Homeostasis and Adaptive Homeostasis

UM2010

Where opportunity creates success

Kathryn Taylor slides adapted from Darrel Brooks/ Allyson Clelland

Learning Objectives

- Define and explain the concept of homeostasis

Explain the processes of homeostasis

- Definition and examples of adaptive homeostasis

Evaluate the effect of failure of homeostasis on health, with examples

Claude Bernard

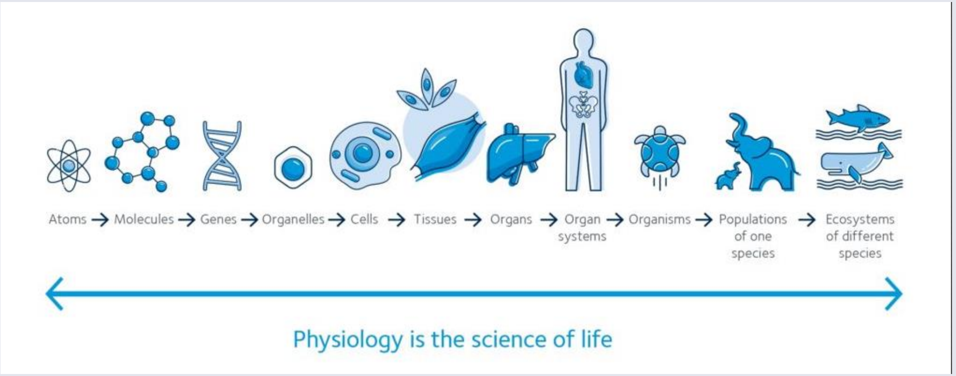
In the 19th Century, Claude Bernard originally proposed the concept of the 'milieu intérieur ' which stated that complex organisms can maintain their internal environment 'fairly constant' in the face of challenges from the external world

In 1926, Walter Cannon extended the concept and coined the term "Homeostasis"

Walter Cannon

Introduction

- The physiology of the body is often described as homeostatic mechanisms that control the cellular environment.
- Cell function relies on an adequate energy supply
- There is integration of activities of different cells through both electrical and chemical signalling molecules
- The cell membrane is important in these functions and forms a barrier between the intracellular and extra cellular environments across which molecules are transported.



Cells, Function and Homeostasis

The elemental constituents of the body are **cells**, whose survival and function are possible only within a narrow range of physical and chemical conditions, such as **temperature, oxygen concentration, osmolarity, and pH.**

Therefore, the whole body can survive under diverse external conditions only by maintaining the conditions around its constituent cells within narrow limits.

The body has an **internal environment,** which is kept constant to ensure survival and proper functioning of the body's cellular constituents. The process whereby the body maintains constancy of this internal environment is referred to as **homeostasis.**

The internal environment

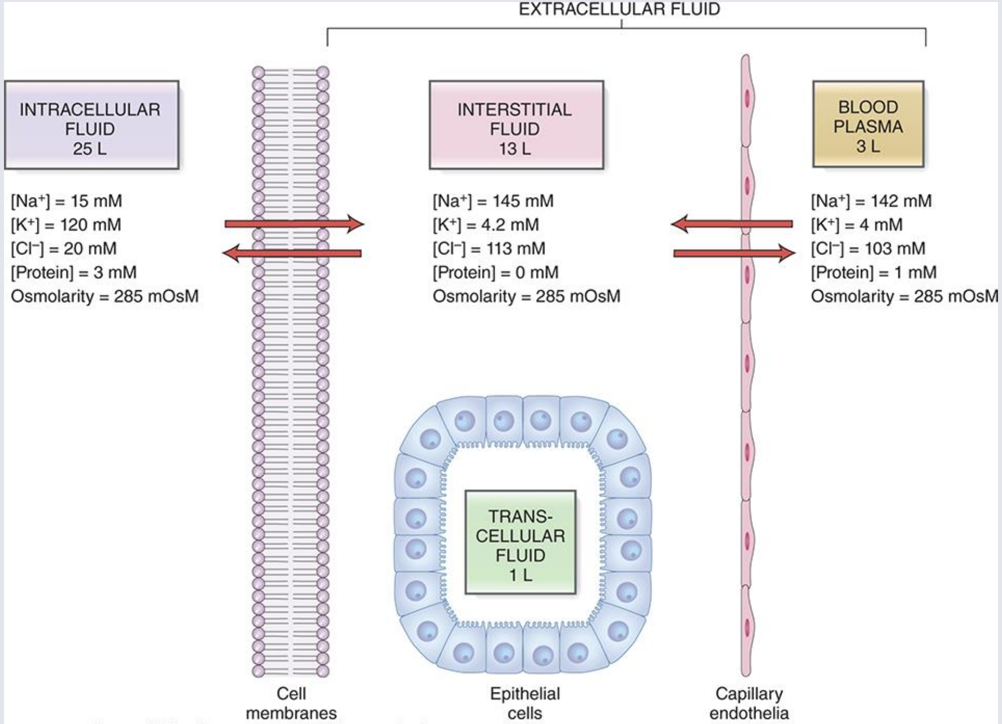
The purpose of homeostasis is to provide an optimal fluid environment for cellular function.

The body fluids are divided into two major functional **compartments:**

Intracellular fluid (ICF) is the fluid inside cells.	**Extracellular fluid (ECF)** is the fluid outside cells, which is subdivided into the **interstitial fluid** and the blood **plasma.**

The concept of an internal environment in the body correlates with the interstitial fluid bathing cells.

Body Fluid Compartments

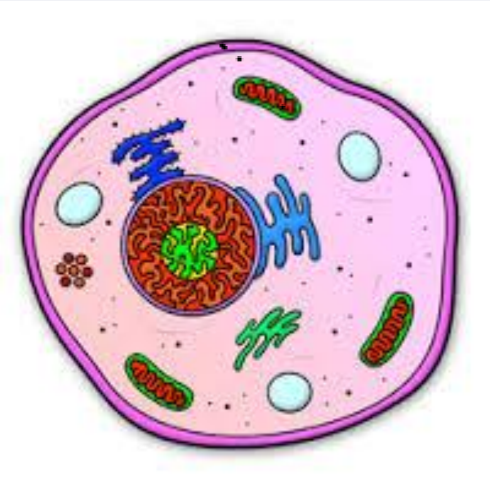


Body fluid compartments. Intracellular fluid (ICF) is separated from extracellular fluid (ECF) by cell membranes. ECF is composed of the interstitial fluid bathing cells and the blood plasma within the vascular system. Interstitial fluid is separated from plasma by capillary endothelia. Transcellular fluid is part of the ECF and includes epithelial secretions such as the cerebrospinal and extraocular fluids. ECF has a high [Na^+] and a low [K^+], whereas the opposite is true of ICF. All compartments have the same osmolarity at steady state.

Citation: Chapter 1 General Physiology, kibble JD. *The Big Picture Physiology: Medical Course & Step 1 Review, 2e;* 2020. Available at: https://accessmedicine.mhmedical.com/content.aspx?sectionid=245544050&bookid=2914 Accessed: January 11, 2021

What is homeostasis

- Internal environment –
- cell cytosol/interstitial fluid

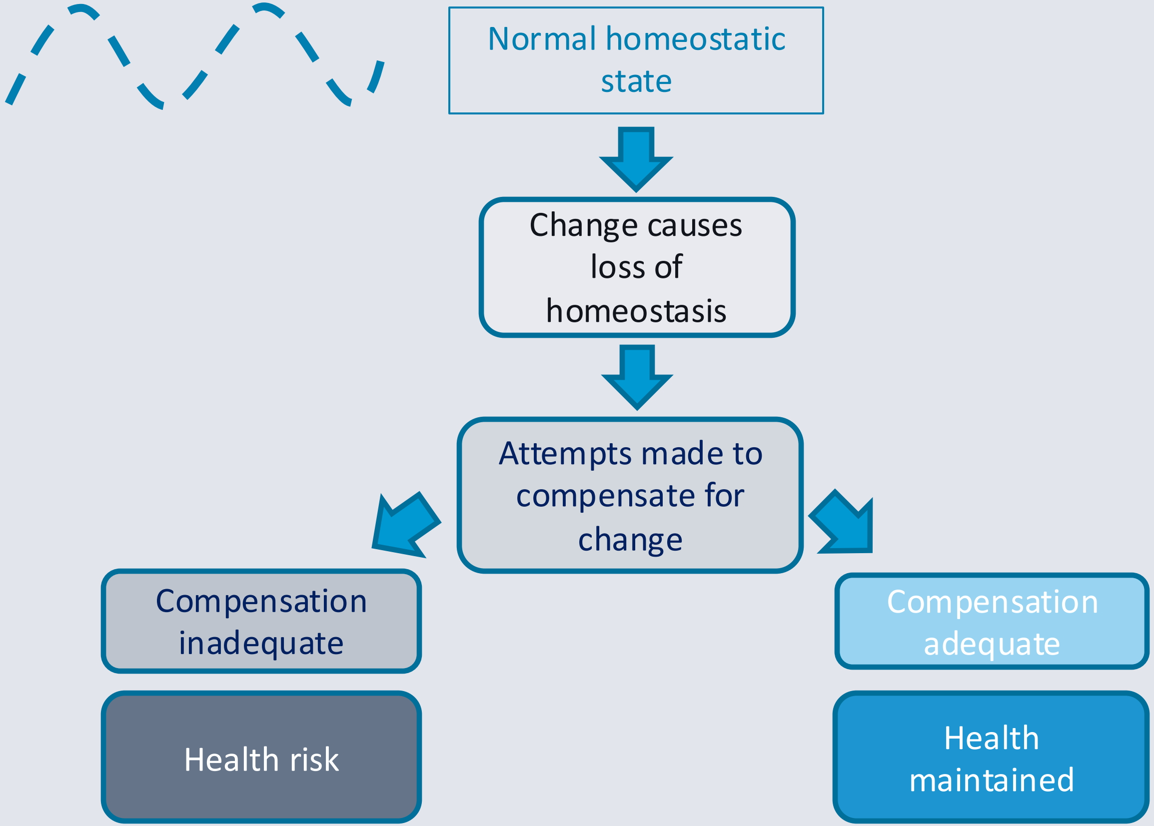


Definition 'maintenance of a relatively constant internal environment despite changes in the external environment

External environment

- Ambient conditions
- Presence or absence of food and drink
- Level of exercise (causing excesses and demands

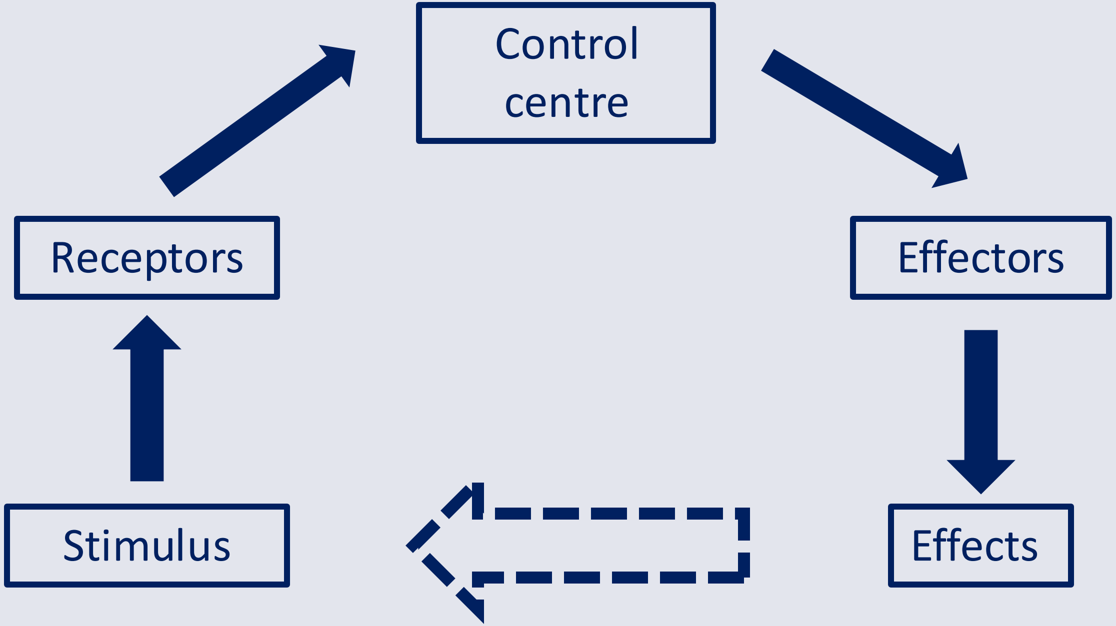
Summary of Homeostasis



Some examples of physiological controlled variables

Controlled Variable (Arterial Blood Sample)	Typical Set Point Value
Arterial O_2 partial pressure	100 mm Hg
Arterial CO_2 partial pressure	40 mm Hg
Arterial blood pH	7.4
Glucose	90 mg/dL (5 mM)
Core body temperature	98.4°F (37°C)
Serum Na^+	140 mM
Serum K^+	4.0 mM
Serum Ca^{2+}	2.5 mM
Mean arterial blood pressure	90 mm Hg
Glomerular filtration rate	120 mL/min

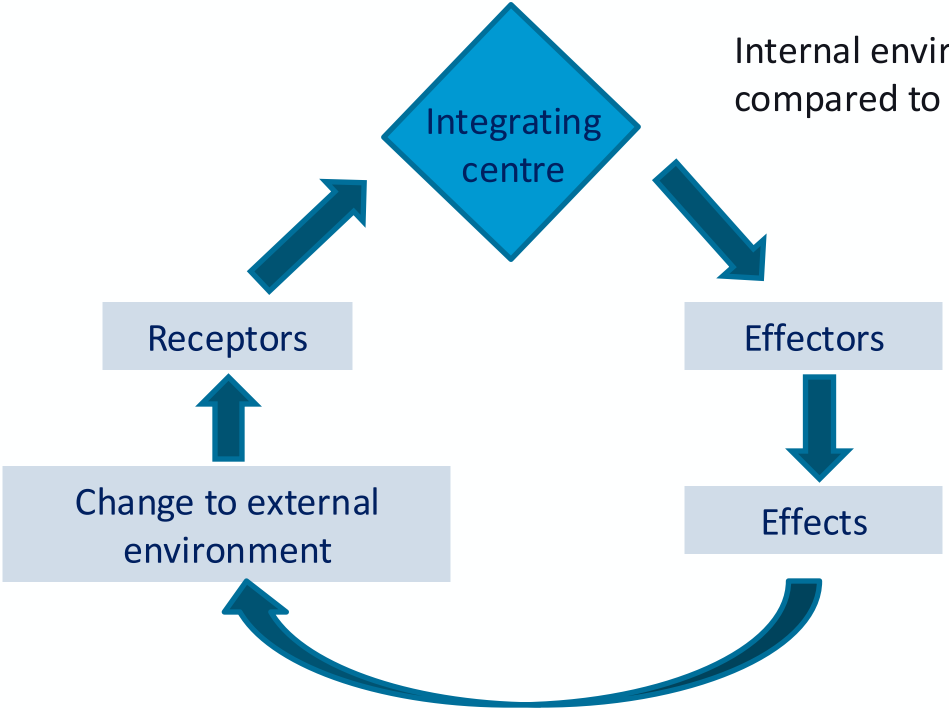
Feedback Loops



Effects negate stimulus

Negative feedback (reflex)

Internal environment compared to a ‘set point’



The effects result in a change back towards the norm

Model of Homeostasis

1. Sensor – measures the value of the regulated variable

2. Mechanism for establishing 'normal range' of values for the regulated variable. i.e. The 'set point'- which can change

3. An 'error detector' that compares the signal being transmitted by the sensor with the (value of the regulated variable) with the set point. The result of this comparison is an error signal that is interpreted by the controller.

4. The controller interprets the error signal and determines the value of the outputs of the effectors.

5. The effectors determine the value of the regulated variable.

Generic homeostatic regulatory system

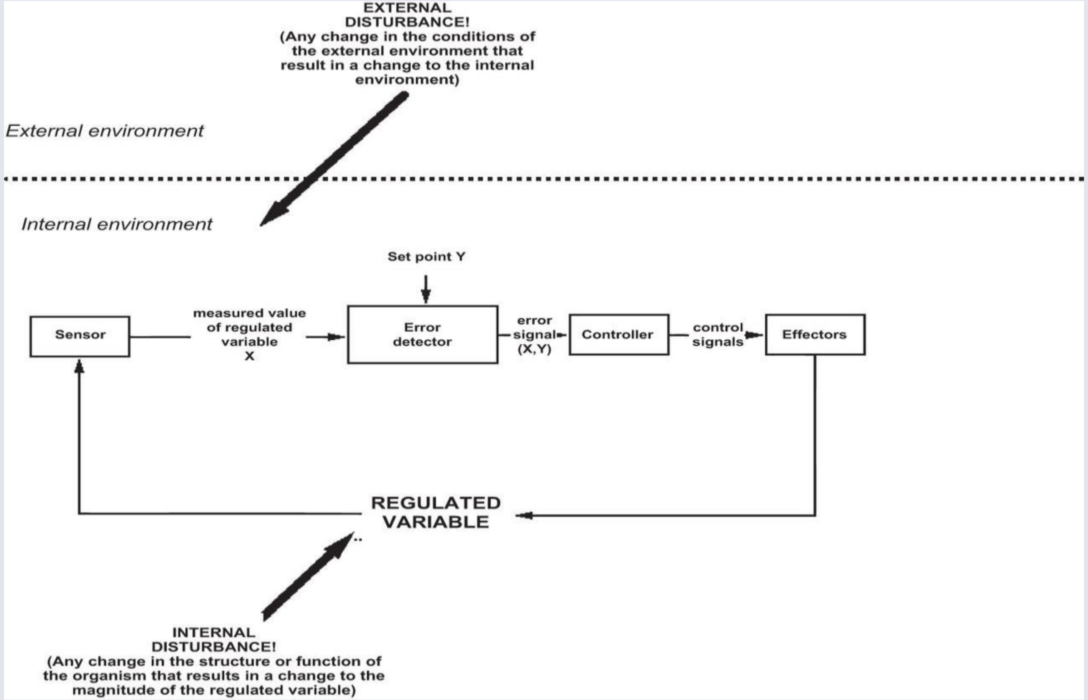


Fig. 1. Diagram of a generic homeostatic regulatory system. If the value of the regulated variable is disturbed, this system functions to restore it toward its set point value and, hence, is also referred to as a **negative feedback system.**

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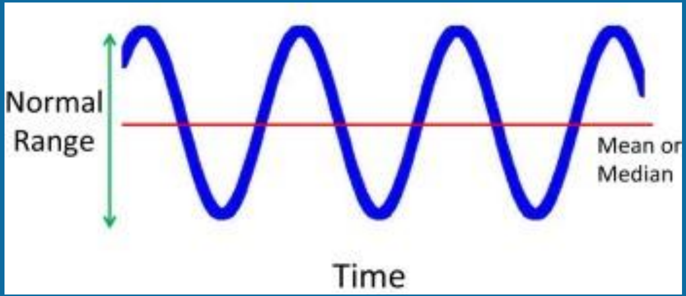
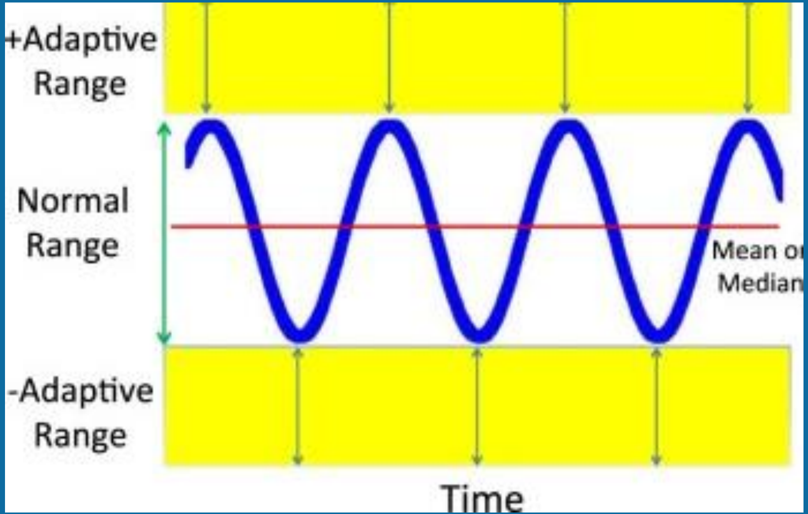

Normal
Range
Mean or
Median
Time


+Adaptive
Range
Normal
Range
Mean or
Median
-Adaptive
Range
Time

Types of Receptors

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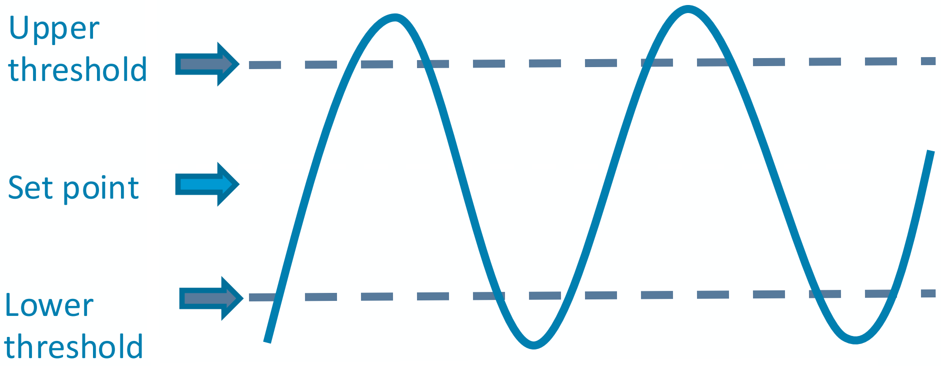
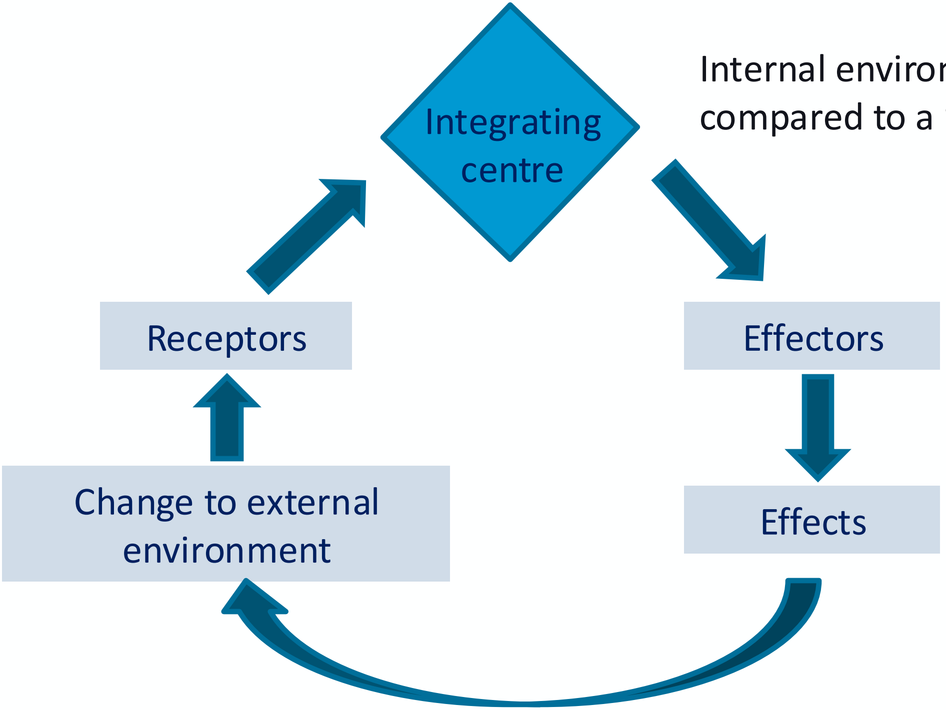
Receptor	Function
Baroreceptors	Monitor pressure e.g. blood pressure in carotid arteries
Chemoreceptors	Monitor level of chemical substances e.g. oxygen, carbon dioxide and pH in carotid arteries
Thermoreceptors	Monitor temperature e.g. in skin and internal organs
Osmoreceptors	Monitor osmolarity (solute concentration)
Glucoreceptors	Monitor level of glucose e.g. beta-cells in pancreas

Negative feedback



- The value (e.g. pH) will increase until it reaches a threshold above the set point
- Reaching the threshold triggers messages to be sent to the effectors to take action
- The action of the effectors causes the value to start to fall
- Once the value falls below a threshold under the set point, it will trigger the effectors to take a different action
- The result is OSCILLATION either side of the set point

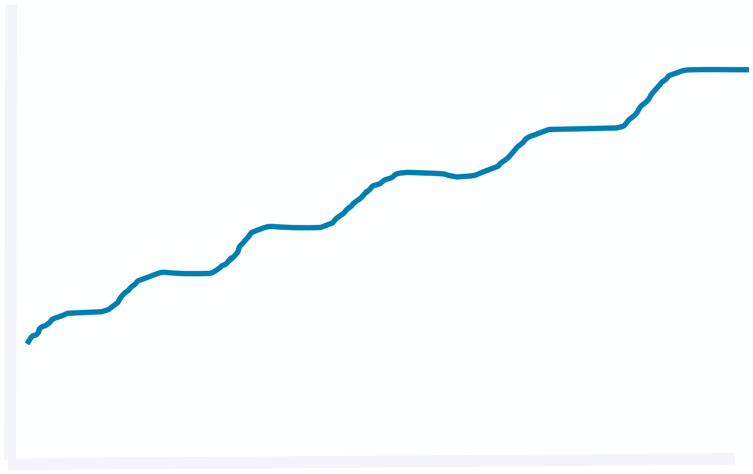
Positive feedback



Internal environment compared to a ‘set point’

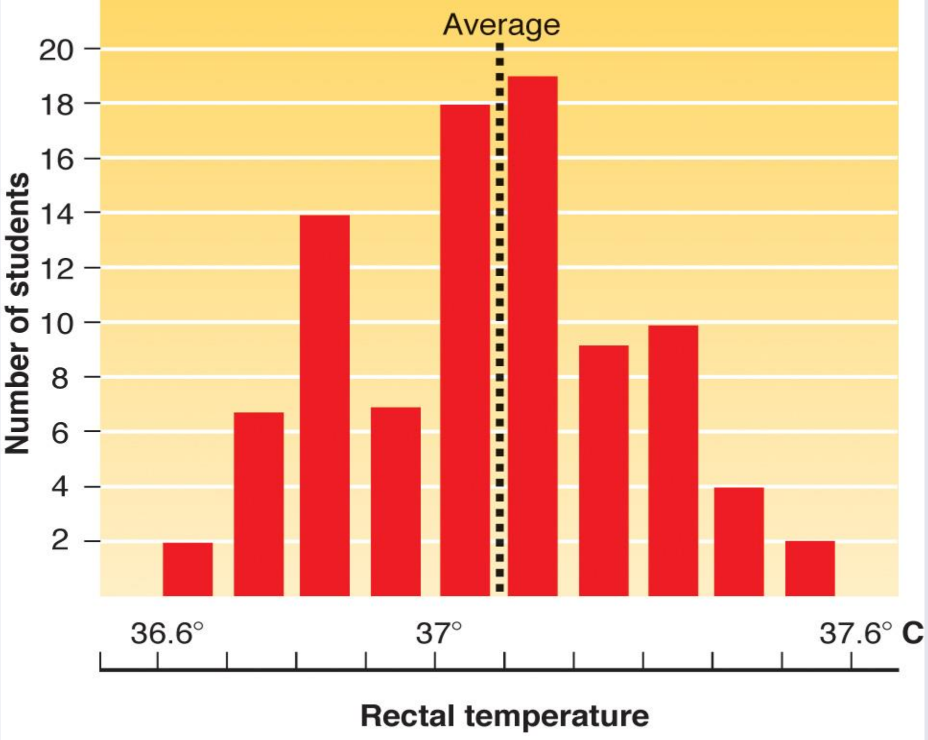
The effects result in a change FURTHER AWAY FROM the norm

Positive feedback



- The value changes in some way (can be up or down)
- The change triggers a further change in the same direction
- An external influence is required to break the cycle
- This is rarely a homeostatic response

Temperature set point



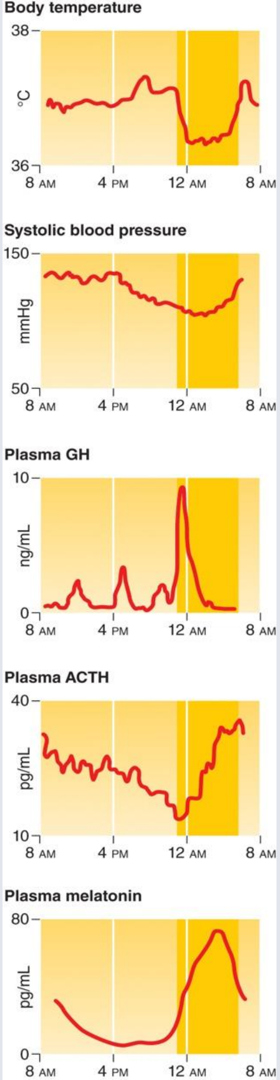
Range of normal body temperatures. In a well-controlled experiment, a group of healthy students show a wide range of normal rectal temperatures. The average (mean) temperature of this group is 37.1°C.

Not everyone's set point, or "normal", body temperature is the same. This Figure shows the difference in body temperatures observed in a group of healthy students. You can see that temperatures varied widely. This explains why some people are comfortable at a temperature that is too cold for others around them—their temperature set point must be naturally lower.

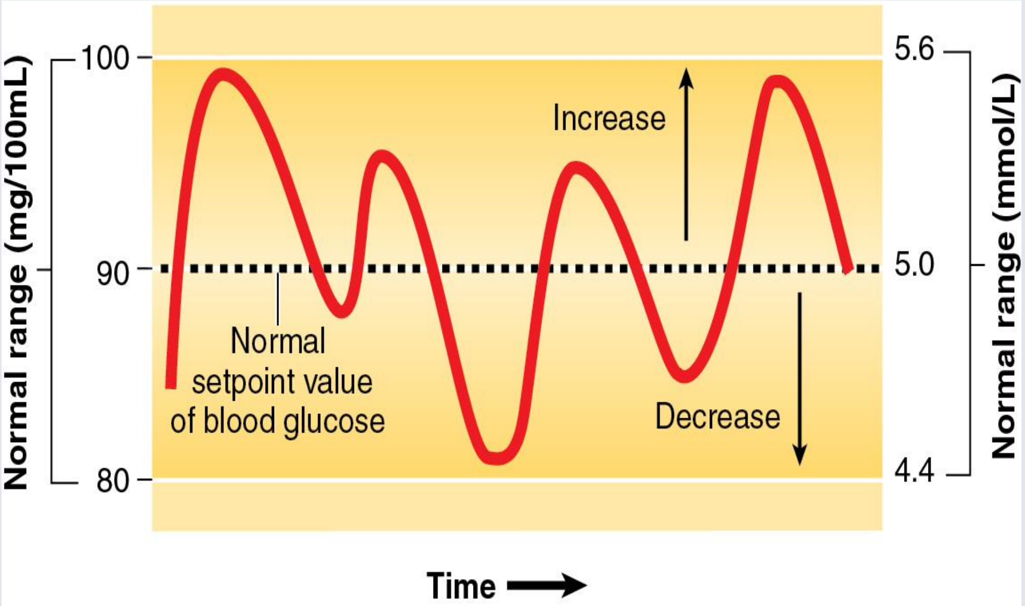
Homeostasis

PATTON, KEVIN T., PhD, Anatomy and Physiology, 2, 23-37

Circadian cycles. The body's internal clock mechanisms raise and lower set points for some variables in a daily high-low rhythm, as these examples show. Shaded areas represent typical sleep times.



Homeostasis of blood glucose

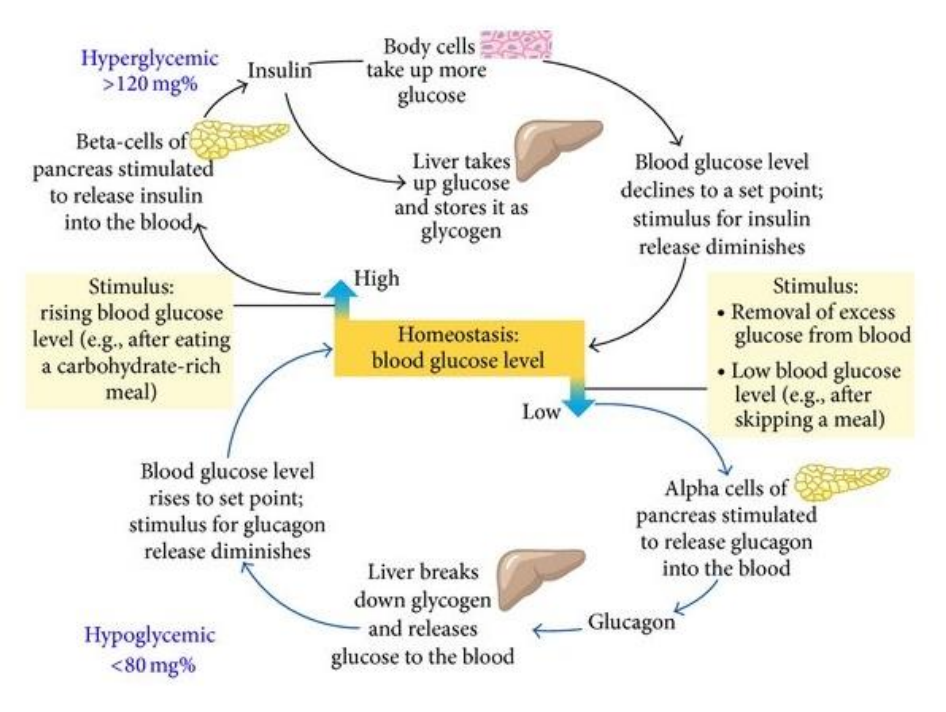


Homeostasis of blood glucose.

The range over which a given value, such as the blood glucose concentration, is maintained is accomplished through homeostasis. Note that the concentration of glucose fluctuates above and below a normal setpoint value 5 mmol/L (90 mg/100 mL) within a normal setpoint range 4.4 to 5.6 mmol/L (80 to 100 mg/100 mL).

Homeostasis
PATTON, KEVIN T., PhD, Anatomy and Physiology, 2, 23-37

Glucose Homeostasis

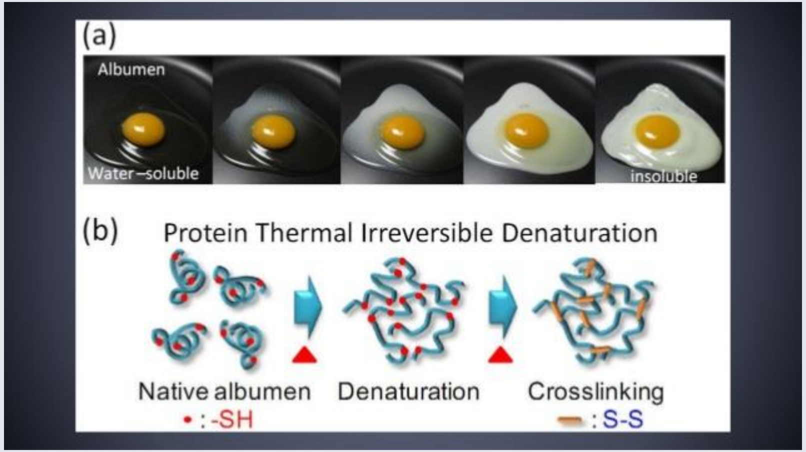


Why is homeostasis so important?

- Changes in the conditions within the cell (such as pH and temperature) can or irreversible damage to proteins

- Important proteins within cells include enzymes, receptors and transport proteins

- Changes to these proteins can threaten the life of the cell



Homeostatic Mechanisms

Regulatory mechanisms that compensate for changes away from a stable condition.

Local/intrinsic mechanisms

- Regulation within a tissue involving no external systems
- May be direct effect or local nerve reflexes

Reflex/extrinsic mechanisms

- Control system outside organ or tissue being controlled
- Involves nervous or endocrine systems and CNS

Intracellular mechanisms

- Action taken within the cells
- modification of enzymes within cells, causing changes to their function

Set-points can be modified:

- Thermoregulation : hypothalamus (integrator)
  Increase in set-point for core body temperature during fever

- one form of acclimatization to environmental oxygen level – some people who have spent a very long time at altitude have a lower set point for P_aO_2

The efficiency of the negative feedback loop can be altered

Sensitivity - more than one stimulus can sensitise the loop

e.g. low P_aO_2 and high P_aCO_2 both trigger increased ventilation, however the response when both occur together is greater than the sum of when they occur independently

Fever

- During a fever, bacteria cause bone-marrow macrophages to secrete substances called endogenous pyrogens
- The endogenous pyrogens are released into the blood stream and cause the hypothalamic set point to be increased
- This results in initiation of feedback mechanisms that increase body temperature
- Body temperature rises above normal

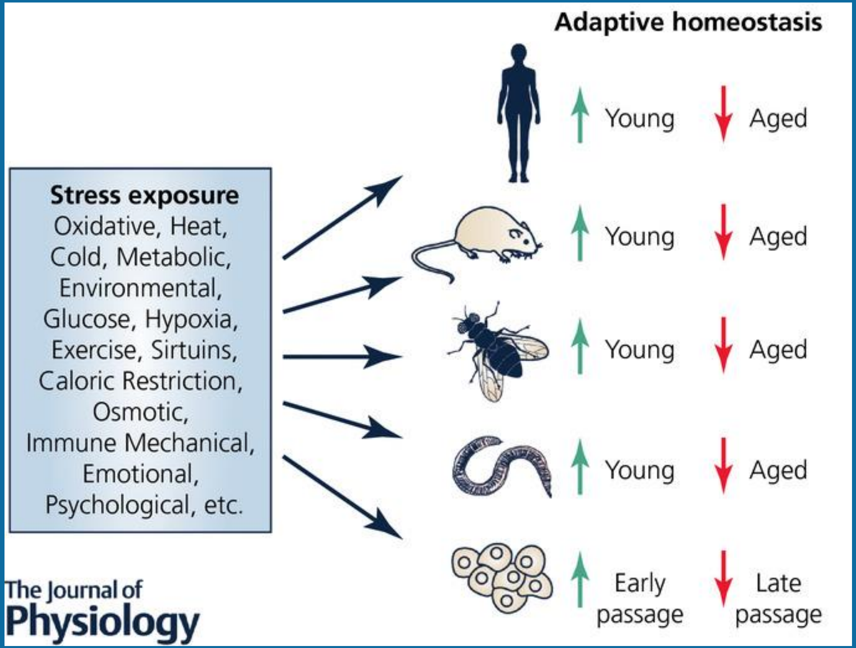
The above-normal temperatures are thought to help defend against microbial invasion because they stimulate the motion, activity, and multiplication of white blood cells and increase the production of antibodies. At the same time, elevated heat levels may directly kill or inhibit the growth of some bacteria and viruses that can tolerate only a narrow temperature range

Importance of Homeostasis

- Optimal cell and system function requires tightly controlled conditions
- Uncontrolled variability in these conditions can cause damage, disease and death.
- Untreated Diabetes:
  - Blood vessel damage from high glucose levels resulting in :
    - Atherosclerosis, retinopathy, kidney disease
  - Nerve damage:
    - foot ulcers, sexual dysfunction, digestive issues (diahorrea / constipation)
  - Organ damage:
    - Pancreas, kidney
  - Ketoacidosis, coma from hypo and hyperglycaemia can be fatal.

Adaptive Homeostasis

Adaptive homeostasis is "the transient expansion or contraction of the homeostatic range for any given physiological parameter in response to exposure to sub-toxic, non-damaging, signalling molecules or events, or the removal or cessation of such molecules or events" (Davies, 2016).



Adaptive Homeostasis

The transient expansion or contraction of the homeostatic range for any given physiological parameter in response to exposure to sub-toxic, non-damaging, signalling molecules or events, or the removal or cessation of such molecules or events" KJA Davies 2016

Allows the body to adapt to greater stresses beyond the normal homeostatic range eg; infection, starvation, hypoxia, cold shock, heat shock, oxidative stress, exercise-induced adaptation, caloric osmotic stress, mechanical stress, emotional stress

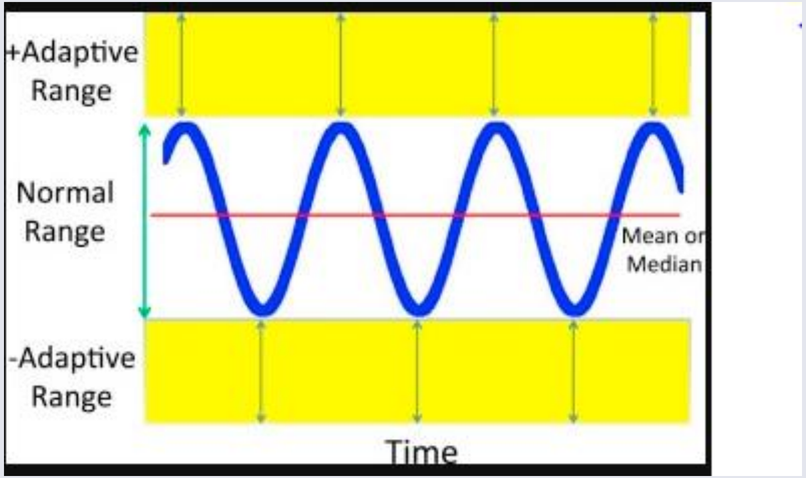
Short term responses to adjust to the environment: can increase stress resistance and protect against more serious episodes of stress.

Adapative homeostasis generally refers to cellular or genetic processes

Positive and Negative Adaptive Homeostasis

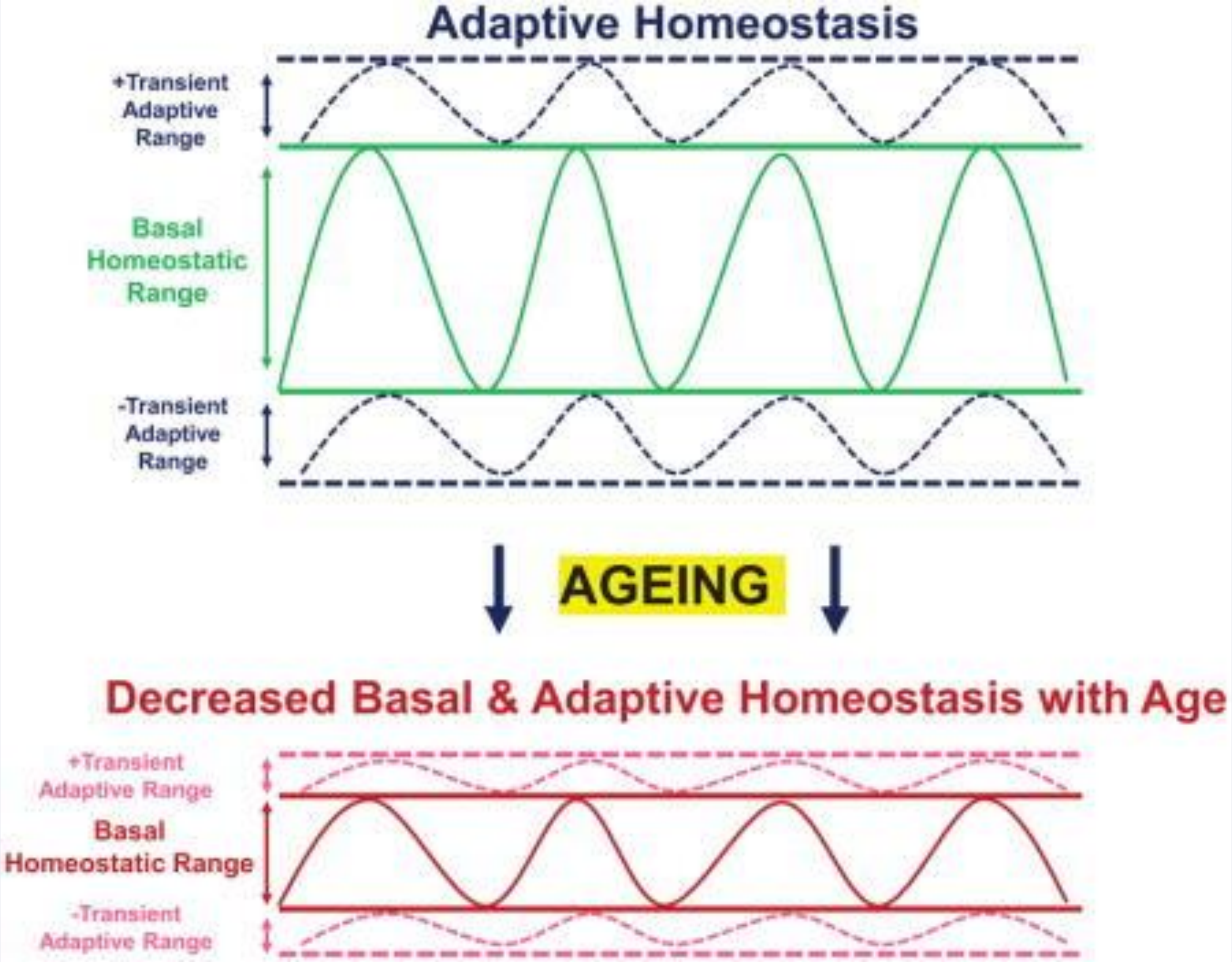
- Positive adaptation:
  - A shift “up” to increase resistance pathways and protect against a greater insult ie oxygen deprivation or levels of toxins

- Negative adaptation:
  - A shift “down” to decrease cellular pathways or gene expression ie decrease in amino acid synthesis following an amino acid rich meal.



Homeostasis and Aging

- Adaptive homeostasis declines with age
- Responses to temperature, metabolic, environmental, oxidative, hypoxia, glucose, exercise, starvation, osmotic, immune, mechanical, emotional, psychological etc are affected
- Cells do not react, react in a minimal way to stimuli, or cannot increase response
- Damage accumulates in cells and tissues related to prior exposure to stimuli/events. Cellular fatigue?



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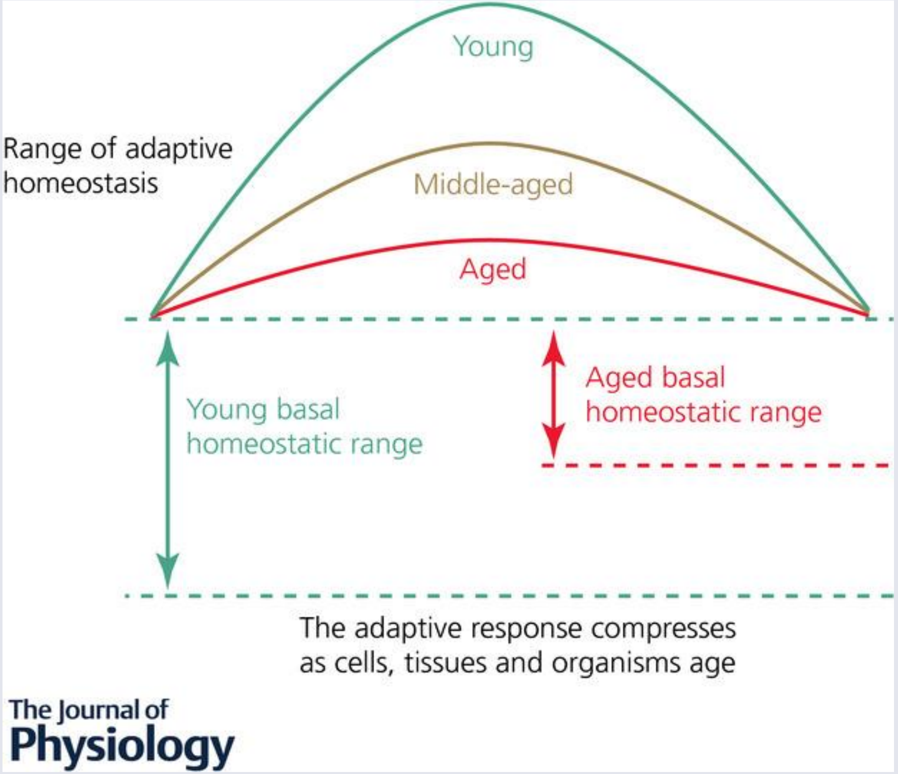


The Journal of Physiology, Volume: 595, Issue: 24, Pages: 7275-7309, First published: 13 October 2017, DOI: (10.1113/JP275072)

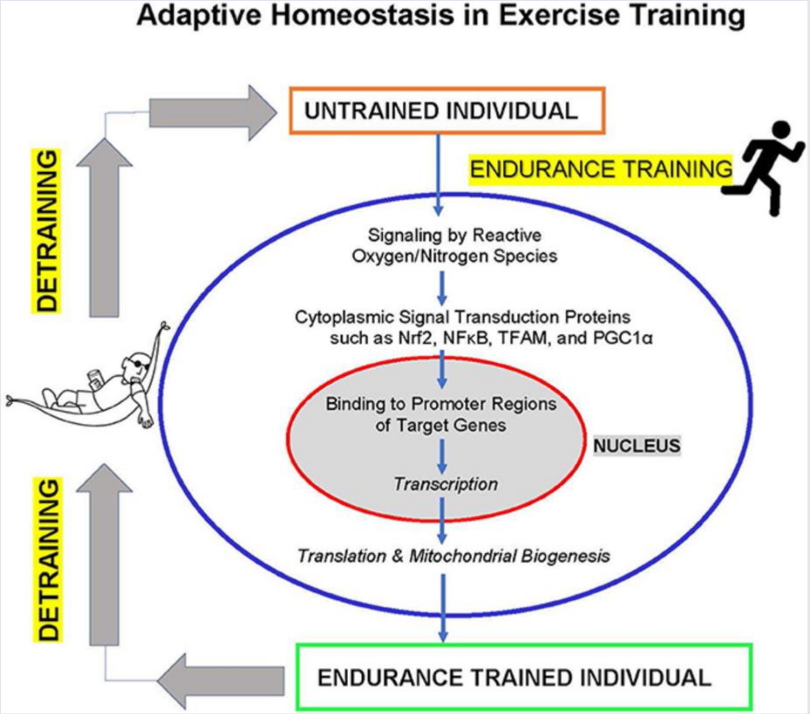
Adaptive Homeostasis, Aging and heart Disease

We know that aging is associated with increased arterial plaque formation, but the body's response to this is affected by aging.

1. Plaque formation leads to a hypoxic environment and elevation in Hypoxia Inducible Factor 1 alpha (HIF-1α).
2. Increase in angiogenesis to increase blood flow
3. Increased remodelling results in smaller infarct size and cardiac damage
4. Aging decreases response, and tissue is more vulnerable to damage

Aging increases the level and number of stresses but the cellular response does not increase, and may decrease, leading to an overall decline in adaptive homeostasis

Cardiovascular Adaptive Homeostasis in Exercise



Adaptive homeostasis in exercise training. Reactive oxygen and nitrogen species such as O·−2, H_2O_2, and $NO^{\bullet}$ activate cytoplasmic signaling proteins such as Nrf2, NFκB, TFAM, and PGC1α to translocate to the cell nucleus where they bind to upstream promoter regions of hundreds of target genes to initiate transcription and (ultimately) translation. The protein products of these target genes include mitochondrial proteins encoded in the nucleus, leading to mitochondria biogenesis, and numerous other adaptive and protective proteins.

These changes in gene expression and increased mitochondrial biogenesis (in addition to other metabolic alterations) lead to increased exercise endurance capacity.

The training effect is a transient process of expanding the range of adaptive homeostasis and it only lasts as long as the training stimulus is maintained. If training is discontinued then detraining results in adaptive homeostasis returning the range of endurance capacity to pre-training levels.

HYPOTHESIS AND THEORY article
Front. Physiol., 01 May 2018
Sec. Redox Physiology
Volume 9 - 2018 | https://doi.org/10.3389/fphys.2018.00369

Homeostasis in the young and old

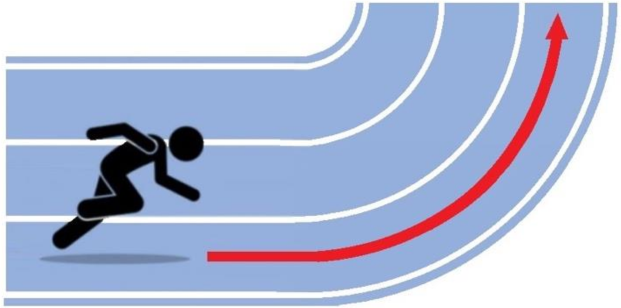
- Preterm infants, newborns and older people have more problems maintaining homeostasis.

- Preterm:
  - Liver development: immature affects blood protein and can lead to hypoproteinemic oedema.
    - Lack of protein decreases oncotic pressure and leads to loss of fluid from the blood vessels into surrounding tissues.
  - Acid-base and blood glucose homeostasis: eg blood limits can be very wide 20-100mg/dl and are more likely to be variable if feeding is irregular
  - Calcium fluctuates more widely, (normal limit? 9-11mg/100ml) which can result in hypo-calcaemic tetany
    - Spontaneous twitch of hands and feet. Increased reflex
    - Low levels of calcium cause an increase in permeability to Sodium and depolarisation

Anticipation

Anticipation (Feed-Forward Control) – the effect can be triggered before any changes have occurred

e.g. increase in heart rate before exercise i.e. before any changes in blood gases have occurred

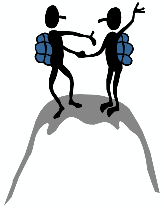


Adaptation responses

What we would normally think of as a homeostatic response

Accommodation: *immediate physiological change in sensitivity of cells to changes in the external environment*

Acclimation; *long term physiological adaptations in response to exposure to artificial or simulated changes in environment*



Acclimatisation: *long term physiological changes resulting from exposure to natural changes in environment*

Acquired responses

Genetic adaptation: *physiological or morphological changes that occur as a result of 'survival of the fittest', following long term exposure to changes in the environment*

Inherited responses