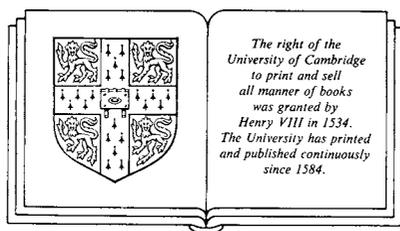


Modeling dynamic phenomena in molecular and cellular biology

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1

Optimal strategies for the metabolism of storage materials

This chapter demonstrates that elementary calculus can be used to illuminate some aspects of the general question of how organisms should employ storage materials, given that they have evolved to be “optimum” in some sense. The material presented here is a slight generalization and expansion of ideas discussed by Cohen and Parnas (1976).

Biological background

Storage materials enable organisms to survive and prosper when there is a temporary shortage of energy. We shall consider only microorganisms in our discussion. For these, a commonly held view is the “excess theory,” according to which microorganisms synthesize storage materials if and only if the supply of external nutrient exceeds the supply necessary for maximal current growth. The approach to be taken here is different and is based on the following hypothesis.

Assumption 1. Storage materials are synthesized in such a manner as to maximize the long-term growth rate.

We shall study photosynthetic algae under circumstances in which a day of uniform light intensity and fixed length is followed by a night with no light. The algae can utilize the light and available nutrients to synthesize proteins required for growth and reproduction. During the day they can also synthesize energy-rich storage materials. These can be used to furnish some or all of the energy that must be supplied at night, when there is no energy flow from the environment and no synthesis – but when energy is required for maintenance and possible cell division. The starchy storage materials supply energy efficiently, but their presence has a cost in diminishing protein production. The sort of question that we shall address here is How much storage material should be synthesized by optimally behaving algae under various possible circumstances? The reader might pause now to try to answer this question, to see whether or

not unaided intuition can arrive at the same conclusions that will be generated by our theoretical arguments.

There is evidence that photosynthesis is depressed during the time in which cells divide. We shall assume that the depression is sufficiently large that division during the night will maximize the expected number of daughter cells.

Assumption 2. Cell division takes place only at night.

At any time t we shall regard a cell as being composed of just two types of materials: biosynthetic materials, denoted by $P(t)$, and storage materials, denoted by $S(t)$. The synthetic materials are largely proteins. In the present context we thus regard “protein” and “synthetic material” as synonymous.

Consider the algae that are contained in some experimental setup, or in some defined natural region. At the beginning of the day, $t=0$, let P_0 and S_0 denote the amounts of protein and storage material that are associated with these algae.¹ [Thus, $P(0) = P_0, S(0) = S_0$.]

Assumption 3. All cellular materials are synthesized at a constant *photosynthesis rate* R per unit amount of synthetic material.

At a given moment, both protein and storage material are synthesized at rates that are proportional to the amount of synthetic material (i.e., protein) that is present. Consequently, as we shall see in detail later, the amount of protein increases exponentially throughout the time it is being synthesized. Suppose that the cell’s “best strategy” requires it to synthesize a certain amount of storage material. The amount of protein at the end of the day will be largest, as required by Assumption 1, if the least possible time is devoted to synthesis of the required storage material. This is accomplished by postponing the period of storage synthesis to the end of the day, when the amount of synthetic machinery is maximal.

The postponement of storage synthesis is really a conclusion of our analysis. We have derived it intuitively, but a rigorous derivation could be given with the aid of optimal control theory.

Conclusion 1. Storage material is synthesized at the end of the day.

¹ A list of symbols and their definitions is provided in the supplement to this chapter. For later chapters, and in general when reading theoretical material, it is recommended that the reader compile such a list.

Calculation of P and S at the end of the day

Given that its synthesis occurs at the end of the day, the amount of storage material is completely determined by the number of hours devoted to its production. Call this number τ (tau). *The purpose of our model is to calculate the optimal value of τ .* The first step is to find mathematical expressions for the amounts of P and S at the end of the day, for any given value of τ .

Let the length of the day be T hours (so that, of course, the length of the night is $24 - T$ hours). Because τ hours at the end of the day are devoted to the synthesis of storage material S , protein P will reach its maximum after $T - \tau$ hours and will remain the same for the rest of the day:

$$P(T) = P(T - \tau).$$

By Assumption 3, if the day is T hours long, it then follows that

$$S(T) = R\tau P(T). \quad (1)$$

[For full accuracy, the initial amount of storage material S_0 should be added to the right side of equation (1), but the relative contribution of this term is negligible.]

We here introduce an abbreviation that we shall employ frequently:

$$\sigma \equiv S(T)/P(T), \quad 0 < \sigma < \infty. \quad (2)$$

The importance of σ (sigma) is evident even at this early stage; it is the ratio of storage material to synthetic material that the cells produce. In economic terms it is the ratio of “capital” (invested for future needs) to production equipment. In terms of (2), equation (1) becomes

$$\tau = \sigma/R. \quad (3)$$

Because R is fixed, instead of calculating the optimal value of τ we can calculate the optimal value of σ - and, indeed, this latter calculation is slightly more convenient.

Assumption 3, that synthesis takes place at a constant rate R , implies that at any time t , $0 < t \leq T - \tau$,

$$dP(t)/dt = RP(t).$$

From the fact that P_0 is the amount of P present at the beginning of the day, it follows (Exercise A1.7) that

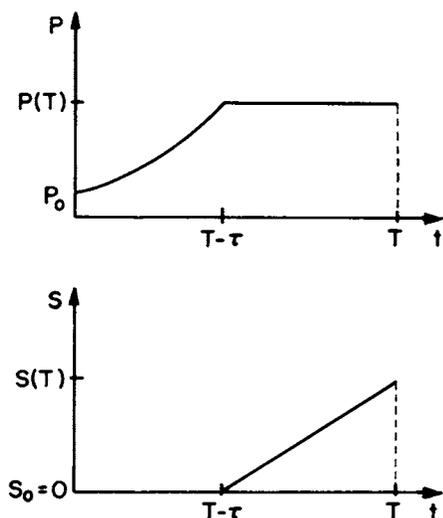


Figure 1.1. Graphs illustrating the result that exponential accumulation of synthetic material P for $T - \tau$ hours is succeeded by uniform synthesis of storage material S for τ hours. (T is the length of the day.)

$$P(t) = P_0 \exp(Rt). \quad (4a)$$

Given that τ is the time allotted for the synthesis of storage material and T is the length of the day, P will be synthesized for $T - \tau$ hours, after which the amount of P will remain constant for the rest of the day. Thus, as we have seen, $P(T) = P(T - \tau)$. Consequently from (4a),

$$P(T) = P_0 \exp[R(T - \tau)]. \quad (4b)$$

See Figure 1.1 for a graphical view of the accumulation of protein and storage material.

We note for later use that the number of new daughter cells N can be calculated from the formula

$$N = [P(T) - P_0] / W, \quad (5)$$

where W is the average weight of a daughter cell.

Calculating the net "profit" from a given amount of storage material

We are examining how storage material enables organisms to operate successfully in the presence of an energy shortage - at night in the present

instance. Storage material is a rich source of the required energy, but it is accumulated at the price of forgoing protein synthesis. We must now calculate precisely the net advantage that flows from the possession of a given amount of storage material – in the two cases in which this amount does or does not furnish the total nocturnal energy requirements.

Assumption 4. During the night, cells need E_M units of maintenance energy per unit weight of synthetic material per hour. Also, the formation of each daughter requires an amount of energy E_d . Thus, a total amount of energy E is required each night, where

$$E = E_M(24 - T)P(T) + E_d N. \quad (6)$$

There are two possibilities:

Case I: Stored energy is less than E .

Case II: Stored energy is greater than E .

In Case II, the cell will convert the excess stored energy into synthetic material. In Case I, synthetic material must be broken down to provide the required energy. We symbolize the various “costs” by

$$P \xrightarrow{k_P} \text{energy}, \quad S \xrightarrow{k_S} \text{energy}, \quad S \xrightarrow{\beta} P. \quad (7)$$

That is, there are k_P (respectively, k_S) energy units per unit amount of P (respectively, S), and conversion of a unit of storage material yields β units of synthetic material.

In the two cases, I and II, we shall now form the expressions for the *gain* in nocturnal cell production due to the presence of storage material (which is an efficient source of required energy) and the *loss* due to the fact that synthesis of protein during the day had to be forsaken because of the production of storage material. We shall then seek a policy that will maximize the “profit,” the gain minus the loss.

Note from (5) that only protein contributes to the formation of new organisms. Thus, we shall measure the *loss* in cell production by the total amount of protein L that was not synthesized during the *day*, because part of the day was devoted to storage synthesis. The *gain* is the total amount of protein G that did not have to be broken down during the *night*, because part of the energy requirements could be met by storage. Gain and loss are each figured out for a given policy. For each policy, one subtracts what did happen from the extreme case in which there is no synthesis whatever of storage material. In the computation of loss, for example, the relevant extreme case is that in which protein

is synthesized all day. From this, the protein actually synthesized is subtracted.

Case I occurs when

$$k_S S(T) < E. \quad (8)$$

In this case the energy available from the stored material is not sufficient, so that an extra amount of energy must be supplied by breakdown of P . If x denotes the amount of protein that must be broken down, then

$$k_P x = E - k_S S(T), \quad \text{i.e., } x = [E - k_S S(T)] / k_P. \quad (9a,b)$$

If there were no storage material, all the necessary energy would have to be extracted from P . The amount of P required would be E/k_P . Subtracting from this the protein that is actually required in Case I, we have a gain G due to the presence of the storage material, given by

$$G = S(T)/\alpha, \quad \text{where } \alpha \equiv k_P/k_S. \quad (10a,b)$$

Case II occurs when $k_S S(T) > E$. Here, instead of having to break down protein to supply the nocturnal energy requirements, there is an excess of stored energy that can be converted into additional protein. Consequently, as the reader is asked to verify,²

$$G = \frac{E}{k_P} + \beta \frac{k_S S(T) - E}{k_S}. \quad (11)$$

In both Case I and Case II the loss L is the same: the amount of P that would have been synthesized if the whole day of length T had been utilized, minus the actual amount synthesized in $T - \tau$ hours. Thus, from (4a),

$$L = P_0 \exp(RT) - P_0 \exp[R(T - \tau)]. \quad (12)$$

Combining (10), (11), and (12), we can calculate the profit $\pi = G - L$, where by profit we mean the increase in synthetic material brought about by the storage policy. After a little rearrangement, we obtain (Exercise 1) the following formulas:²

$$\blacklozenge \text{ I: } \pi = P_0 \exp(RT) \left[\left(1 + \frac{\sigma}{\alpha} \right) e^{-\sigma} - 1 \right] \quad \text{when } k_S S(T) < E. \quad (13a)$$

$$\begin{aligned} \blacklozenge \text{ II: } \pi = P_0 \exp(RT) [(1 + \beta\sigma)e^{-\sigma} - 1] \\ + E \left(\frac{1}{k_P} - \frac{\beta}{k_S} \right) \quad \text{when } k_S S(T) > E. \end{aligned} \quad (13b)$$

² On first reading, (11) and (13) should be accepted. Verification should be attempted later, as explained in the Preface.

The final mathematical problem: maximize profit

By Assumption 1, we wish to maximize π . More precisely, because the possible storage “strategy” of the cells is expressed in their choice of σ , we wish to *select the synthetic/storage ratio σ that will maximize $\pi(\sigma)$* . The italicized phrase constitutes the mathematical problem to which we have been led by our model building.

A simplified model

We shall now make an assumption that will make the problem considerably simpler. To this end, note from (13) that Case II occurs if and only if $k_S S(T) > E$. Because σ is the variable with which we are concerned, it is natural to use (2) and to write the condition for Case II in the form

$$k_S \sigma > E/P(T). \quad (14)$$

But this key condition for distinguishing Cases I and II is not a simple one, because $E/P(T)$ depends on σ . To see this, first observe that (6) and (5) imply³

$$\frac{E}{P(T)} = E_M(24 - T) + \frac{E_d N}{P(T)} = E_M(24 - T) + \frac{E_d}{W} \left(1 - \frac{P_0}{P(T)}\right). \quad (15)$$

By (4) and (3), the right side of (15) depends on σ [through $P(T)$]. Consequently, (14), together with (15), presents a somewhat complicated inequality to be solved for σ .

We can circumvent the difficult nature of (14) by limiting our considerations to situations in which there is so much protein production (because of intense light) that

$$P_0 \ll P(T). \quad (16)$$

Now the “nonconstant” term $P_0/P(T)$ in (15) can be neglected.

To take advantage of our finding that $E/P(T)$ can be regarded as a constant if (16) holds, we reformulate our problem with the aid of the definition

$$\bar{\sigma} \equiv E/[k_S P(T)]. \quad (17)$$

We now see from (14) that Case II holds when $\sigma > \bar{\sigma}$. From (15) and (16) it follows that

³ Formula (15) can at first be accepted without checking, but a reader with pencil in hand (see Preface) should experience no difficulty in rapidly verifying it.

$$\bar{\sigma} \approx E_M(24 - T)/k_S + (E_d/Wk_S) = \text{constant.} \quad (18)$$

Using (17) to replace E , we find that expression (13b) for the profit in Case II becomes

$$\pi = P_0 \exp(RT) \left\{ e^{-\sigma} \left[\bar{\sigma} \left(\frac{1}{\alpha} - \beta \right) + \beta\sigma + 1 \right] - 1 \right\}. \quad (19)$$

Now our mathematical problem is to maximize the function $\pi(\sigma)$ given by (13a) when $\sigma < \bar{\sigma}$ and by (19) when $\sigma > \bar{\sigma}$, where $\bar{\sigma}$ is a constant.

Solution of the simplified mathematical problem

Let us begin with Case II, where $\sigma > \bar{\sigma}$. From (19) we can easily verify (Exercise 1) that

$$\partial\pi/\partial\sigma = P_0 \exp(RT - \sigma) [\beta - \beta\sigma - \bar{\sigma}(\alpha^{-1} - \beta) - 1]. \quad (20)$$

We have a zero derivative, the classic necessary condition for a maximum, if

$$\beta\sigma = \beta - \bar{\sigma} \left(\frac{1}{\alpha} - \beta \right) - 1, \quad \text{i.e., if } \sigma = \bar{\sigma} - \frac{\bar{\sigma}}{\alpha\beta} - \frac{1}{\beta} + 1. \quad (21a,b)$$

But $\sigma > \bar{\sigma}$ in the region under consideration, so that σ is certainly greater than the right side of (21b) – for we expect that

$$\beta < 1, \quad \text{so that } \frac{1}{\beta} > 1, \quad -\frac{1}{\beta} + 1 < 0. \quad (22a,b,c)$$

[Equation (22a) records the biological assumption that something is lost in converting storage material to protein; see the definition of β in (7).] We thus see that the derivative in (20) is always negative, and the largest value of $\pi(\sigma)$ in Case II occurs on the boundary of the region, where $\sigma = \bar{\sigma}$. Let us now check Case I. Here we find, from (13a) [Exercise 1], that

$$\partial\pi/\partial\sigma = P_0 \exp(RT - \sigma) (1 - \sigma - \alpha)/\alpha. \quad (23)$$

The derivative vanishes when

$$\sigma = 1 - \alpha. \quad (24)$$

Note that the right side of (24) will be positive, because $\alpha \equiv k_p/k_S$ is certainly expected (Exercise 2) to satisfy

$$\alpha < 1. \quad (25)$$

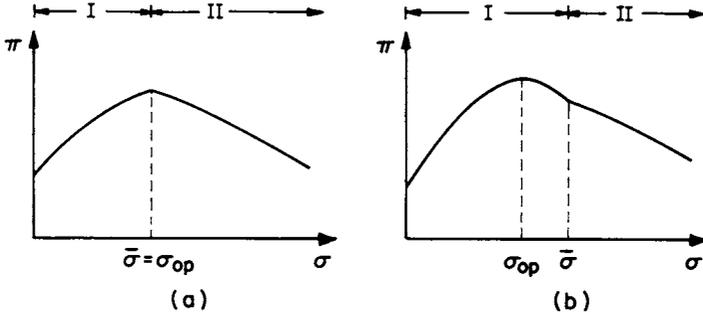


Figure 1.2. Schematic shape of the profit function (in the simplified problem) when (a) $1 - \alpha > \bar{\sigma}$, (b) $1 - \alpha < \bar{\sigma}$. Note that in case (a) the derivative does not vanish at the maximum; the derivative at $\bar{\sigma}$ does not exist.

The point $\sigma = 1 - \alpha$ is within the region $\sigma < \bar{\sigma}$ if and only if

$$1 - \alpha < \bar{\sigma}. \tag{26}$$

If (26) does not hold, the derivative when $\sigma < \bar{\sigma}$ is positive, and the maximum value of π within this region occurs when $\sigma = \bar{\sigma}$. See Figure 1.2.

Let σ_{op} be the optimal value of the ratio $\sigma = S(T)/P(T)$, that is, the value that gives a maximum profit $\pi(\sigma)$. Summarizing the results of our calculations we obtain the following.

Conclusion 2

◆◆ $\sigma_{op} = 1 - \alpha \quad \text{if } 1 - \alpha \leq \bar{\sigma}, \tag{27a}$

◆◆ $\sigma_{op} = \bar{\sigma} \quad \text{if } 1 - \alpha \geq \bar{\sigma}. \tag{27b}$

In practice, typical values of the parameters are $0.1 \leq \bar{\sigma} \leq 0.25$ and $\alpha = 0.4$ (Parnas and Cohen, 1976, p. 36). Thus, (27b) holds, and we predict that *storage materials are generally produced during the day in the exact amount needed at night.*

Conclusions from the mathematical results

We shall be content to draw only one further conclusion from the present results. This requires studying the effect of the rate of photosynthesis R on the optimal time interval τ_{op} during which storage material is synthesized. Assuming that the algae have evolved to operate under optimal conditions, we note that (27a) and the relation $\tau_{op} = \sigma_{op}/R$ of (3) yield

$$\partial \tau_{op} / \partial R = -(1 - \alpha) / R^2 < 0. \tag{28}$$

If (27b) holds, then, similarly,

$$\partial\tau_{\text{op}}/\partial R = -\bar{\sigma}/R^2 < 0. \quad (29)$$

Conclusion 3. The optimal length of time for the synthesis of storage material decreases when photosynthesis increases.

Conclusion 3 is particularly interesting, for it is opposite to what is expected from the excess theory. In fact, Assumption 1 and Conclusion 1 have been verified for a number of microorganisms. Conclusion 3 has been verified by Cohen and Parnas (1976) for *Chlamydomonas reinhardtii*.

The full problem

We have proceeded under the assumption that the last term in (15) can be neglected. When light intensities are strong, as many as eight daughter algae appear during the night from the division of a single large cell; in this case the simplification is justified. On the other hand, when light intensities are weak, we can still proceed – without simplifying – by employing a little more sophisticated mathematics.

We recall that, in general, $\bar{\sigma}$ is not constant (i.e., $\bar{\sigma}$ depends on σ); this is the root of our difficulty. To proceed, it is convenient to define the constants ψ (psi) and ϕ (phi) by

$$\psi \equiv \frac{E_M(24-T)}{k_S} + \frac{E_d}{k_S W}, \quad \phi \equiv \frac{E_d}{k_S W} \exp(-RT). \quad (30a,b)$$

With these constants, the exact expression for $\bar{\sigma}$ is

$$\bar{\sigma}(\sigma) = \psi - \phi e^{\sigma}, \quad (31)$$

combining (17), (15), and (4b). Consequently,

$$\sigma > \bar{\sigma} \quad \text{if and only if} \quad \sigma > \psi - \phi e^{\sigma}. \quad (32a,b)$$

For (32b) to hold, the graph of $y = \sigma$ must lie above the graph of $y = \psi - \phi e^{\sigma}$. These graphs are depicted in Figure 1.3. It follows from the figure that

$$\sigma > \bar{\sigma} \quad \text{if and only if} \quad \sigma > \sigma^*. \quad (33)$$

Here σ^* is a constant, defined by the intersection of the two graphs:

$$\sigma^* = \psi - \phi \exp(\sigma^*). \quad (34)$$

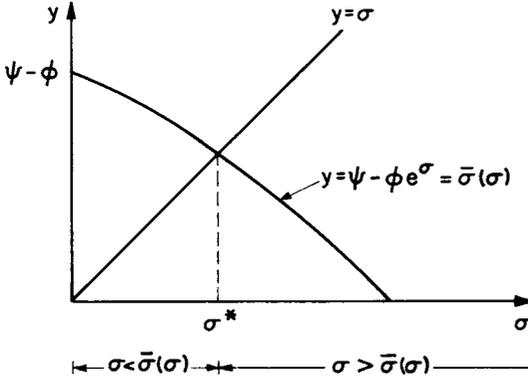


Figure 1.3. Graph for determining when σ is less than or greater than $\bar{\sigma}(\sigma) \equiv \psi - \phi e^\sigma$.

Our problem is now seen to require the maximization of a function $\pi(\sigma)$ given by (13a) when $\sigma < \sigma^*$ and by (19) when $\sigma > \sigma^*$.

Let us first consider Case II, when $\sigma > \sigma^*$. Noting from (31) that

$$\frac{\partial \bar{\sigma}}{\partial \sigma} = -\phi e^\sigma, \tag{35}$$

we differentiate (19) to find (Exercise 3) that for Case II,

$$\frac{\partial \pi}{\partial \sigma} = P_0 \exp(RT - \sigma) \left[-(1 - \beta) - \beta\sigma - \left(\frac{1}{\alpha} - \beta \right) (\bar{\sigma} + \phi e^\sigma) \right]. \tag{36}$$

The positivity of $\bar{\sigma} + \phi \exp(\sigma)$ follows from (31). Consideration of (22a) and (25) thus shows that $\partial \pi / \partial \sigma$ remains negative when $\sigma > \bar{\sigma}$ even when the simplifying assumption (16) is not made.

Because $\bar{\sigma}$ does not appear in (13a), $\partial \pi / \partial \sigma$ is computed in region I as before. We conclude that if simplification (16) is not made, Conclusion 2 [equation (27)] must be modified to

$$\blacklozenge \quad \sigma_{\text{op}} = 1 - \alpha \quad \text{if } 1 - \alpha \leq \sigma^*, \tag{37a}$$

$$\blacklozenge \quad \sigma_{\text{op}} = \sigma^* \quad \text{if } 1 - \alpha \geq \sigma^*. \tag{37b}$$

We have no explicit expression for the constant σ^* . But from (34), by implicit differentiation (Exercise 3), we can find the useful formula

$$\frac{\partial \sigma^*}{\partial R} = \frac{T\phi}{\phi + e^{-\sigma^*}}. \tag{38}$$

Equation (38) shows that when $1 - \alpha \geq \sigma^*$, σ_{op} is an increasing function

of the photosynthesis rate R . Equation (38) is also necessary in recalculating (29), for when $1 - \alpha \geq \sigma^*$,

$$\tau_{\text{op}} \equiv \frac{\sigma^*}{R}, \quad \frac{\partial \tau_{\text{op}}}{\partial R} = \frac{R(\partial \sigma^*/\partial R) - \sigma^*}{R^2}. \quad (39a,b)$$

It might be argued that it is “obvious” that the optimal length of time τ_{op} during which storage material should be photosynthesized must decrease as the intensity of sunlight increases (Conclusion 3). But in (39b) our more general model shows that the sign of $\partial \tau_{\text{op}}/\partial R$ can, in principle, be either positive or negative – so that the behavior of τ_{op} could be counter-intuitive. In fact, on substituting typical numerical values, it can be shown that $\partial \tau/\partial R$ retains the negative sign found in (29).

Final remarks

This chapter can be regarded as giving one example of an optimization approach that has been used in many biological contexts. Another example is provided by optimum foraging studies that proceed under the hypothesis that animals adopt feeding strategies that maximize the rate of net energy gain. See Hainsworth and Wolf (1979) for a review and Townsend and Calow (1981) for a recent example of several texts concerned with the adaptive significance of physiological characteristics.

A particularly extensive and interesting treatment of optimization arguments in biology can be found in the Oster and Wilson (1978) study of social insects. Of special value is the critique of optimization theory found in the last chapter. For example, these authors point out that optimization arguments, as in the present case, leave open the question of how the optimum strategy is implemented. (This is not a fatal flaw, because successful theories may well raise more interesting questions than they answer.) They remark that careful examination of a biological situation often reveals several conflicting goals, so that the question may not be one of optimization, but rather how “conflicting interests . . . can be resolved in a stable fashion.” They stress the crucial difference between engineers who use optimization theory to arrive at a most efficient design and theoretical biologists who use the theory “to infer ‘nature’s design’ already created by natural selection.” It might also be added that engineers can, in principle, build structures in an entirely novel fashion, whereas organisms can improve themselves only relatively gradually, by tinkering with their existing structure. In addition, some traits may not be adaptive at all, as evolution lags a changing environment or promotes some traits as side effects of others (Maynard Smith, 1978).

In short, optimization theory has already provided many biological insights, but, perhaps even more than other theoretical frameworks, it must be employed with taste and restraint.

Exercises

1. Verify equations (11), (13), (20), and (23).
2. Why is (25) expected on biological grounds?
3. Verify equations (36) and (38).
4. How would the various formulas and conclusions be changed if Assumption 3 were modified to take into account different constant rates of synthesis for P and S ?
5. Try to supply convincing intuitive reasons to support result (27a) that under certain circumstances the optimal cell behavior is to synthesize (during the day) less storage material than is required to provide the energy needed at night.
6. (a) Show that the function $\pi(\sigma)$ is continuous at $\sigma = \bar{\sigma}$ by demonstrating that $\pi(\sigma)$ has the same limit as $\sigma \rightarrow \bar{\sigma}$, whether $\sigma < \bar{\sigma}$ or $\sigma > \bar{\sigma}$.
(b) Show that different answers are obtained for

$$\lim_{\sigma \rightarrow \bar{\sigma}} \frac{d\pi(\sigma)}{d\sigma}$$

depending on whether $\sigma < \bar{\sigma}$ or $\sigma > \bar{\sigma}$ when the limit is taken. That is, show that $\pi(S)$ has a discontinuous derivative at $\sigma = \bar{\sigma}$.

(c) Show that $\psi - \phi > 0$, as is assumed in Figure 1.3. In addition, show that $\bar{\sigma}(\sigma) \geq 0$ for all biologically reasonable parameter values.

7. Implicit in equations (5) and (6) is the assumption that not much of the synthetic material $P(T)$ is broken down at night to supply energy. Conclusion 2 indicates that this assumption is generally valid. Nonetheless, even though cases in which $P(T)$ is significantly broken down occur only rarely, discuss the extensions of the mathematical model that would be required to deal with this phenomenon. [Remarks: (i) The problem is not fully specified, as is of course true for most research problems. For example, one needs to know something about the timing of the nocturnal cell divisions. (ii) A full discussion would assume the dimensions of a miniproject. Even with very limited time, however, something can be learned by beginning an account of some of the issues involved and by making some explicit, not-unreasonable assumptions concerning the biology – which properly should be the subject of literature review and/or experiment.]
8. What do you anticipate to be the behavior of the fraction of storage materials as a function of light intensity for algae cells growing in continuous light? After pondering the matter, compare your thoughts with those expressed by Parnas and Cohen (1976, pp. 10–11).
9. By checking the second derivative, verify that (24) provides a minimum [when (25) holds].
- † 10. (a) Consider the function f given by

$$f(x) = x^2 \quad \text{when } x \leq 1;$$

$$f(x) = [(x-b)/(1-b)]^2 \quad \text{when } x \geq 1, b \neq 1.$$

For what value of x is f a minimum? A maximum? Sketch the graph of f .

(b) Repeat (a) for the function given by

$$f(x) = x^2, \quad -\infty < x \leq 1;$$

$$f(x) = 4 - 3x, \quad 1 \leq x.$$

11. Sketch the graph of $f(x)$ for $0 \leq x \leq 4\pi$ if

$$f(x) = x \quad \text{when } \sin x \geq \cos x;$$

$$f(x) = -x \quad \text{when } \sin x < \cos x.$$

12. Consider the function f given for $x \geq 1$ by

$$f(x) = x^2 - 4x \quad \text{when } \ln x - x + 2 \geq 0;$$

$$f(x) = (\ln x + 2)^2 - 4x \quad \text{when } \ln x - x + 2 \leq 0.$$

(a) By sketching on one graph the curves $y = \ln x$ and $y = x - 2$, show that the equation $\ln x - x + 2 = 0$, $x \geq 1$, has a single solution x^* , where $x^* > 2$.

(b) Show that the function f is continuous at $x = x^*$.

†

(c) Show that if $g(x) = (\ln x + 2)^2 - 4x$, then $dg/dx \leq 0$ for $x \geq 1$.

(d) Sketch the graph of $f(x)$ for $x \geq 1$. In particular, show that there is a maximum at $x = x^*$.

(e) Sketch the graph of $f(x)$ for $x \geq 1$ if

$$f(x) = (\ln x + 2)^2 - 4x \quad \text{when } \ln x - x + 2 \geq 0;$$

$$f(x) = x^2 - 4x \quad \text{when } \ln x - x + 2 \leq 0.$$

The following is taken from a discussion by A. Perelson (Segel, 1980, Section 5.3) of histamine release in basophil cells. Virtually no knowledge of the biology is required to answer the various questions.

13. Let C , m , and M be concentrations of free, singly bound, and doubly bound antigen molecules. At steady state, it is found that

$$M = \frac{mK_i(S_0 - m)}{2(1 + mK_i)}, \quad (40a)$$

where m satisfies

$$(1 - \beta)K_i m^2 + m - \beta S_0 = 0; \quad (40b)$$

$$\beta \equiv KC / (1 + KC).$$

Here K and K_i are dissociation constants, and S_0 is the total receptor concentration.

(a) Show that there is exactly one meaningful solution of the quadratic equation (40b).

(b) Show that on substituting the solution of (40a) into (40b) we obtain

$$M = S_0 \frac{1 + 2\delta - (1 + 4\delta)^{1/2}}{4\delta}, \quad \delta \equiv \beta(1 - \beta)K_i S_0.$$

Find the constants a_0 , a_1 , and a_2 in the series

$$(1 + 4\delta)^{1/2} = a_0 + a_1\delta + a_2\delta^2 + \dots,$$

and use the result to derive the approximation

$$M \approx \frac{1}{2} S_0 \delta, \quad 0 < \delta \ll 1.$$

(c) It is desired to find the value of β that maximizes M . To do this, it is sufficient to set $dM/dm=0$ (m , not $\beta!$). Why? Show from (40a) that $dM/dm=0$ if $m^2 K_i + 2m - S_0 = 0$.

(d) Conclude that M is maximized when $\beta = \frac{1}{2}$.

14. (a) Calculate the net amount of protein synthesis, over the day and night, if no storage material is made.
 (b) Repeat (a) when τ hours at the end of the day are used to synthesize storage material.
 (c) Use (a) and (b) to provide an alternative derivation of (13).

Supplement: List of symbols and their definitions

$P(t)$	Weight of protein at time t
$S(t)$	Weight of storage material at time t
P_0	Weight of protein at beginning of day
S_0	Weight of storage material at beginning of day
R	Rate of synthesis of cellular material per unit amount of P
τ (tau)	Hours per day devoted to production of S
T	Length of day
σ (sigma)	$S(T)/P(T)$
W	Average weight of daughter cell
E_M	Maintenance energy/unit weight of P /hour
E_d	Energy required for the formation of each new cell
E	Total energy required each night, for maintenance and reproduction
k_P	Energy units/unit weight of P
k_S	Energy units/unit weight of S
β (beta)	Units of S obtained on conversion of one unit of P
α (alpha)	k_P/k_S
G	Gain in P , owing to storage
L	Loss in P , owing to storage
π	Profit: gain minus loss
$\bar{\sigma}$	$E/[k_S P(T)]$
σ_{op}	Value of σ that maximizes profit
ψ, ϕ (psi, phi)	Combinations of constants defined in (33)
σ^*	Particular value of σ depicted in Figure 1.3
τ_{op}	Value of τ , when $\sigma = \sigma_{op}$