Topic 3. Living Systems as Engineering Systems

TOPICS
- systems analysis
- acceleration of reactions
- energy coupling
- control systems

Systems Analysis

What is it? How the parts work together to make the whole system serve the purpose or objective for which it was designed. The ability to perform this type of analysis is one of the defining characteristics of an engineer.

We began our discussion of the systems engineering aspects of life in terms of the material balance. Noting that mass must be conserved, we can track how matter enters and leaves a system, or a part of a larger system, and how matter is converted from one form to another. This is one of the key aspects of how the various parts of a system work together to achieve a purpose or objective.

What is the objective of a living system? To survive and propagate.

To perform a systems analysis, we must first define what the system is. We could consider a cell as our system – this would be particularly appropriate for single-celled organisms. We could also designate our system as the entire organism for multicellular organisms. For complex organisms, we could consider an organ as a system. For eukaryotic cells, we could also consider an organelle as the system. What we select as our system will be based on the level of detail we desire from our analysis.

For example, if, in our analysis, we wanted to describe the total amount of heat given off by the human body, we could designate the entire body as our system for our analysis, or we could designate each organ as a system and sum up the results over all organs, or we could designate each cell in the body (over 100 trillion!) as a system and then sum up the results over all cells. If we just wanted the total amount of heat given, without regard to the heat given off by individual organs or even by individual cells, we would designate our system as the entire human body.

Let's consider a cell as our system. Cells can be thought of as miniature reactors (10^{-12} to 10^{-11} mL) containing thousands of compounds with thousands of chemical reactions occurring simultaneously. What is required for this system to meet its objective – to survive and propagate?

1. Reactions must be accelerated.

Consider a cell metabolizing glucose to provide the energy it needs to carry out its life processes.

a glucose → b CO_2 + c H_2O + d "energy"

where we are indicating that some unit amount of energy d is liberated for every a moles of glucose consumed. That is the rate of energy production is related to the rate of glucose consumption as

$$R_{glucose} = \frac{a}{d} R_{energy}$$

The rate of most biochemical reactions can be expressed in a functional form that is similar to the Monod model. If we call the glucose concentration inside the cell S, then we can write the rate of glucose consumption in the cell, i.e., the rate at which the glucose concentration in the cell decreases, as

$$\frac{R_{glucose}}{V_{cell}} = \frac{kS}{K+S}$$

This relationship is known as the Michaelis-Menten equation. At low glucose concentrations (S << K), this rate is essentially linear in S, but at high glucose concentrations (S >> K), this rate becomes independent of glucose concentration. This is because the biochemical machinery of the cell can be saturated.

Then the rate of energy production will be

$$R_{energy} = V_{cell} \frac{kS}{K+S} \frac{d}{a}$$

Taking for example the limit of S << K, then

$R_{energy} = V_{cell} \frac{kd}{Ka} S$, or more simply, $R_{energy} = V_{cell} k' S$ where k' is a rate constant that indicates how intrinsically fast the chemical reaction is.

If energy must be produced at a high rate in order to achieve the objective, then the cell has three choices

- increase the size of the cell, V_{cell} – but the bigger the size of the cell, the harder it is to materials (mass) and energy in and out of the cell at fast enough rates to address needs
- have a large glucose concentration, S – but typically the glucose inventory in a cell may be low, so it doesn't have the option of having S large. And, when glucose levels get too high, other deleterious side reactions may occur (e.g. hyperglycemia in diabetics)
- increase the reaction rate constant, k'. Many reactions that occur in living systems are actually quite slow if they are not aided by **catalysts** called **enzymes**. Enyzmes are proteins.

A catalyst is a molecule that speeds up the rate of a chemical reaction, but it is not actually consumed by the reaction. (It is neither a reactant nor a product, but it makes the reaction faster.) Enzymes are proteins that serve as catalysts for biochemical reactions. For example, glucose conversion to CO_2 and H_2O requires O_2. It is the equivalent of combustion, but if you mix glucose and oxygen at body temperature, the reaction will be immeasurably slow. But in the presence of the enzyme glucose oxidase, the reaction occurs fast enough for glucose to be an effective source of energy to run cellular processes.

2. Energy must be provided to drive non-spontaneous processes.

Reactions that liberate energy can happen spontaneously. Many reactions in living systems actually consume energy, rather than liberate it. If no energy is provided to the reaction it will not happen spontaneously. A car does not drive itself spontaneously – energy has to be liberated from the fuel in order to move the car. This is an example of how a reaction that liberates energy can be coupled with a non-spontaneous process to make that process occur. The word *coupled* here is key – there has to be a direct coupling. In the car, the combustion of fuel happens in a piston, so the energy released by the chemical reaction is directly harnessed to power the car. There is a direct coupling. What if instead of combusting the fuel inside the pistons, we instead just burned a tank of fuel in a parking lot next to the car? The car would not run – there is no direct coupling between the fuel combustion and the supply of energy to the pistons that drive the car.

In biochemical terms, the amount of energy consumed or released by a reaction is called the free energy of reaction, ΔG_{rxn}. ("G" after J.W. Gibbs, one of the founders of thermodynamics)

If $\Delta G_{rxn} > 0$, the process is not spontaneous and energy is consumed.
If $\Delta G_{rxn} < 0$, the process is spontaneous and energy is released.

In this context, the free energy, G, is an accounting of all the forms of energy a chemical species will have at constant temperature and pressure:

G = internal (thermal) energy + potential for pressure-volume work – level of disorder (entropy)
$G = U + PV - TS$

Consider two reactions. If reaction one is spontaneous, with $\Delta G_{rxn,1} < 0$, and reaction two is non-spontaneous with $\Delta G_{rxn,2} > 0$, both reactions can be made to occur by coupling them together if $\Delta G_{rxn,1} + \Delta G_{rxn,2} < 0$, but again, only if $\Delta G_{rxn,1}$ can be directly harnessed to drive reaction two.

The coupling of reactions to drive otherwise non-spontaneous processes is the hallmark of living systems. If we mixed all the ingredients for life in a beaker, but we left out the enzymatic machinery for coupling chemical reactions, we would not get life.

2. Control and Communications Systems.

Because so many events (reactions) are occurring simultaneously, events must be coordinated so that chaos doesn't occur.

Cells have well-defined compositions; cells, organisms, species, ecosystems tends towards steady state or a state of stable composition = **homeostasis**.

Control systems are used by cells, organisms to assess how the system (cell, organism) is behaving and make changes so that the system behaves as it should = **set point**.

Key points concerning homeostasis

- internal environment of cell, organism must be kept within a tolerable range throughout the life cycle, even if external conditions change.

- Some homeostatic systems are more important than others – i.e. some conditions, when far from the set point, are more life-threatening than others

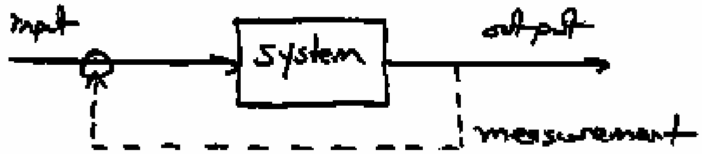
  - Blood pH must be close to 7.4
  - Body temperature must be close to 37°C
  - Pulse should be close to 60 beats per minute at rest

  - Homeostasis consists of a large set of setpoints.

- Some set points may change in a regular way – biorhythms over day, month, season, year, lifetime (infradian <24 hr, circadian 24 hr, ultradian >24 hr)

Types of Control Systems

Feedback Control

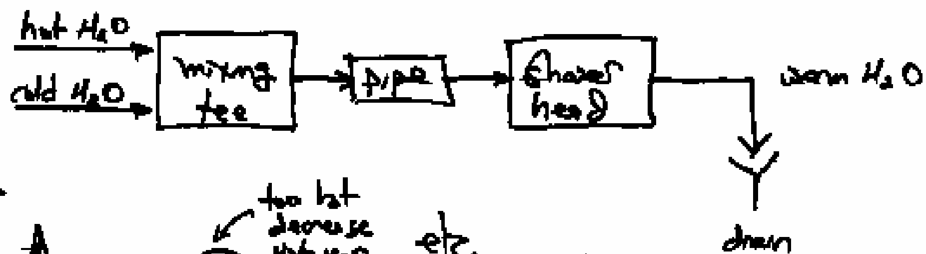


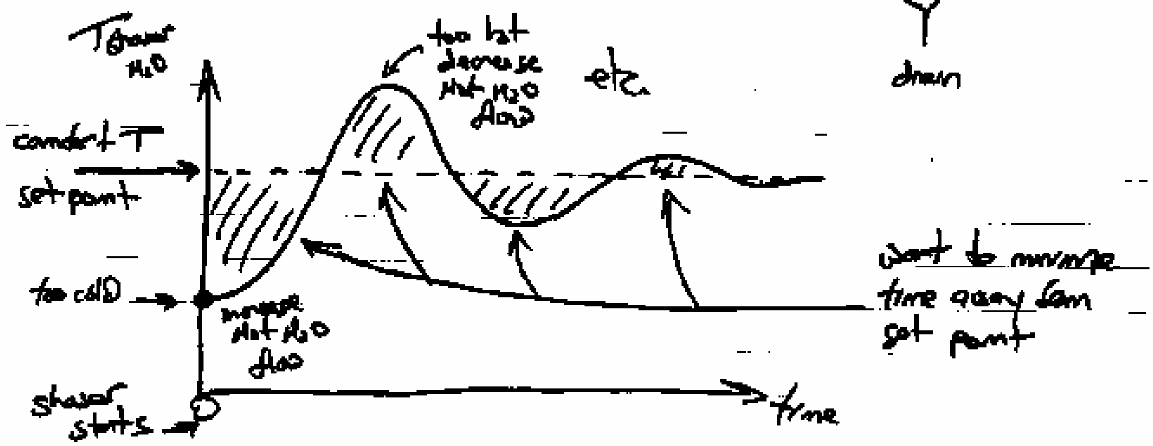
feedback control loop
- used to manipulate input so that it matches output desired

① negative feedback control
the difference between the set point and the actual value is assessed, the error signal, input is manipulated to move output in opposite direction, towards set point value

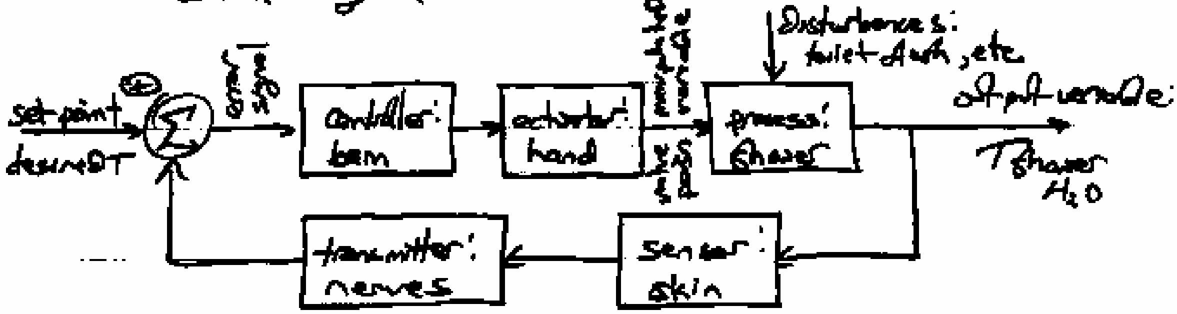
error = (set point value − actual value)

Consider a shower
process diagram: tracks material flow





Control diagram: tracks information flow



sensor – measures output variable
transmitter – sends signal from sensor to controller
controller – determines what action to take based on the error signal
actuator – changes the manipulated variable to drive output variable closer to the set point

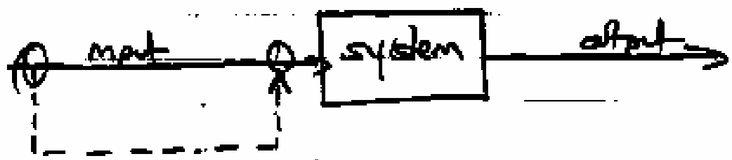
examples of negative feedback control
maintaining intracellular pH, T

② positive feedback control
input signal is amplified, causing output to continue moving in same direction

associated with instability in a system
– e.g. "feedback" that is obtained when microphone of a PA system is held next to the PA speaker...

Some examples
sexual arousal
urination & defecation
parturition (uterine contractions that expel fetus)

Feed-forward Control



feedforward loop
used to anticipate changes in environment to maintain desired output – take action before changes in inputs work their way through system

examples
- pursuit of food, prey; avoiding predator
- steering a car

rather than waiting for an actual error signal to take action, future error is estimated based on present course of action

Modes of Control

① Continuous – manipulated variable is continuously adjusted to achieve set point

e.g. shower example, can manipulate hot/cold valves continuously to achieve desired temperature

② Discrete or ON/OFF – manipulated variable can take one of several (often two) states such as "on" or "off"

e.g. window air conditioner – based on signal from thermostat, air conditioner is either on, giving cold air, or off.