1 Introduction into Biomaterials Science

1.1.1 Define the following terms: Biomaterial, biologically derived material, (medical) implant, biocompatibility

A **biomaterial** is a material intended to interface with biological systems to evaluate, treat, augment or replace any tissue, organ or function of the body. (*ESB Consensus Conference 2*)
A **biologically derived material** is any material that originates from living organisms. Denaturised bone, for example, can be used as an implant.
A **(medical) implant** is defined as a medical device made of condensed matter (one or more solid state materials; rather seldom a liquid or liquid-like medium), intentionally placed within the body, either totally or partially beneath an epithelial surface.
Biocompatibility is the ability of a material to perform with an appropriate host response in a specific application.(*The Williams dictionary of Biomaterials, DF Williams, 1999, ISBN 0-85323-921-5*)

1.1.2 How is biocompatibility quantified today?

To quantify the biocompatibility of material which has no unit, different tests are applied according to defined standards (in vitro ISO10993). In general it includes:

- physico-chemical properties tests (guided by physicist, chemist);
- in vitro cell experiments (guided by biologist);
- in vivo animal tests (guided by veterinary doctor);
- clinical trials and studies (guided by medical doctor).

1.1.3 How can biocompatibility be quantified in general?

To quantify biocompatibility, one compares certain properties of materials under certain conditions, for example:

- particle release
- water uptake

- conductivity
- surface charges
- mechanical stimuli
- mechanical properties
- anisotropy
- surface chemistry
- surface morphology

1.2 Please define the term *biosensor*. Please explain how the five *human biosensors* work, in principle. Please provide the equivalent technical devices and give their working principles.

A **Biosensor** is a device to detect an analyte that combines one or more biological components with a physico-chemical detection unit.

Human biosensors:

(a) Nose $\Longrightarrow$ smell.
It works on a principle of receptor binding (chemical binding). Molecules of odorant suspended in air travel up the nose through the notrils. On the roof of the nasal cavity is the olfactory epithelium that contains specific receptors. Odor can stimulate these receptors. A single odorant molecule can bind to a number of olfactory receptors. After binding, the receptor undergoes structural changes. It creates chemical and electrical signals that travel along the nasal cavity to the olfactory bulb and afterwards to the brain.

(b) Tongue $\Longrightarrow$ taste.
It works according to principle of (chemical) receptor binding. Humans detect taste with taste receptor cells. These are clustered in taste buds. Each taste bud has a pore that opens out to the surface of the tongue enabling molecules and ions taken into the mouth to reach the receptor cells inside. The receptor cells respond by sending signals to the gustatory areas of the brain.

(c) Ear $\Longrightarrow$ hear.
In the ear, sound vibrations in the air lead to resonant vibrations of the basilar membrane inside the cochlea. The movement of hair cells, located all along the basilar membrane, creates an electrical disturbance that can be picked up by the surrounding nerve cells. Signals are transmitted to the brain by the cochlear nerve.

(d) Eye $\Longrightarrow$ see.
The retina contains two major types of light-sensitive photoreceptor cells used for vision: rods and cones. Rods cannot distinguish colours, but are responsible for low-light (scotopic) monochrome (black-and-white) vision. Cones are responsible for colour vision. When rods and cones are stimulated by light, the nerves send impulses through these fibres to the brain.

(e) Finger (skin) $\Longrightarrow$ touch. (Also sensitive to its chemical environment.)
The finger works like a force sensor and thermometer simultaneously. The receptors in the finger work only in a restricted physiological range. Signals are communicated to the brain via seneory nerves through tracts in the spinal chord.

The equivalent technical devices to human biosensors:

(a) Artificial nose
An artificial nose works like a chemical sensor. For example:

i. A quartz crystal vibrating at a known frequency, coated with a material that can absorb molecules only of a very specific size and shape. When this happens, its mass increases slightly, changing the frequency of the crystal's vibration. A simple circuit detects the change and signals that the chemical in question is present. Given an array of these sensors, each with a coating that responds to a different chemical, you can detect a wide range of species.

ii. A series of flexible, microscopic silicon beams each coated with a different polymer. When one of the beams absorbs a specific chemical, it bends slightly; the chip to which the beams are attached detects this change.

iii. Vapour-sensitive dyes called metalloporphyrins change color when exposed to certain chemicals. By examining the states of an array of

these dyes before and after exposure to analyte(s), a computer can essentially see smells.

iv. Synthetic systems that work in membranes which mimic cell walls use pattern recognition to create "fingerprint"' for specific odorants. (See Montenegro et al, Chemistry:a European Journal, vol 16 (47), 2010, pp14159-14166)

(b) Artificial tongue
The artificial tongue works like a chemical sensor. The general principles of its work are the same as for artificial nose.

(c) Artificial ear - Sensitive microphone
A microphone works like a pressure sensor. It is an acoustic-to-electric transducer or sensor that converts sound into an electrical signal. Most microphones today use electromagnetic induction (dynamic microphone), capacitance change (condenser microphone), piezoelectric generation, or light modulation to produce an electrical voltage signal from mechanical vibration.

- In the condenser microphone the diaphragm acts as one plate of a capacitor, and the vibrations produce changes in the distance between the plates. The voltage maintained across the capacitor plates changes with the vibrations in the air.

(d) Artificial eye - high resolution camera
An image sensor normally consists of a charge-coupled device (CCD) and a capacitor array (the photoactive region). When light strikes the sensor it is held as an electrical charge in each capacitor. The charge is proportional to the incident light intensity. The charges are connected to voltage one pixel at a time as they are read by the CCD. Additional circuitry in the camera converts the voltage into digital information.

(e) Artificial skin

i. Force sensor - haptic
Most early designs of haptic feedback use electromagnetic technologies such as vibratory motors with an offset mass, such as the pager motor which is in most cell phones or voice coils where a central mass or output is moved by a magnetic field. The electromagnetic

motors typically operate at resonance and provide strong feedback, but have limited range of sensations. Next-generation actuator technologies are beginning to emerge, offering a wider range of effects thanks to more rapid response times. Next generation haptic actuator technologies include electroactive polymers, piezoelectric, and electrostatic surface actuation.

ii. Thermal sensor - thermometer

1.3 What is the role of biomaterials in the field of tissue engineering?

The role of biomaterials in the field of tissue engineering is extremely important. Tissue engineering combines biological cells, **engineered materials**, and to a certain extent also suitable biochemical factors to improve or replace biological functions in an effort to effect advance medicine. As a result, the choice of a biomaterial is very important (type, shape etc.).

1.4 How can the hydrophobicity (wetting behavior) be quantified (formula)? Why can the contact angle of a droplet on a material covered by a monolayer of water not be directly measured? Please suggest different experiments for contact angle measurements.

Hydrophobicity can be quantified by measuring the contact angles of water droplets on a surface.
The contact angle θ_0 can be derived from the consideration of the thermodynamic equilibrium between the liquid droplet *(l)*, the solid substrate *(s)*, and the gas/vapor environment (ambient atmosphere - *(v)*).
At equilibrium, the solid-vapor interfacial energy γ_{sv}, the solid-liquid interfacial energy γ_{sl} and the liquid-vapour energy of the surface tension γ_{lv} can be written as the YOUNG equation. By the measurement of θ_0 , the equation can be used to determine one interfacial energy, if the other one is known. But if the material is unknown, we will have two unknown interfacial energies in one equation.

$$\gamma_{sv} = \gamma_{sl} + \gamma_{lv} cos\theta_0$$

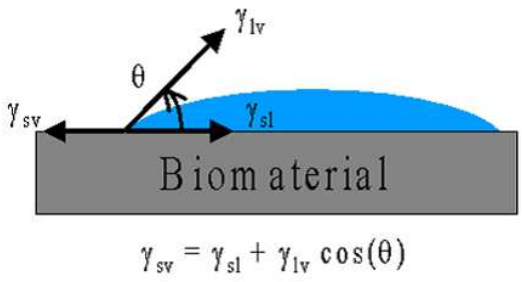

Figure 1: Measuring the contact angle.

The contact angle of a droplet on a material covered by a monolayer of water cannot be directly measured, because water always leads to the highest contact angle. If we have a water film there is no chance to measure, the contact angle will be zero.

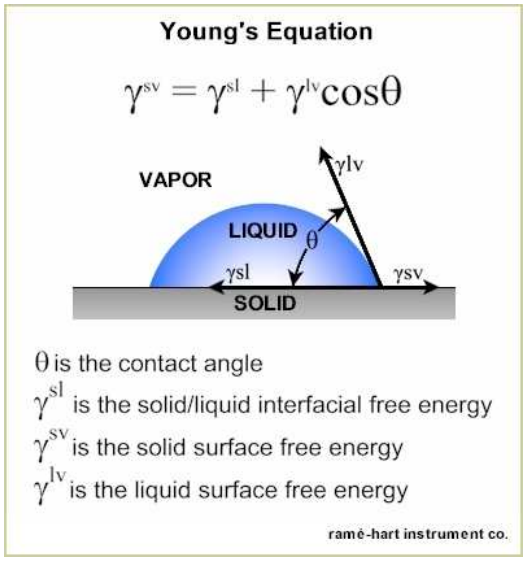

Figure 2: Measuring the contact angle.

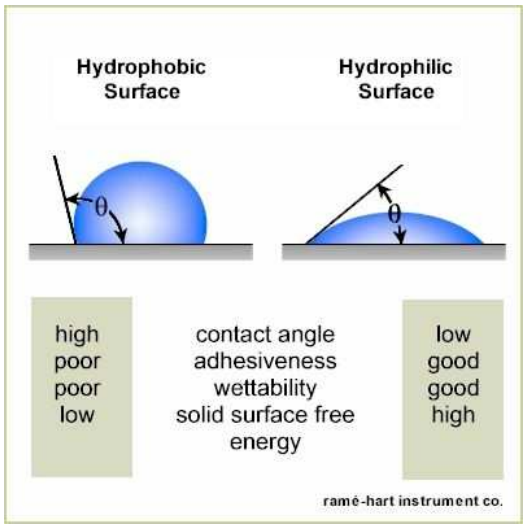

Figure 3: Hydrophobicity.

Ways to measure the contact angle:

(a) Sessile or Static drop
This is the most common type of measurement. A single reading on a static sessile drop shortly after its creation. A static contact angle is captured when a thermodynamic equilibrium is reached between the three phases: solid, liquid, and gas.

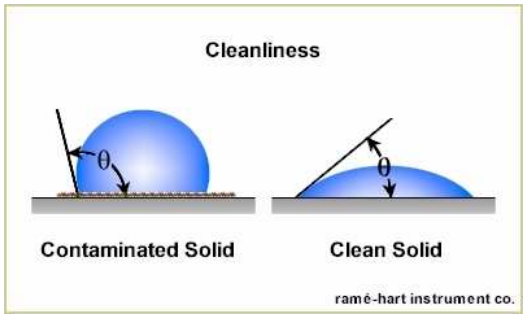

Figure 4: Sessile or Static drop.

(b) Plate method or Wilhelmy Method

An alternate method for measuring the contact angle involves lowering a plate into a test liquid and then removing it; and while doing so, measuring the force on the plate. This method is more complicated than the sessile drop method, requires large volumes of liquid, does not determine heterogeneity, and requires that the solid samples be fabricated to exact dimensions and have two identical surfaces. It also requires a precision force scale.

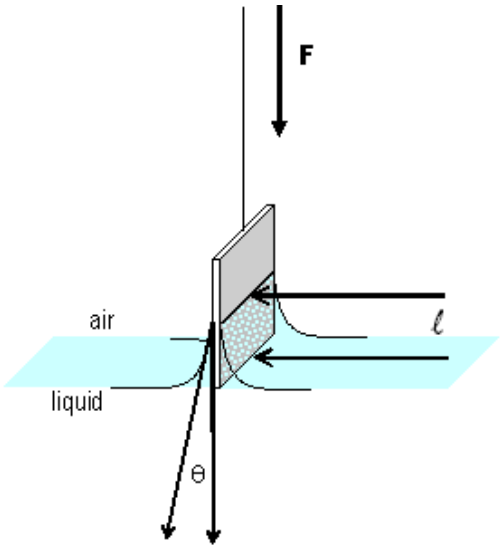

Figure 5: Wilhelmy Method.

(c) Captive air bubble method

An alternative to the Wilhemly plate method is the captive air bubble method. In this method, the contact angle is measured between an air bubble of defined volume and the solid surface immersed in the temperature controlled bath.

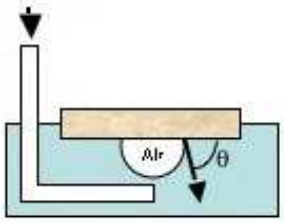

Figure 6: Captive air bubble method.

(d) Capillary rise method
The capillary rise method presents the only method of contact angle measurement available for the measurement of tubular materials and coatings. Temperature may be maintained in this method over a short period of time.

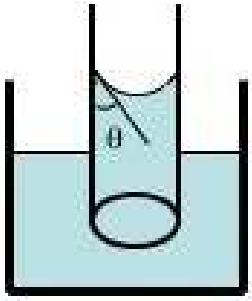

Figure 7: Capillary rise method.

(e) Tilting substrate method
The tilting plate method captures the contact angles measurements on both the left and right sides of a sessile drop while the solid surface is being inclined typically from 0 to 90^0. As the surface is inclined, gravity causes the contact angle on the downhill side to increase while the contact angle on the uphill side decreases. Respectively, these contact angles are referred to as advancing and receding angles. The difference between them is the contact angle hysteresis. In some cases, the drop will roll off the solid as wetting occurs at the roll-off angle. The last valid readings

are captured and normally represent the advancing and receding contact angles. In some cases, the solid can tilt all the way to 90^0 without the drop releasing. In this case, the final left and right contact angles are used.

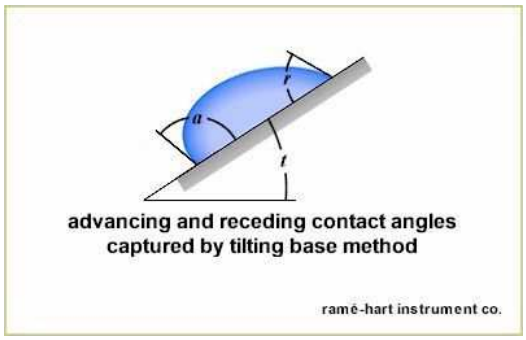

Figure 8: Tilting substrate method.

(f) Add and Remove Volume Method

This is a study that requires adding volume to the drop dynamically to the maximum volume permitted without increasing the three-phase line. The resulting maximum possible contact angle is referred to as the advancing angle. Volume is then removed from the drop. When the maximum volume that can be removed without reducing the three-phase line is reached, the resulting contact angle is measured. This angle is the receding angle. When the receding angle is subtracted from the advancing angle, the result is called the contact angle hysteresis. This method produces good results for determining the advancing angle. However, it is difficult to capture the receding contact angle using this method as the needle which must be imbedded in the drop to remove the volume is also disturbing the geometry of the drop profile. An alternate method for capturing the receding contact angle is the **evaporating method**. The drop is measured repeatedly as the volume evaporates. Just prior to dewetting and subsequent reduction in the three-phase line, the receding contact angle is measured.

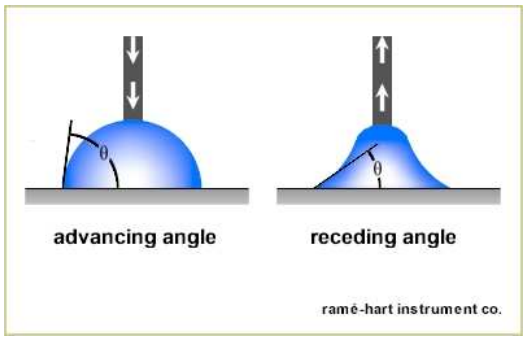

Figure 9: Add and Remove Volume Method.