natural to choose a perpendicular direction for the other frame coordinate; the normal direction. (I’m leaving out the issue of how to choose the sign here.)

Proving that the gradient points in the maximal up-hill direction by attaching such a local (tangent, normal) coordinate system, or *frame*, to the level set is easy. Suppose, in particular, that an arbitrary vector \vec{u} were pointing uphill. If we expand \vec{u} into the two frame components,

$$\vec{u} = \vec{u}_{\parallel} + \vec{u}_{\perp}$$

one denoting the component of \vec{u} parallel to the level set curve (that is, in the direction of the tangent) and the other in the direction perpendicular to the level set curve, then it is immediate that any motion along the level set (following the tangent to it, \vec{u}_{\parallel}) is wasted motion—there is no change in height. Thus to walk most rapidly uphill we require the magnitude of $\|\vec{u}_{\parallel}\| = 0$ or that the gradient is perpendicular to the level set contours.

2.4 Gradient Ascent in the “food function”

We now have the machinery necessary to return to our analysis of *A. coli*. Since it is a multi-dimensional problem, it is instructive to plot the gradient vector field for our food distribution – see Fig. 2.14.

The trick for *A. coli* is to sample the gradient direction, take a step in that direction, resample the gradient direction, take another step, and so on until the gradient is 0. (Remember, what defines the max of the food function.)

Schematic Algorithm: Gradient Ascent

- INITIATION: Start at point $P^0 = (x_0, y_0)^T$ in domain of f
- REPEAT: calculate gradient contribution at position $(x_n, y_n)^T$: $\Delta P := \nabla f(x, y)$
update position as function of gradient: $P^{n+1} = P^n + h\Delta P^n$
- STOPPING CONDITION Stop when $\|P^{n+1} - P^n\| \leq \epsilon \approx 0$.

In this algorithm, n is an iteration number, hence it represents “time” along the path that *A. coli* swims. ϵ is a threshold for termination, because we have to

2.5. A MORE ADVANCED VIEW:

PATHS AS CURVES THROUGH A VECTOR FIELD IN THE ENVIRONMENT

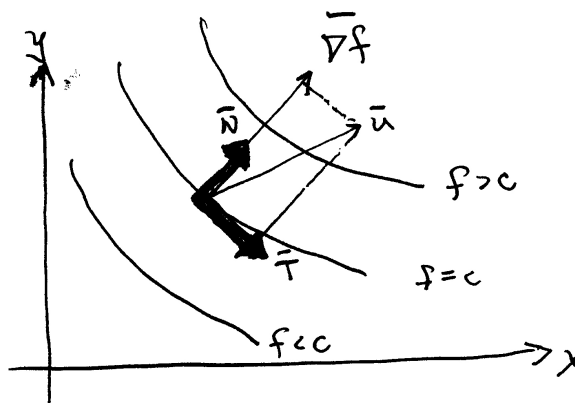


Figure 2.12: Proving that the gradient points in the maximal up-hill direction is facilitated by attaching a local (tangent, normal) coordinate system, or *frame*, to the level set. See text.

specify what “0” means for this animal. h is the step size, relating to the run length. An important point for theoretical computer science is that the gradient trajectory remains in the domain of the food function.

For *A. coli* the gradient is not available exactly, so the function F involves both an approximation of the exact gradient and a randomization of the step.

What is *A. coli*’s use of the stopping criterion?

Does *A. coli* need the random component in F ? Why?

Do the exact parameters matter for *A. coli*? See Fig. 2.15.

2.5 A more advanced view:

Paths as Curves through a Vector Field

A VECTOR FIELD is an attachment of vectors to every point in a plane or manifold.

It is smooth if the vectors vary smoothly with the point of attachment.

Since *A. coli* is wandering through its domain, if we “smooth” the trajectory to imagine that it no longer has the discontinuities at the tumbles, then we can think of the velocity along its path.

Note: if the path is a curve, the instantaneous velocity points in a direction tangent

2.5. A MORE ADVANCED VIEW:
 CHAPTER 2. *A. COLI*: COMPLEXITY IN THE ENVIRONMENT

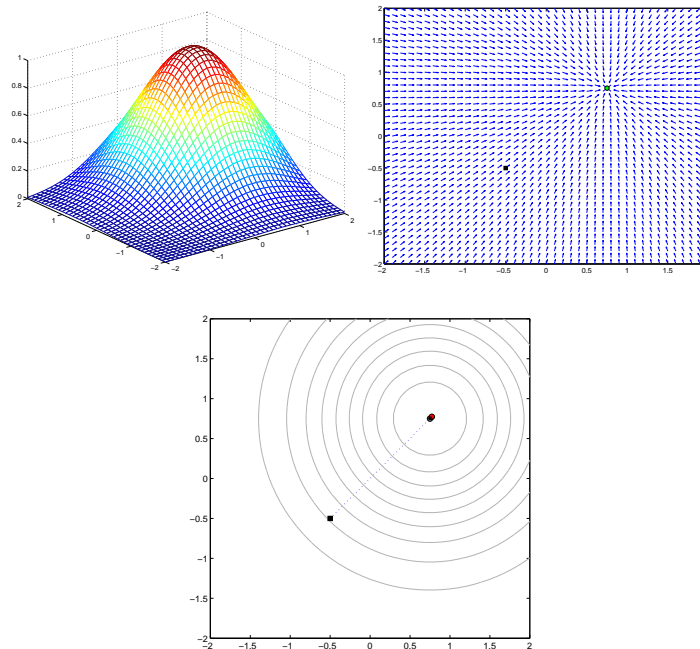


Figure 2.13: The computer scientist’s version of how to search for food: just march directly “uphill” in the gradient direction. (TOP, LEFT) Food “potential” function plotted as height against position. (TOP, RIGHT) Unit gradient vector field for the food potential. (BOTTOM) Path of gradient ascent.

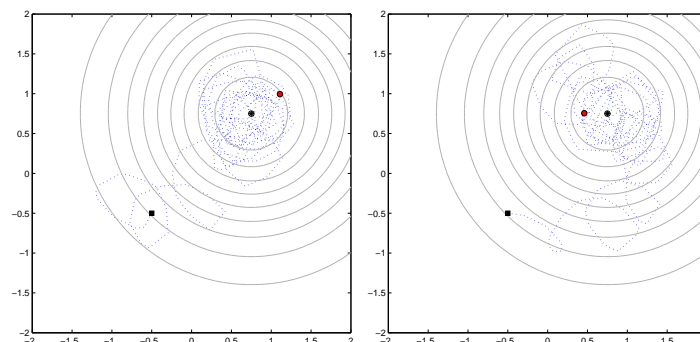


Figure 2.14: Run and tumble for our *A. coli* plotted against the level sets of the food distribution. Notice now how they “tend” to move uphill.

2.5. A MORE ADVANCED VIEW: PATHS AS CURVES THROUGH COMPLEXITY IN THE ENVIRONMENT

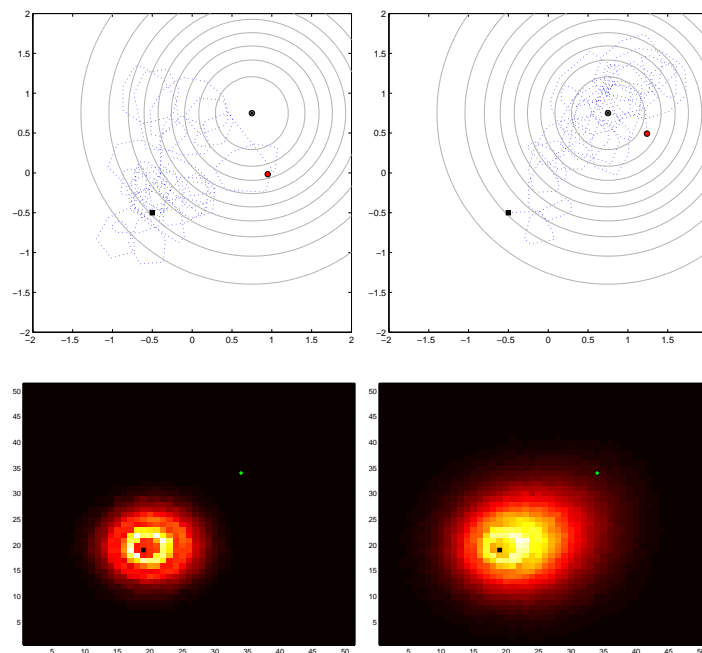


Figure 2.15: Run and tumble for a modified *A. coli*; in this case when positive gradient is detected, the animal restricts the tumble angle only by about 20% rather than in half. (TOP) Two runs (BOTTOM) Histograms for runs of 15 and 75 steps. How does this compare with the original *A. coli*?

to this curve (the magnitude of the velocity is *A. coli*'s speed.)

Something special happens when this tangent vector (along the path) is parallel to the gradient vector of the food distribution function at every point along the path. This agreement is very special indeed. We have an *integral trajectory* $\gamma(t)$ of a vector field $a(x)$ if and only if the velocity vector

$$\frac{d\gamma(t)}{dt} = a(\gamma(t)).$$

Note that a really interesting equation has emerged here, with a derivative on one side; such equations are called differential equations. As with our discussion of the calculus, one should think of the derivative on the left side as indicating the (infinitesimal) change in position over an (infinitesimal) time dt . Eventually we shall worry about solving such equations. Nevertheless, since we seek the curve γ , it should come as no surprise that an integral is involved. Hence the name. In short,

integral trajectories of a vector field are solutions of a system of differential equations.

$$\dot{x}(t) = a(x(t))$$

If this is smooth, there always exists a solution for sufficiently small t . This is a basic theorem from ordinary differential equations. See Fig. 2.16.

Notice that, in this smooth case, it's as if *A. coli* is making an infinite series of infinitesimal decisions about which way to go by reading out the gradient of the food. Perception will involve fewer, and bigger, decisions.

2.6 Why Abstraction?

Different notions of abstraction can be important for different purposes. A rather different model from the picture suggested at the beginning of this lecture (fig. 2.2 arises when we consider the 'gradient view' rather than the 'position view.' This new viewpoint will be extremely important for understanding vision. To introduce it, see Fig. 2.17

More generally, *E. coli* is a rather complicated organism. Here we illustrate how much we left out and why finding principles that unify function across different organisms is so important to basic science.

2.6.1 *A. coli* as a model of *E. coli*

The question with which we opened this lecture—how does *E. coli* find food?—now can be answered, but only in a certain sense. Rather than studying the biologically-real animal, we developed a model for it, which we called *A. coli*. This model abstracted certain of its properties, such as run-and-tumble movements, but largely



Figure 2.16: Gradient ascent is guided by a vector field. (a) A sketch of the gradient vector field for the food function in Fig. /reffig:level-sets. Notice how it “points” to the two peaks. (What happens to the gradient field in the “valley” between the peaks?) (b) Zooming in on a region near the major peak, we show the path that would be followed by a gradient ascent algorithm starting at position 1 and ending at position 2. Notice how the infinitesimal “step” at each time instant is in the direction of the gradient attached to that position.

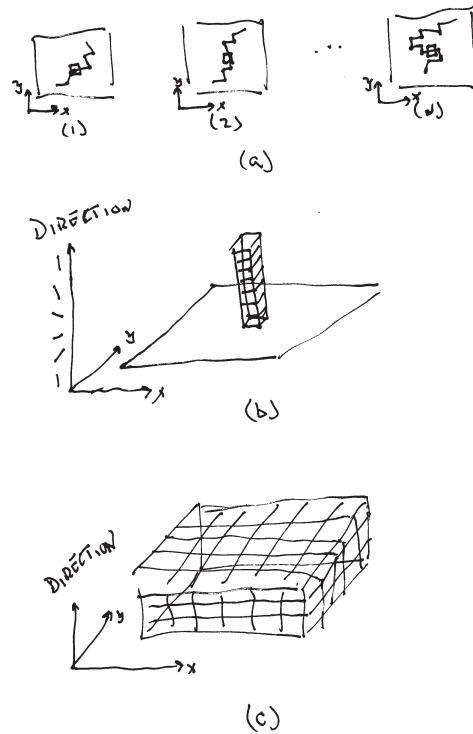


Figure 2.17: A rich representation of all possible paths for *A. coli* through its square domain. (a) N different *A. coli* follow different paths through the domain, even though all are basically “flowing” from the bottom left to the upper right. Focusing on the tiny ‘square pixel’ at the center of the domain, note that its direction may span the full circle of possibilities. (b) Isolating this pixel, we can think of the different (quantized) directions arranged as a ‘column’ above it. This creates a new, third dimension that is very abstract from the two spatial directions in which we often think. (c) For a zillion *A. coli* swimming through the domain, one might pass through any position at any direction. This fills in the ‘cube’ of possibilities in the $(x, y, \text{direction})$ representation.

2.6. WHY ABSTRACTION? *A. COLI*: COMPLEXITY IN THE ENVIRONMENT

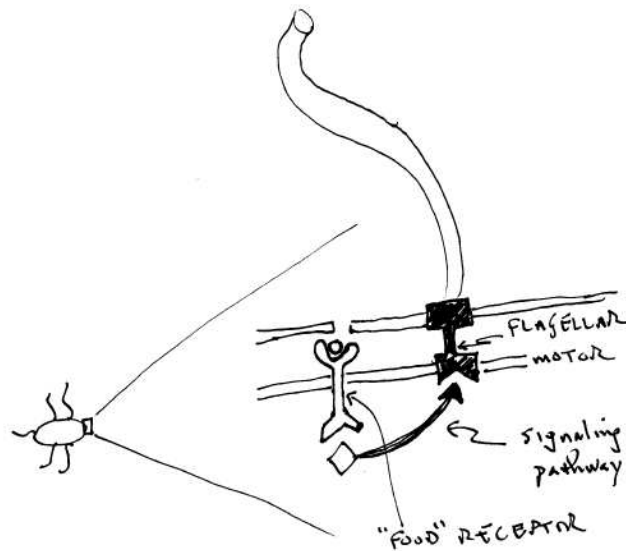


Figure 2.18: The membrane surrounding *E. coli* consists of several structures, including a molecular motor that drives each of the flagella and receptors sensitive to molecules in the environment. When appropriate ligands (think food particles from this lecture) bind to the receptor, a chemical signalling pathway is activated that causes the motor to spin in the correct way; when not activated, motor spins oppositely.

ignored others; e.g., how food is sensed and how these sensations are translated into movements. The model was useful in that its analysis revealed a similarly abstract characterization of behaviour: gradient ascent in the field of food particles. Such fields are very special because, at least in the idealistic sense, any tiny (infinitesimal) movement of *A. coli* corresponded exactly to the gradient of the food field at that point. Moreover, the idealistic case is efficient: by marching up the gradient exactly no effort is wasted. The trajectory followed by *A. coli* goes directly toward the source. Even with the random perturbations, when it got close to the source it remained there. On average, this sequence of steps diminished the distance between *A. coli* and the source uniformly; ideally every step brought it closer.

The control mechanism of *E. coli* is illustrated in Fig. 2.18. Here there is a

2.6.2 Pirouette movement in *C. elegans*

The second major role in abstraction is to find common principles by which very different organisms function. *C. elegans* is the nematode worm with a nervous system

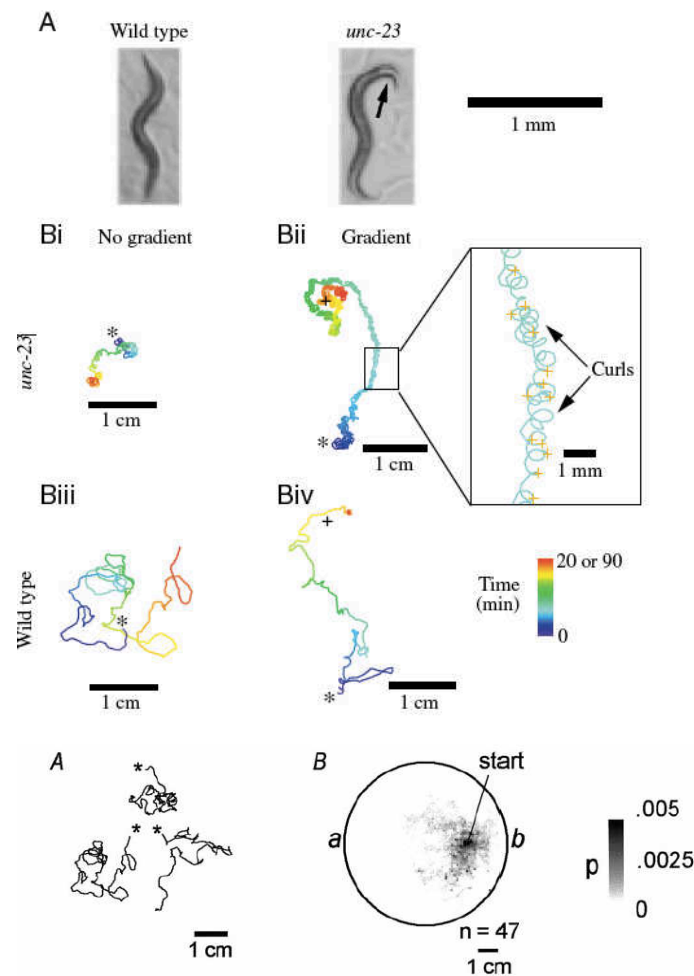


Figure 2.19: Illustration of pirouette movement in *C. elegans* Figs. from Pierce-Shimomura et al, 2005, 1999

consisting of

quote from Chemosensation in *C. elegans**, Cornelia I. Bargmann, www.wormbook.org/chapters/

“Direct observation reveals that during chemotaxis, *C. elegans* responds not to the absolute level of attractant, but to the change in attractant concentration over time (Pierce-Shimomura et al., 1999). When an animal travels up a gradient of attractant, it moves in long forward bouts with rare changes of direction called pirouettes. When an animal travels down a gradient of attractant, it pirouettes frequently. By changing the rate of pirouettes, the animal makes long movements in the right direction, and short movements in the wrong direction. Over time it accumulates at the peak of the gradient. As is true in bacteria, the direction of the turn during

chemotaxis is random, indicating that *C. elegans* does not sense a spatial gradient over its body to decide which way to turn (Pierce-Shimomura et al., 2005).

This temporal chemotaxis strategy requires animals to compare current levels of attractant to recent levels. To ask whether *C. elegans* can perform such a comparison, animals were subjected to rapid uniform changes in their chemical environment. When animals were moved from high to low attractant levels, they responded with a bout of pirouettes; when animals were moved from low to high attractant levels, pirouettes were suppressed (Dusenbery, 1980b; Miller et al., 2005). The rate of pirouettes then returned to baseline through rapid adaptation, updating the short-term memory to match the new attractant conditions. The molecular basis of temporal sensing and rapid adaptation in ASE is unknown.

The neurons downstream of ASE in chemotaxis are not well understood. The AIY interneurons are prominent targets of ASE; they suppress pirouettes, but genetic results indicate that they are not required for chemotaxis to ASE-sensed chemicals (Tsalik and Hobert, 2003). ASE has additional targets including AIA and AIB interneurons that may also regulate pirouette frequency.

The biased random walk is not the optimal strategy for chemotaxis in a perfect linear gradient, but it is well-suited to following attractants in noisy, turbulent natural conditions. Its strength as a behavioral strategy is that it emphasizes empirical progress - an increase in attractant concentrations. It is remarkable that unicellular bacterial flagellar motors and multicellular *C. elegans* nervous systems use such a similar strategy for chemotaxis.

2.7 Summary

The natural world is, of course, never perfect. There might be local maxima in the food field due to turbulence or source mixing, and measurements of concentration and their translation into *runs* are subject to error. But this suggests a purpose for the randomized component of the movement: it helps the animal to get over the local bumps to find the true source, if one exists. The perception—action cycle, for *A. coli* can be summarized as gradient ascent in the food field.

2.8 Notes

For the review of calculus, read e.g. Thomas, **Calculus and Analytic Geometry**, or whatever textbook you used earlier.

Two additional references that are very clear from a physics perspective:

- Schey, H. M., **div, grad, curl and all that**, Norton, 1997.
- Feynman, R. P., Leighton, R. B., and Sands, M., **The Feynman Lectures on Physics**, vol II, Addison-Wesley, Reading, MA, 1965.

Read the books by Howard C. Berg to learn about E. coli: (i) **Random Walks in Biology**; and (ii) **E. coli in Motion**. They're both gems.