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Background

1 | Anatomy and Physiology

The following chapter outlines the functions of the cardiovascular system and focuses on its microcirculatory part. Further the phenomena of vasomotion is illustrated.

1.1 Macrocirculatory system

The main function of the cardiovascular system is the blood supply of the whole body and the transportation of metabolites. The propulsion of this is the heart. It generates the systolic blood pressure through the strength of left ventricle. The pressure difference between the heart and the periphery emerging from there, ensures the blood flow. The blood flows from regions with high pressure, like the aorta, to regions with low pressure, like the periphery.[**martini2012**]

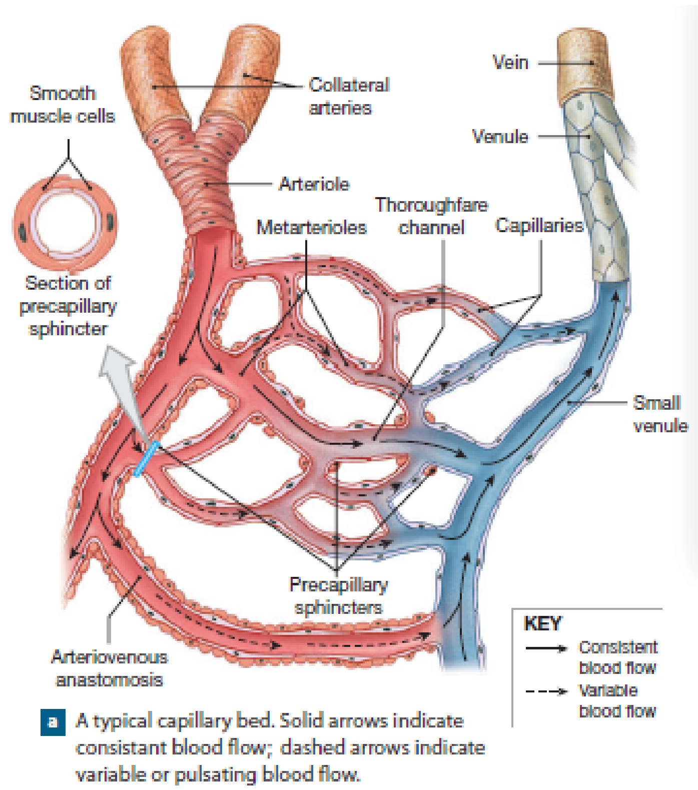
The heart supplies the body through the systemic and the pulmonary circuit with blood. Through these circuits the heart regulates the blood allocation with adjustment of stroke volume and heart frequency. The oxygen-rich blood accumulates in the left ventricle. From there the blood is pushed out through the aortic valve into the aorta and via the arteries spread into the whole body. The venous system returns the meanwhile low in oxygen blood back to the heart into the right atrium. From there the blood flows into the right ventricle and is pushed out through the pulmonary valve into the lung arteries. In the lungs gas exchange of the blood happens. Subsequent the oxygen-rich blood flows via the pulmonary veins back to the left heart to supply the body.[**martini2012**]

As mentioned, there are two types of vessels, arteries and veins. The difference between those two types of vessels is that arteries transport the blood away from the heart and veins solely transport blood to the heart. There are also some differences in the structure of arteries and veins. Arteries consist of three different layers, tunica interna, tunica media and tunica externa. The tunica interna consists of vascular endothelium, the tunica media consists of smooth muscle cells and elastic fibres, the tunica externa consists of connective tissue and also elastic fibres. Furthermore, there are two different types of arterial vessels. In arteries of the elastic type prevail the elastic fibres in the tunica media. This allows an abrupt extension of the vessel during the systole and ensuing constriction, due to this the blood is transported. This phenomena is called windkessel function. In arteries of the muscular type prevail the muscular fibres in the tunica media. This allows regulation of the lumen by constriction and dilatation, whereby the resistance and the blood flow in the organs is regulated.[**martini2012**]

Venous vessels are similarly structured like arterial vessels, however they are thinner and have also semilunar valves inside, to inhibit back flow inside the vessels. This system is supported by the skeletal muscles which help to hold up blood flow. The arterial and the venous vessel system are connected through the capillary system in the microcirculatory system.[**martini2012**]

1.2 Microcirculatory system

The heart and larger arteries and veins are associated with the cardiovascular system, but those are only used for transportation of blood. Instead it is the capillaries, that permeate most tissues, that is responsible for the perfusion of tissue. These are the only vessels which permit exchange between the vessel and the surrounding interstitial fluids. Factors that affect tissue perfusion is cardiac output, peripheral resistance and blood pressure. Capillaries are made not of single individual fluid conductors like veins and arteries, but instead formed into capillary beds. Here they work as a interconnected network of vessels. As mentioned before the arteries decrease in size the further they expand into the peripheral system. The small arteries divide into arterioles which further divide into dozen of capillaries. The capillaries merge into a venule after the blood has been deoxygenated. A capillary is divided into two segments, first the metarteriole and second the capillary. The blood flow between arterioles and venules can also be a direct connection, made by an arteriovenous anastomosis. This works as a bypass diverting blood flow around the capillary bed. An example of the structure of the capillary bed can be seen on figur 1.1.[**martini2012**]



Figur 1.1: The basic structure of a capillary bed, with arteriole on the left side of the bed and a venule on the right[**martini2012**].

Each capillary entrance is controlled by a precapillary sphincter, which is composed of smooth muscle cells, that are able to contract or relax and thereby limit access of blood flow to certain capillaries. The blood flows relatively slow within the capillaries giving time for the two way exchange of nutrients and wastes. [**martini2012**]

1.2.1 Vasomotion

The flow within the capillaries varies. This is among other thing due to the earlier mentioned precapillary sphincters opening and closing. The opening and closing of sphincters is part of the autoregulation process performed at a local level, to control the blood flow. The vascular system does not contain blood enough for every vessel a capillary beds to be filled with blood. Therefore only 25% of the vessels in a capillary bed contains blood, and vessels activity needs to be well coordinated. Thermoregulation and control of nutrition balance are the primary functions of the microcirculatory system. Local changes in concentration of chemicals and interstitial fluids eg. dissolved oxygen concentrations in tissue modulates the vascular smooth muscles activity. Constriction and dilation of the vessel is thereby regulated by this periodic activity, also known as vasomotion. [**martini2012**, **geyer2004**]

Under normal circumstances cardiac output remains stable and the control of local blood flow happens through local peripheral resistance within local tissues. The regulation of cardiovascular activity is controlled by local homeostatic mechanism. These make sure that demands such as oxygen and nutrients are meet and wastes are disposed.[**martini2012**]

Physiological mechanism controlling vasomotion are not yet fully understood, but vascular smooth muscle activity has been shown to be roughly proportional to the tissue's metabolic demand for oxygen.[**geyer2004**] Further have some factors that trigger homeostatic mechanism to alter the vasomotion been said to have an impact. Factors that trigger dilation is called vasodilators and can be some of the following:[**martini2012**, **geyer2004**]

- Decreased oxygen level or increased CO2 level
- Lactic acid or other acids generated from tissue cells
- Nitric oxide NO released from endothelial cells
- Rising concentrations of potassium ions or hydrogen ions in the interstitial fluid
- Chemicals released during local inflammation
- Elevated local temperature

A vasodialation will result in increased oxygen, nitrients, buffers released to recreate homeostasis. Factors that stimulate contriction is called vasoconstricters and can happen due to following:[**martini2012**]

- Damaged tissue
- Aggregating platelets

2 | Hemodynamics

Hemodynamics explains the movement or flow of blood. It is influenced by parameters like blood pressure, blood volume, cardiac output, blood composition, etc. It is possible to measure some of the hemodynamic parameters non-invasive, and also to calculate parameters.[**martini2012**, **thiriet2008**]

2.1 Physiological Base

The regulation of the blood pressure happens with baroreceptors in the walls of the big arteries in chest and neck area. These receptors register the changes of the elongation of the vessels and transmit this information to medulla oblongata. With the received pressure informations initiates the medulla oblongata, if necessary, regulatory measures. For the short-term regulation is the sympathicus responsible. Both, middle-term and long-term regulation, is made by the kidneys. For middle-term regulation messenger substance are released, which entail vasoconstriction. The long-term regulation occurs per pressure diuresis or reabsorption in the kidneys.It is possible to measure different blood pressures at different places in the cardiovascular system, for example the mean arterial pressure (MAP). The MAP increases in relation to the stroke volume and decreases when blood flows into the peripheral system. The central venous pressure (CVP) states the pressure in the venous system and complies approximately the pressure in the right ventricle. CVP depends on the filling volume of the venous system. Cardiac output, total periphery resistance and the viscosity of blood affect the blood pressure.[**martini2012**, **thiriet2008**]

The cardiac output (CO) states the blood volume, which is pumped by the heart per time unit (HR). The calculation of the CO as follows.[**martini2012**]

$$CO = HR \times strokevolume \tag{2.1}$$

The total periphery resistance (TPR) is the flow resistance of the systemic circulation and results from the sum of all vessel resistances. TPR depends on MAP , CVP and CO. [**martini2012**]

$$TPR = \frac{MAP - CVP}{CO} \tag{2.2}$$

2.2 Physical Base

To consider the hemodynamics, it is possible to draw conclusions by analogy of physical laws. Especially of Ohm's law $R = \frac{U}{I}$ or rather $I = \frac{U}{R}$. A special case of Ohm's law constitutes Hagen-Poiseuille's law in the field of fluid dynamic and rheology. Hagen-Poiseuille's law describes the laminar flow of an homogeneous Newtonian fluid through a rigid pipe depending on characteristics of the fluid and of the pipe.[**noordergraaf2011**, **thiriet2008**]

Blood is an inhomogeneous suspension of liquid and corpuscular components, whose viscosity η depends on more factors than the temperature, and is consequently no Newtonian fluid. Nevertheless it is possible to draw conclusions by analogy out of Hagen-Poiseuille's law for the computation of the hemodynamics.[**noordergraaf2011**, **thiriet2008**]

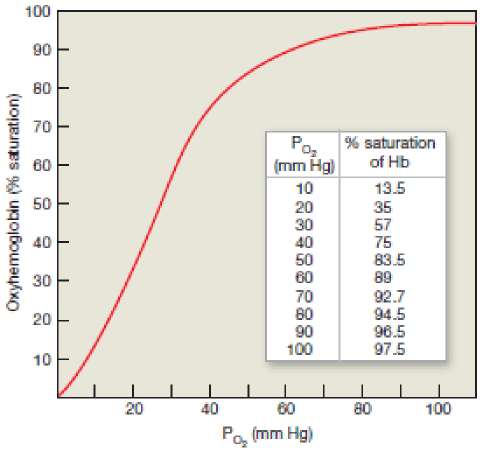
$$\frac{V}{t} = \frac{r^4 \times \pi \times \Delta P}{8 \times \eta \times I} \tag{2.3}$$

Here is the volume flow equivalent to the electrical current I and the pressure difference ΔP to the electric voltage U. Thus, the calculation of the resistance as follows.[**noordergraaf2011**, **thiriet2008**]

$$R = \frac{8 \times I \times \eta}{r^4} \tag{2.4}$$

Thereby volume flow increases 16 times and the resistance decreases 16 times for double radius r.[**noordergraaf2011**, **thiriet2008**]

In the blood, oxygen is tied to a large extent by hemoglobin. The oxygen saturation (sO_2) describes the percentage of the oxygenated hemoglobin. With rising oxygen partial pressure (pO_2) increases the oxygen saturation. This relation between sO_2 and pO_2 is showed by the oxygen binding curve.[**martini2012**, **hasan2013**]



Figur 2.1: The oxygen binding curve shows the relation between sO_2 and pO_2 [**martini2012**].

The oxygen content (cO_2) of the blood depends on both, the oxygen saturation and the oxygen partial pressure. cO_2 is calculated by the sum of the hemoglobin bounded and the physical dissolved oxygen.[**martini2012**, **hasan2013**]

$$cO_2 = Hb \times 1,34\frac{ml}{g} + pO_2 \times 0,003\frac{ml \times dl}{mmHg} \tag{2.5}$$

The available oxygen (DO_2) is calculated by the oxygen content of the blood and the cardiac output.[**martini2012**, **hasan2013**]

$$DO_2 = cO_2 \times CO \tag{2.6}$$

The consumption of oxygen (VO_2) is calculated by the difference between the available oxygen in the arterial and the venous blood and the cardiac output.[**martini2012**, **hasan2013**]

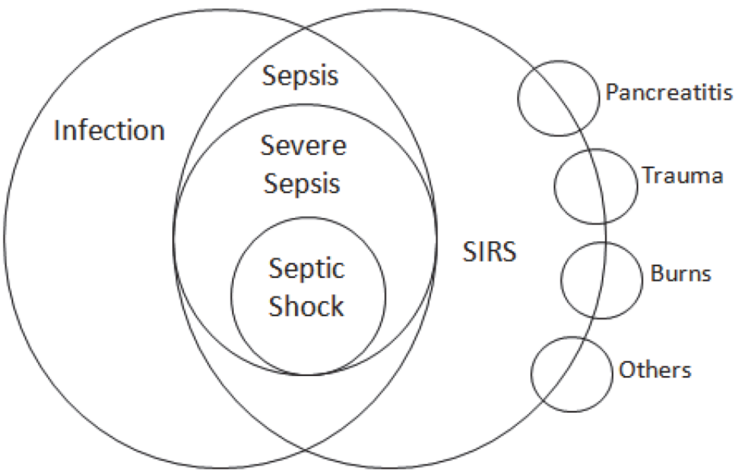
$$VO_2 = (c_aO_2 - c_vO_2) \times CO \tag{2.7}$$

Therefore one can draw a conclusion from the available and the consumption of oxygen to the cardiac output.

3 | Vasomotion in disease

This chapter describes pathologic incidents in the cardiovascular system and organs during sepsis. Sepsis is used as an example of a disease where vasomotion plays a role.

Sepsis is a condition, that develops on behalf of systemic inflammatory response syndrome (SIRS) with pressence of an infection or bacteria in the tissue, within the body which triggers an immune response. This response often overburdens the immune system, to fight the inflammation or bacteria. The infection or bacteria can be anywhere in the body's tissue. Some of the normal macrohaemodynamics of sepsis are abnormal body temperature, abnormal heart rate, oxygen extraction and abnormal blood pressure.[**plunta2010**, **kanta2014**] Sepsis is increasing condition in the population. Different studies suggest estimates of the incidence of sepsis, but the identification of diagnosis of sepsis can vary, why the numbers may also vary from place to place.[**baudouin2008**, **kanta2014**] The Dr. Foster Organisation found an increase by 53% from 1996 to 2002 in the hospitals in the United Kingdom. Causes for the increase in incidence can be due to the increasing elderly population, with cronic conditions undergoing invasive procedures [**baudouin2008**]. Sepsis is often associated with three stages, sepsis, severe sepsis and septic shock. This is illustrated in figure 3.1.



Figur 3.1: Relation between SIRS and infection. Showing the stages in sepsis and some of the causes of SIRS which include pancreatitis, trauma, burns etc.[**kanta2014**]

3.1 Sepsis

Under the stage of sepsis several things happen, mainly to the micro circulatory system at the capillary level, that leads to impaired homeostasis in the body. Infection or other bacteria that is responsible for causing some irregularity is present in the blood and in the tissues around the vessels. Among the first things that happens when the body encounters an infection, white blood cells are recruited to release molecules that will fight the infection. Molecules that interact with the endothelial in the blood vessels, like nitric oxide (NO), are released. The interaction causes the vessels to dilate to increase the blood vessel diameter and permeability. The increased diameter slows down the blood flow, which causes a drop in blood pressure. Also the vessels permeability is increased. This reaction happens multiple places in the body where there is infected tissue present and will cause systemically vessel dilation. The characterization of sepsis is SIRS as a result of infection.[**baudouin2008**, **kanta2014**]

3.2 Severe sepsis

When the permeability of the vessels is increased there will be more fluid in the tissue and the cells will get less oxygen because the oxygen has a harder time to get to the demanding tissue. Also the endothelial of the vessels will get damaged when the white blood cells try to destroy the pathogens. This triggers coagulation and clotting is formed in the damaged areas in the blood vessels. These clots can break off into the blood and cause further harm eg. stroke. At a point the damaged vessels leads to more leakage, because there will be a point where the coagulation cannot keep up. Organs will start to dysfunction at this stage. The characterization of severe sepsis is presence of sepsis with organ dysfunction and hypoperfusion is often included in this state. The mortality rate for patients with severe sepsis are about 25 to 30% [**baudouin2008**, **kanta2014**].

3.3 Septic shock

Septic shock occurs when the body has undergone sepsis for a greater duration of time. This stage is characterized by a condition with hypotension even after adequate fluid resuscitation is given. Because of lactic acidosis the cells are not getting a sufficient supply of oxygen and therefore the cells will begin to die. This can lead to a very dangerous state, where organs begin to fail because they get to damaged to function. When multiple organs get damaged the state in septic shock reaches multiple organ failure also called multiple organ dysfunction syndrome (MODS)[**baudouin2008**, **kanta2014**]. The mortality for patients with septic shock are in the region of 40 to 70% [**kanta2014**].

4 | Infrared Thermal Imaging

The following chapter will include an introduction to infrared imaging, where some general concepts and physical principals will be explained. Furthermore it will be elaborated how a device measures infrared radiation.

Infrared imaging is an technique that utilizes infrared radiation emitted from nearly any objects. The existence of infrared radiation was first discovered in 1800 by Sir Frederick William Herschel. His experiments lead to the knowledge that there were a light spectrum beyond the visual spectrum humans are able to perceive.[**ignacio2017**, **optris2009**]

Infrared thermography is commonly used to calculate surface temperatures and important concepts in the understanding of this are heat and temperature. Temperature is a measure for the internal energy within an object and can be defined as the average kinetic energy of the object. Heat is the energy that passes from a warm object to another colder object. A warm object will decrease in internal energy and a cold object will increase due to the temperature difference and therefore the heat transfer. In the human body, a constant temperature is keep, due to several factors and therefore the temperature will not decrease even though a heat transfer to the surrounding environment occurs. The environmental temperature do have an impact on how large the heat transfer gradient is. If a body is in a cold environment, the emitted heat will be greater than the absorbed. In the same way, if the environment is much warmer than 37°C, a greater absorption than emission will occur and the body will increase in temperature.[**ignacio2017**]

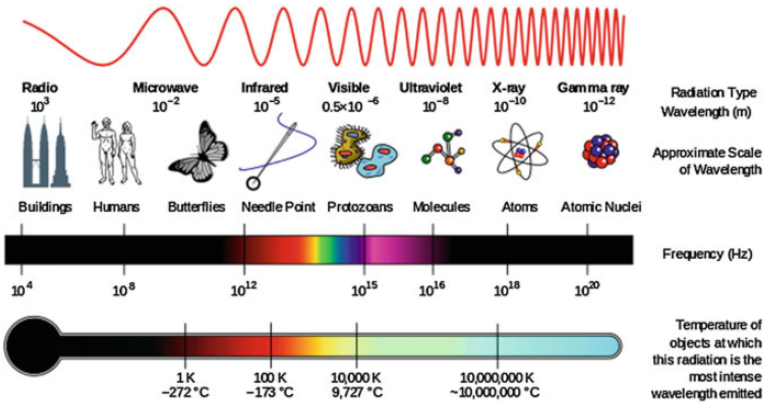
4.1 Physical principals

Any object above absolute zero emits energy-electromagnetic radiation depending on its temperature. Absolute zero is $0K$ or -273.16°C. To put that into perspective the human body has a temperature around 37°C.[**ignacio2017**, **optris2009**]

Electromagnetic radiation is a propagation of energy trough a medium without the transportation of mass. An electromagnetic wave is made of the relationship between frequency f, wavelength λ and the speed of light c. This is stated in the equation of wave motion.[**ignacio2017**]

$$\lambda = \frac{c}{f} \tag{4.1}$$

Depending on the frequency and wavelength certain characteristics arise from what is called the electromagnetic spectrum. The electromagnetic spectrum is the electromagnetic energy that is emitted. This extends from radiation of low energy such as radio waves and infrared, to waves of higher energy in form of eg. X-rays. A graphical representation of the electromagnetic spectrum can be seen on figur 4.3.[**ignacio2017**]

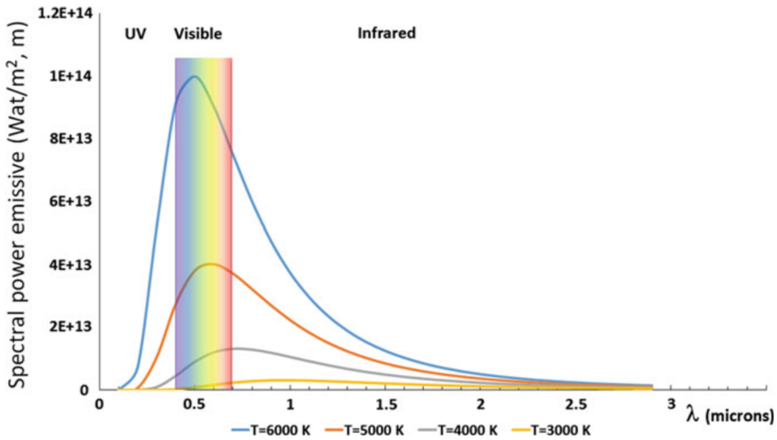


Figur 4.1: The electromagnetic spectrum with wavelength, emitters, frequency and temperature.[**ignacio2017**]

Infrared radiation is also known as thermal radiation because of the relationship between temperature and infrared radiation. Temperature of the human body permits radiation in the infrared spectrum, but objects of much higher temperature are capable of emitting radiation in the visible and UV spectrum. This has to do with the difference between object and environmental temperature. If the temperature of these are relatively close to each other, the radiation emitted will be within infrared wavelengths. Infrared radiation has a wavelength from 769 nm to 1 mm. Objects emit more radiation in some region regions compared to others. Because of this is the infrared spectrum classified in the three regions, near, middle and far infrared. Near is between 769 nm and 2.5 μm, middle 2.5 μm to 50 μm and far 50 μm to 1 mm. The human body emits most radiation in the far infrared part, and most thermal cameras are build with this in mind. Near and middle cameras are used to measure gases.[**ignacio2017**]

4.2 Measuring thermal energy

The theory of the black body is important to understand the absorption and emission of light relative to temperature, because the theory of the black body is used to describe the laws of infrared radiation and its relationship to temperature. The black body is an ideal perfect emitter of infrared radiation because it absorbs all electromagnetic radiation permitted to it, and it emits the same amount of radiation as it absorbs, the absorption and emission are both equal to one. Spectral emissive power, also denoted E_λ is the energy emitted by a surface in relation to time and range of wavelength. Figure 4.2 shows an graphical illustration of spectral emissive power of the black body for specific wavelengths when the temperature changes. [**ignacio2017**]



Figur 4.2: Spectral power emissive as a function of wavelength for different temperatures [**ignacio2017**]

The knowledge of this principle helps in the understanding of how infrared radiation behaves, and how temperature affects the wavelength of the signal. The radiation from the human body which has a temperature at 37°C emits the maximum energy of 9.3μm, which means that most of the radiation is in the far infrared spectrum.[**ignacio2017**]

Physical laws including Wien's displacement law and Stefan-Boltzmann's law are important for explaining how the infrared radiation behaves at different temperatures. [**ignacio2017**]

Wien's displacement law tells that the wavelength of the peak of the black body radiation curve decreases as the body temperature increases. This law can be used to describe different wavelengths according to the temperature of the black body which emits the radiation. Wien's law has the following equation:

$$\lambda_{max} = \frac{a}{T} \tag{4.2}$$

In Wiens displacement law 'a' denotes the Wien's displacement constant, this constant has the value $2.897 * 10^{-3} mK$. 'T' denotes the absolute temperature in kelvin. 'λ_{max}' denotes the wavelength of emission peak with unit in meters.[**ignacio2017**]

Stefan-Boltzmann's law tells that small changes in temperature will lead to big changes in emissive power. This is seen in Stefan-Boltzmann's equation because it states that the total emissive power is proportional to the fourth power of the absolute temperature. [**ignacio2017**]

$$E = \varepsilon * \sigma * T^4 \tag{4.3}$$

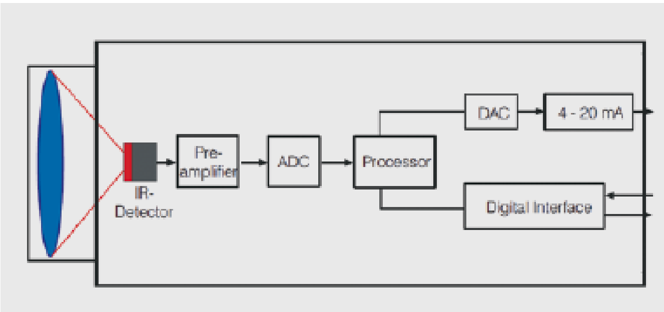
In Stefan-Boltzmann's equation 'E' denotes the total emissive power with unit W/m^2. 'σ' denotes the Stefan-Boltzmann's constant, this has a value of $5.67 * 10^{-8} W/m^{-2}K^{-4}$ and 'T' is the temperature in kelvin. 'ε' denotes the emissivity and is normally not a part of the Stefan-Boltzmann's law, but part of the modified Stefan-Boltzmann's equation, because it is used for calculation of temperature in most thermal cameras. Emissivity is different for all materials. Skin have an emissivity between 0.95 to 9.99, why these values typically are used when assessing the temperature of the skin of the human body with thermography. This law is important when considering infrared thermography because the sensitivity when calculating the temperature from the emissive power is big. [**ignacio2017**]

Region of interest

Region of interest (RIO) is an important consideration when doing measurements with thermal imaging. One of the reasons why this is an important aspect is because it is the RIO that lays the foundation of the data that goes into the statistical analysis. A minimum of 25 pixels is recommended for the RIO to reduce error in the data. To get the best measurement the RIO should be filling most of the image to get the best thermal data and better resolution in the area you want to measure. [**ignacio2017**]

Thermal cameras

The radiation emitted from an object is focusing the RIO onto a detector via a lens in the thermal camera. The radiation emitted to the detector generates an electric output proportional to the radiation. The output is then undergoing amplification before further signal processing that digitalizes the signal into pixels. This allows the final output signal to be viewed as a temperature for the object on an monitor, this is also illustrated on figure 4.3. [**optris2009**]



Figur 4.3: Simplified block diagram of an standard infrared camera.[**optris2009**]

The infrared radiation is made into an electrical signal in the camera, this data can be used in calculating the temperature for an object by knowing certain variables and putting these into Stefan Boltzmann's equation 4.3. The emissive power denoted E, is the radiation that the detector in the camera is getting. The variables σ are known and ε is specified for the object that is being measured, eg. the human skin with emissivity between 0.95 to 0.99. The temperature are then the only variable to calculate and this is done for each pixel in the image to make up the complete thermal image of the object. Each pixel will be representing one thermal data. [**ignacio2017**]

5 | The use of infrared imaging in vasomotion

In the following chapter an introduction to different techniques of measuring vasomotion will be giving. Here their methods and applicability for measuring vasomotion will be presented, with main focus directed towards thermal imaging as applied technique.