TECHNISCHE UNIVERSITÄT WIEN
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Biocompatible materials
LV 308.106

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Non-metallic Materials

NMW

Dates and Lecture theatre

Monday 8:15 – 9:45 a.m. EI 1 Petritsch Hörsaal

03/10/2011	10/10/2011	17/10/2011
24/10/2011	31/10/2011	07/11/2011
14/11/2011	21/11/2011	28/11/2011
05/12/2011	12/12/2011	19/12/2011
09/01/2012	16/01/2012	23/01/2012

Assignment due to final grading

- Written examination (Dates and Rooms -> TISS)

  1 h 30 min
  no multiple choice test
  questions to be answered (ca. 12-15) about e.g.,
  - basics
  - definitions
  - testing of (bio)materials
  - materials and their application
  - damage mechanisms in biomaterials

  No standards or values to be known by heart!

Content (I)

1. Introduction
2. Biological environment and materials
    - 2.1. Basics and Definitions
    - 2.2. Biocompatibility, Material properties, Corrosion, Sterilisation, Surface
3. The biological system and its constituents
    - 3.1. Cell
    - 3.2. Tissue
    - 3.3. Immune System
4. Reactions of the Human Body on Materials and Components
5. Determination of Biocompatibility with *in vitro* and *in vivo* Methods

Content (II)

6. Biocompatible materials

6.1. Medical engineering materials

6.2. Anisotropic biocompatible fibre composites (Osteosynthesis plates, Screws)

6.3. Implants for the muscoloskeletal system

- Hip joint endoprosthesis
- Knee endoprosthesis
- Problems with (polymeric) sliding surface replacements
- Bone cements
- Testing methods (wear, fatigue, strength ...)

Content (III)

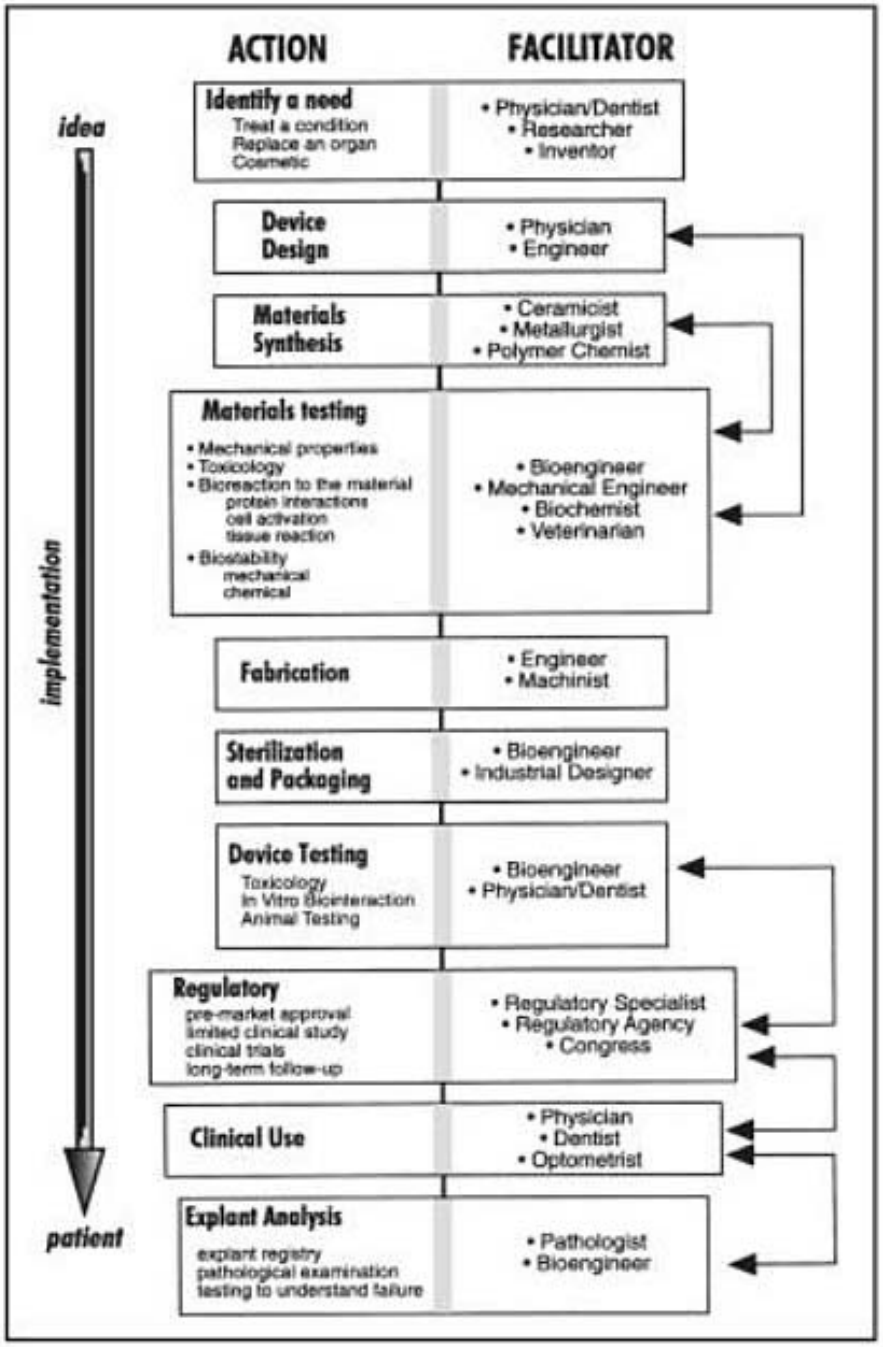
6. Biocompatible materials (continuation)
   - 6.4. Degradable osteosynthesis system for maxillofacial surgery
   - 6.5. Natural polymers
   - 6.7. Wound dressings and suture materials
   - 6.8. Implants for the blood circulatory system
   - 6.9. Materials and implants in ophthalmology
   - 6.10. Material applications in dentistry
   - 6.11. Controlled therapeutical systems
   - 6.12. Failure of implants

Further reading – Books (not exhaustive)

- J. Black, J. Hastings: Handbook of Biomaterial Properties *Chapman & Hall, London Weinheim, 1998*
- S. Dumitru: Polymeric Biomaterials
  Marcel Dekker, New York, 1994
- J.A. Helsen, H. J. Breme (eds.): Metals as Biomaterials
  John Wiley & Sons, Chicester, 1998
- R. Marxkors, H. Meiners: Taschenbuch der zahnärztlichen Werkstoffkunde *Hanser, München Wien, 1993*
- J. Park, R.S. Lakes: Biomaterial – An Introduction
  Springer, Berlin Heidelberg, 2007
- R. C. Portnoy: Medical Plastics - Degradation Resistance & Failure Analysis, *Plastics Design Library, Norwich, 1998*
- B. D. Ratner, A.S. Hoffman, F. J. Schoen and J.E. Lemons: Biomaterials Science - An Introduction to Materials in Medicine
  Academic Press, San Diego, 1996
- R. Schmid: Werkstoffverhalten in biologischen Systemen - Grundlagen, Anwendungen, Schädigungsmechanismus, Werkstoffprüfung, *Springer, Berlin Heidelberg, 1999*
- E. Wintermantel, S.-W. Ha: Medizintechnik mit biokompatiblen Werkstoffen und Verfahren, *Springer, Berlin Heidelberg, 2002*

Further reading – Journals (not exhaustive)

- Advanced Engineering Materials
- Advanced Functional Materials
- American Journal of Roentgenology
- Biomaterials
- Bio-Medical Materials and Engineering
- International Journal of Nano and Biomaterials
- International Journal of Oral Surgery
- Journal of Applied Biomaterials and Biomechanics
- Journal of Applied Polymer Science
- Journal of Biomaterials Applications
- Journal of Biomaterials Science Polymer Edition
- Journal of Biomedical Research
- Journal of Biomimetics, Biomaterials and Tissue Engineering
- Journal of Bone and Joint Surgery
- Journal of Oral & Maxillofacial Implants
- Journal of Prosthetics Dentology



Disciplines involved in biomaterials science and the path from a need to a manufactured medical device

B.D. Ratner et al., Biomaterials science, 2004

Uses of biocompatible materials

Problem area	Examples
Replacement of diseased or damaged part	Artificial hip joint, kidney dialysis machine
Assist in healing	Sutures, bone plates and screws
Improve function	Cardiac pacemaker, contact lens
Correct functional abnormality	Harrington spinal rod
Correct cosmetic problem	Augmentation mammoplasty, chin augmentation
Aid to diagnosis	Probes and catheters
Aid to treatment	Catheters, drains

J.B. Park, R.S. Lakes, An introduction to biomaterials, 1992

Biocompatible materials in organs

Organ	Examples
Heart	Cardiac pacemaker, artificial heart valve
Lung	Oxygenator machine
Eye	Contact lens, eye lens replacement
Ear	Artificial stapes, cosmetic reconstruction of outer ear
Bone	Bone plate
Kidney	Kidney dialysis machine
Bladder	Catheter

J.B. Park, R.S. Lakes, An introduction to biomaterials, 1992

European Regulations and International Standards

concerning medical devices with respect to biocompatible materials

(examples)

MEDICAL DEVICES SECTOR - LEGISLATION

European Directives regulate the marketing and putting into service of medical devices

- Directive 2007/47/EC of the European Parliament and of the Council of 5 September 2007 amending Council Directive 90/385/EEC on the approximation of the laws of the Member States relating to active implantable medical devices, Council Directive 93/42/EEC concerning medical devices and Directive 98/8/EC concerning the placing of biocidal products on the market.
  - Directive 2007/47EEC - OJ L247/ 21.9.07

- Active Implantable Medical Devices (AIMDD)
  - Directive 90/385/EEC - OJ L189/ 20.7.90

- Medical Devices Directive (MDD)
  - Directive 93/42/EEC - OJ 169/ 12.7.93

- In Vitro Diagnostic Directive (IVDD)
  - Directive 98/79/EC - OJ331/ 7.12.98

Directive Area: Active implantable medical devices 90/385/EEC

CEN Technical Body: CEN/CENELEC Joint Working Group on Active Implantable Medical Devices (CEN/CLC/JWG AIMD)

- EN 45502-1:1997:: Active implantable medical devices - Part 1: General requirements for safety, marking and information to be provided by the manufacturer
- EN 45502-2-1:2004:: Active implantable medical devices - Part 2-1: Particular requirements for active implantable medical devices intended to treat bradyarrhythmia (cardiac pacemakers)

Directive Area: Active implantable medical devices 90/385/EEC

CEN Technical Body: Sterilization of medical devices (CEN/TC 204)

- EN ISO 11135-1:2007:: Sterilization of health care products - Ethylene oxide - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices
- EN ISO 17665-1:2006:: Sterilization of health care products - Moist heat - Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices
- EN ISO 11137-1:2006:: Sterilization of health care products - Radiation - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices
- EN ISO 11137-2:2006:: Sterilization of health care products - Radiation - Part 2: Establishing the sterilization dose (corrected version 2006-08-01)
- EN ISO 11737-1:2006:: Sterilization of medical devices - Microbiological methods - Part 1: Determination of a population of microorganisms on products
- EN 556-1:2001:: Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices
- EN 556-2:2003:: Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 2: Requirements for aseptically processed medical devices

Directive Area: Medical devices 93/42/EEC
CEN Technical Body: Non-active surgical implants (CEN/TC 285) (I)

- EN ISO 5840:2005:: Cardiovascular implants - Cardiac valve prostheses
- EN ISO 7439:2002:: Copper-bearing intra-uterine contraceptive devices - Requirements, tests
- EN 12011:1998:: Instrumentation to be used in association with non-active surgical implants - General requirements
- EN ISO 9713:2002:: Neurosurgical implants - Self-closing intracranial aneurysm clips
- EN ISO 7197:2006:: Neurosurgical implants - Sterile, single-use hydrocephalus shunts and components
- EN 12006-2:1998:: Non active surgical implants - Particular requirements for cardiac and vascular implants - Part 2: Vascular prostheses including cardiac valve conduits
- EN 12006-3:1998:: Non active surgical implants - Particular requirements for cardiac and vascular implants - Part 3: Endovascular devices

Directive Area: Medical devices 93/42/EEC
CEN Technical Body: Non-active surgical implants (CEN/TC 285) (II)

- EN 14299:2004:: Non active surgical implants - Particular requirements for cardiac and vascular implants - Specific requirements for arterial stents
- EN ISO 14630:2008:: Non-active surgical implants - General requirements
- EN ISO 14602:1998:: Non-active surgical implants - Implants for Osteosynthesis - Particular requirements
- EN ISO 21534:2007:: Non-active surgical implants - Joint replacement implants - Particular requirements
- EN ISO 21535:2007:: Non-active surgical implants - Joint replacement implants - Specific requirements for hip-joint replacement implants
- EN ISO 21536:2007:: Non-active surgical implants - Joint replacement implants - Specific requirements for knee-joint replacement implants
- EN ISO 14607:2007:: Non-active surgical implants - Mammary implants - Particular requirements

Directive Area: Medical devices 93/42/EEC
CEN Technical Body: Non-active medical devices (CEN/TC 205)

- EN 1618:1997:: Catheters other than intravascular catheters - Test methods for common properties
- prEN ISO/DIS 3826-2:2007:: Plastics collapsible containers for human blood and blood components - Part 2: Graphical symbols for use on labels and instruction leaflets
- EN ISO 3826-3:2006:: Plastics collapsible containers for human blood and blood components - Part 3: Blood bag systems with integrated features
- EN ISO 10555-1:1995:: Sterile, single-use intravascular catheters - Part 1: General requirements
- EN 13726-1:2002:: Test methods for primary wound dressings - Part 1: Aspects of absorbency
- EN 13726-2:2002:: Test methods for primary wound dressings - Part 2: Moisture vapour transmission rate of permeable film dressings
- EN 13726-3:2003:: Non-active medical devices - Test methods for primary wound dressings - Part 3: Waterproofness
- EN 13726-4:2003 Non-active medical devices - Test methods for primary wound dressings - Part 4: Conformability
- EN 13726-6:2003:: Non-active medical devices - Test methods for primary wound dressing - Part 6: Odour control
- EN 14079:2003:: Non-active medical devices - Performance requirements and test methods for absorbent cotton gauze and absorbent cotton and viscose gauze

Directive Area: Medical devices 93/42/EEC
CEN Technical Body: Dentistry (CEN/TC 55)

- EN 1639:2004:: Medical devices for dentistry - Instruments
- EN 1640:2004:: Medical devices for dentistry - Equipment
- EN 1641:2004:: Medical devices for dentistry - Materials
- EN 1642:2004:: Medical devices for dentistry – Dental implants

Directive Area: Medical devices 93/42/EEC
CEN Technical Body: Medical devices utilizing tissues (CEN/TC 316)

- EN ISO 22442-1:2007:: Medical devices utilizing animal tissues and their derivatives - Part 1: Application of risk management
- EN ISO 22442-2:2007:: Medical devices utilizing animal tissues and their derivatives - Part 2: Controls on sourcing, collection and handling
- EN ISO 22442-3:2007:: Medical devices utilizing animal tissues and their derivatives - Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents

Directive Area: Medical devices 93/42/EEC
CEN Technical Body: Ophthalmic optics (CEN/TC 170)

- EN ISO 11979-8:2006:: Ophthalmic implants - Intraocular lenses - Part 8: Fundamental requirements
- EN ISO 14534:2002:: Ophthalmic optics - Contact lenses and contact lens care products - Fundamental requirements
- EN ISO 12870:2004:: Ophthalmic optics - Spectacle frames - Requirements and test methods

Directive Area: Medical devices 93/42/EEC
CEN Technical Body: Respiratory and anaesthetic equipment (CEN/TC 215)

- EN ISO 15001:2004:: Anaesthetic and respiratory equipment - Compatibility with oxygen
- EN ISO 5356-1:2004:: Anaesthetic and respiratory equipment - Conical connectors - Part 1: Cones and sockets
- EN ISO 5356-2:2007:: Anaesthetic and respiratory equipment - Conical connectors - Part 2: Screw-threaded weight-bearing connectors
- EN ISO 5366-1:2004:: Anaesthetic and respiratory equipment - Tracheostomy tubes - Part 1: Tubes and connectors for use in adults
- EN 1820:2005:: Anaesthetic reservoir bags
- EN 12342:1998:: Breathing tubes intended for use with anaesthetic apparatus and ventilators
- EN 13014:2000:: Connections for gas sampling tubes to anaesthetic and respiratory equipment
- EN 739:1998:: Low-pressure hose assemblies for use with medical gases
- EN 13544-2:2002:: Respiratory therapy equipment - Part 2: Tubing and connectors
- EN 1782:1998:: Tracheal tubes and connectors
- EN 1282-2:2005:: Tracheostomy tubes - Part 2: Paediatric tubes

Directive Area: Medical devices 93/42/EEC
CEN Technical Body: Assistive products for persons with disability (CEN/TC 293)

- EN ISO 22523:2006:: External limb prostheses and external orthoses - Requirements and test methods
- EN ISO 10328:2006:: Prosthetics - Structural testing of lower-limb prostheses - Requirements and test methods
- EN ISO 22675:2006:: Prosthetics - Testing of ankle-foot devices and foot units - Requirements and test methods

Directive Area: In vitro diagnostic medical devices 98/79/EC

CEN Technical Body: In vitro diagnostic medical devices (CEN/TC 140)

- EN ISO 20776-1:2006:: Clinical laboratory testing and in vitro diagnostic test systems - Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices - Part 1: Reference method for testing the in vitro activity of antim
- EN 13641:2002:: Elimination or reduction of risk of infection related to in vitro diagnostic reagents
- EN 12286:1998:: In vitro diagnostic medical devices - Measurement of quantities in samples of biological origin - Presentation of reference measurement procedures
- EN 12287:1999:: In vitro diagnostic medical devices - Measurement of quantities in samples of biological origin - Description of reference materials
- EN 14254:2004:: In vitro diagnostic medical devices - Single-use receptacles for the collection of specimens, other than blood, from humans
- EN 591:2001:: Instructions for use for in vitro diagnostic instruments for professional use
- EN 13975:2003:: Sampling procedures used for acceptance testing of in vitro diagnostic medical devices - Statistical aspects
- EN 14820:2004:: Single-use containers for human venous blood specimen collection

Biological system and materials

What is a biological system?

Biological System and Materials

The whole direct natural environment is the biological system that is in contact with the material.

Biocorrosion

Interaction between biological system and material as consequence of the direct contact; for investigations the direct environment is considered

Influence of far-ranging effects influenced by the transport systems of the cells

→ Long-time behaviour

Biological System and Materials

- Biocorrosive material damage
  - Partial degradation on polymers (e.g., plasticizer (Weichmacher))
    - Negative: brittleness of sealing materials in the waste water field
    - Positive: Recycling by biodegradation
  - Destruction of surfaces by colonisation with e.g., bacteria and lichen (Flechten) as well as their metabolites
  - Biofilms
- Damage by higher organisms
- Usage of material surfaces as places for colonisation
- Bio-chemical engineering (Organisms as producers)

Selection of materials

1. Translation
2. Screening
3. Ranking
4. Consider the limiting factors

Requirements on materials and components for medical use

- Biocompatibility
- Mechanical properties
- Corrosion resistance
- Sterility
- Surface properties

Historical overview about recent metallic biomaterials (R. Schmidt, 1999)

Material	Alloy	Application	
		since	for
CrNi steel	CrNi 18.8	1919 1926	dentistry orthopaedics
CrNiMo steels	CrNiMo18.10.2	ca. 1935	orthopaedics
Co basis alloys	CoCrMo cast alloy	1932 1936	dentistry orthopaedics
	CoCrWNi wrought alloys	1952	orthopaedics
	CoCrNiMo wrought alloys	1970	orthopaedics
Ti basis	Pure titanium	1951	orthopaedics
Tantalum		1938	orthopaedics

Implants

- Support or replacement of cell or tissue functions
- The materials selection depends on
  - **Kind** and
  - **function of the tissue that has to be replaced e.g.,**
    - Implants with the function load application or load transfer (like hip implants) -> optimum stiffness and fatigue strength
    - Implants for the blood circulatory system (like artificial vessels) -> chemical composition of the material surface, flexibility
- Relevant factors for the success of an implant are:
  - Biocompatibility
  - Patient's health state
  - Characteristics of the surgery and the following therapy

Implants

Interactions

- Demands on biocompatibility depend among others from the state of health of the patient
- Implant materials influence healing processes:
  - **Specific surface** influences the interface which allows the controlling of the ingrow of the tissue
  - **Tissue reactions** are influenced by
    - Chemical composition
    - Surface energy
    - Hydrophilic character of the materials surface
    - Corrosion
    - Relative motions
- Geometry and dimension must also be considered

Implants

Influences on Biocompatibility

- Intrinsic properties
- Processing
  - High fatigue strength of cobalt based alloys is only reached by forging
  - Ceramic components in the hip joint (ball, cup) must have an optimum surface quality (low average grain size)
- Clinical after-treatment (sterilisation)
  - For polymers the selection of the sterilisation method is of great importance (long-time behaviour)
  - Some ceramics are sensitive to moisture at high temperature

Materials and Application in Implantology (Selection)

Application	Materials			
	Metals	**Polymers**	**Ceramics**	**Composites**
Osteosynthesis / Joint replacement	Stainless steels Ti and Ti alloys CoCr alloys; Tantalum	PE (PE-UHMW), LCP PMMA, PEEK, PCU PLA/TMC/PGA	Aluminium oxide Zirconium oxide Calcium phosphate	CFR-PEEK
Vascular / cardiac surgery	Stainless steel CoCr alloys Ti alloys (Nitinol) Ta alloys, gold	PET PTFE Polysiloxanes PUR	Pyrolytic carbon	
Dentistry	Ti and Ti alloys CoCr alloys Amalgam (HgAgSn) Gold alloys	PMMA Polyacrylic acids	Aluminium oxide Zirconium oxide Calcium phosphate Porcelain	“Composites” (dental fillings)
Ophthalmology		PMMA, PHEMA Polysiloxanes, Hydrogels PE (PE-HD)	Calcium phosphate	
Surgical devices	Stainless steels Ti alloys	POM (Bone cement mixer components)		CFR-PEEK

Technical materials

Metals

- metallic bonding in the solide state (mixtures or solutions -> alloys)

Polymers

- Carbon containing materials that are joined in a chain-like structure by covalent bonding

Ceramics (inorganic glasses)

- inorganic materials with ionic or covalent bonding; Carbon is often associated with ceramics because of its ceramic-like properties

Composites

- in engineering a material that consists of at least two distinct parts

Chemical bonds in materials

Table 2.1 Strength of different chemical bonds reflected from their heat of vaporization*

Bond type	*Substance*	*Heat of vaporization (KJ/mol)*
Van der Waals	He	0.14
	N_2	13
Hydrogen	Phenol	31
	HF	47
Metallic	Na	180
	Fe	652
Ionic	NaCl	1062
	MgO	1880
Covalent	Diamond	1180
	SiO_2	2810

*Adapted from Harris and Bunsell (1977).

Designed biomaterials

in the 1960s specially designed materials for medical devices

- Silicones
- Polyurethanes
- Polytetrafluoroethylene (Teflon®)
- Hydrogels
- Poly(ethylene glycol)
- Poly(lactic/glycolic acid)
- Hydroxyapatite
- Titanium
- Bioglass®

Basics in materials properties as a recapitulation

Loading of materials and components

Mechanical/structural loads

- Tension / compression
- Shear
- Bending
- Torsion
- Hydrostatic pressure

Mode of action

- static
- dynamic
- cyclic

Behaviour of materials towards external load

- Reversible deformation
- Irreversible deformation
- Rupture

Types of material behaviour

- Elastic
- Non-linear elastic
- Visco-elastic
- Plastic
- Isotropic vs. Anisotropic

- Brittle (fracture before yield)
- Ductile (yield before fracture)

The elastic modulus

Elastic modulus, Young‘s modulus, modulus of elasticity

= slope of the stress-strain curve in the elastic deformation range

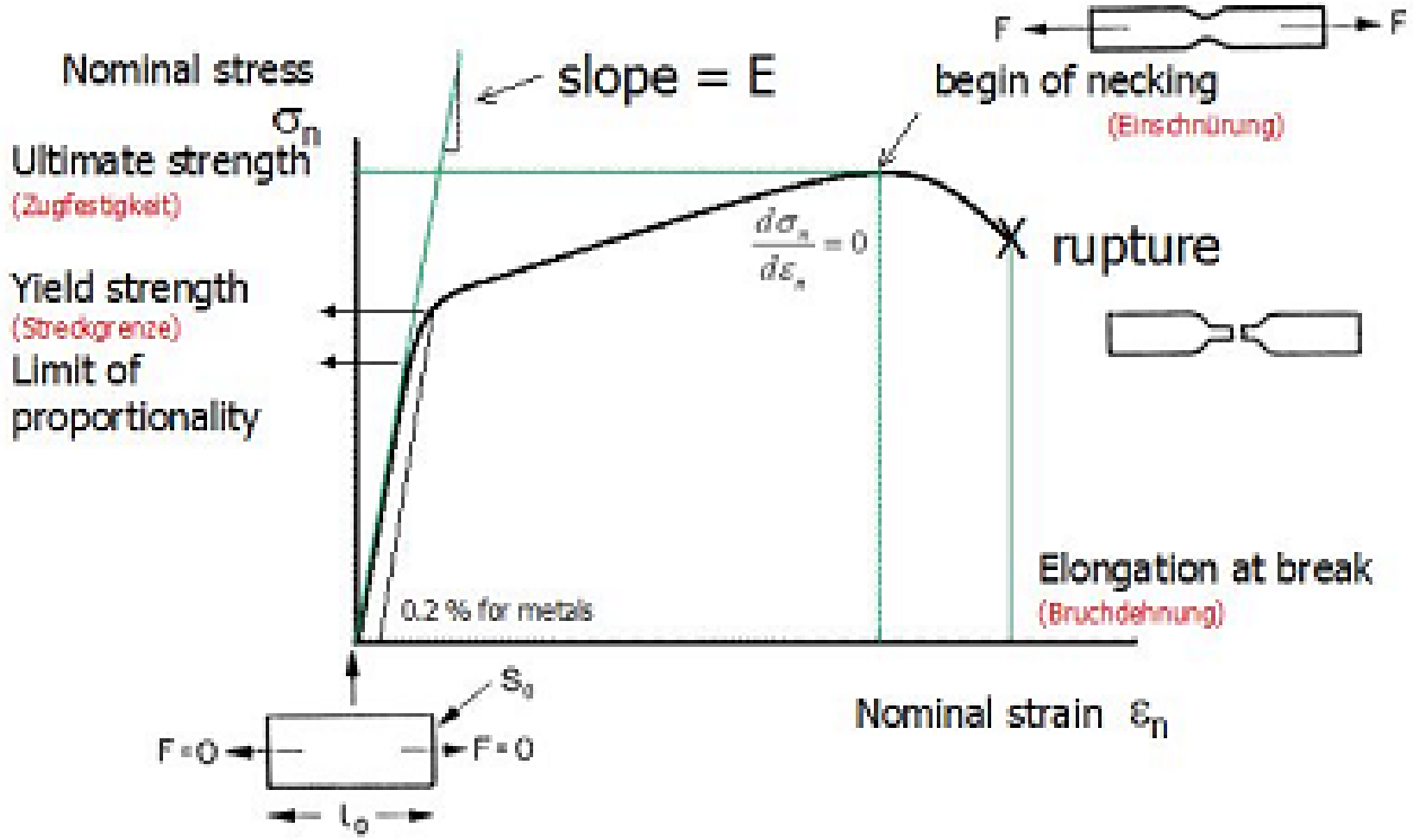
$$\sigma = E.\ \varepsilon$$

Stress (σ) = F/A F...force causing the deformation; A...Area to which the force is applied ($N.mm^{-2}$ or Pa)

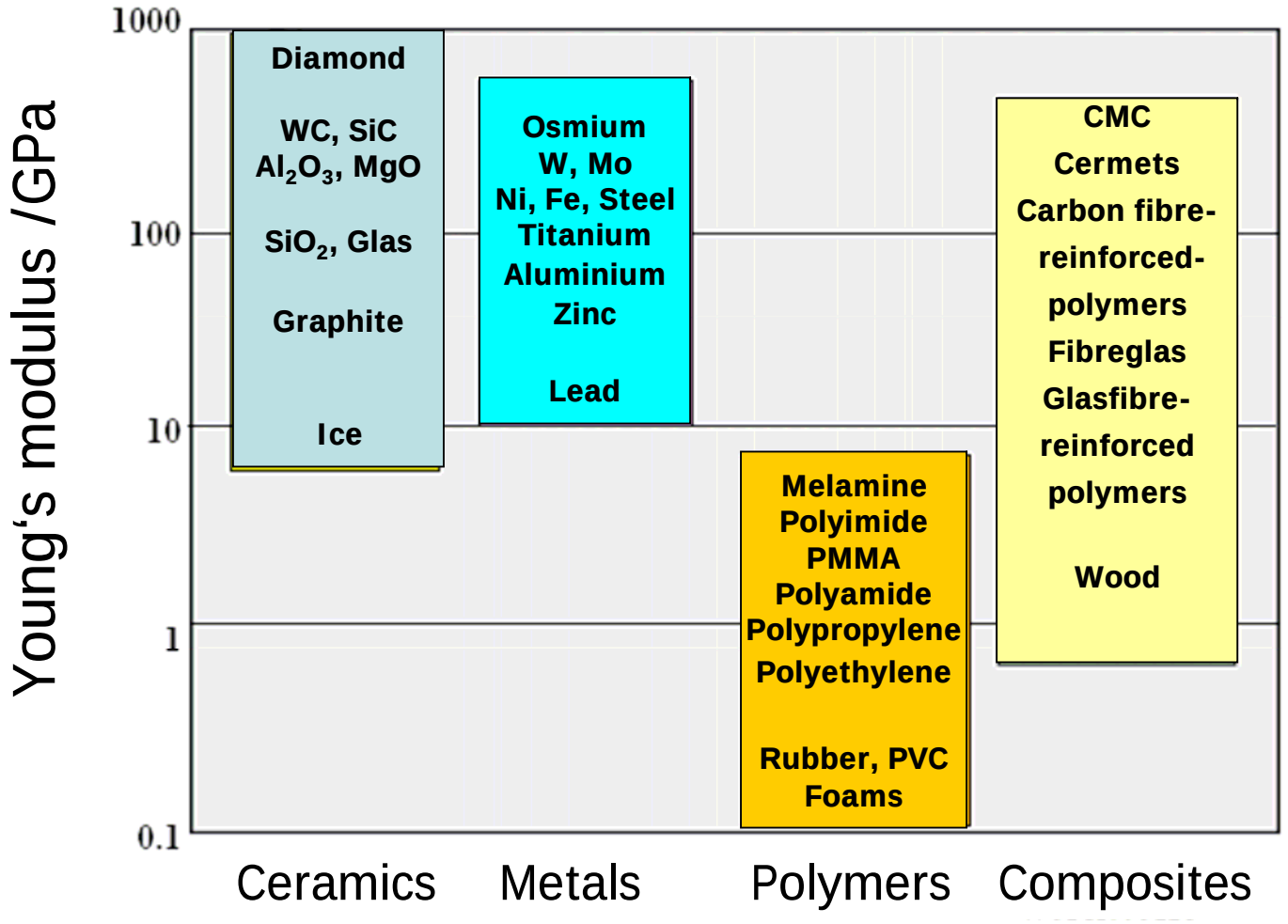
Strain (ε) = $\Delta l/l$ Δl...Change in length; l...Initial length (unitless)

Elastic modulus or Young‘s modulus (E) ($N.mm^{-2}$ or Pa)

Elastic modulus from tensile testing

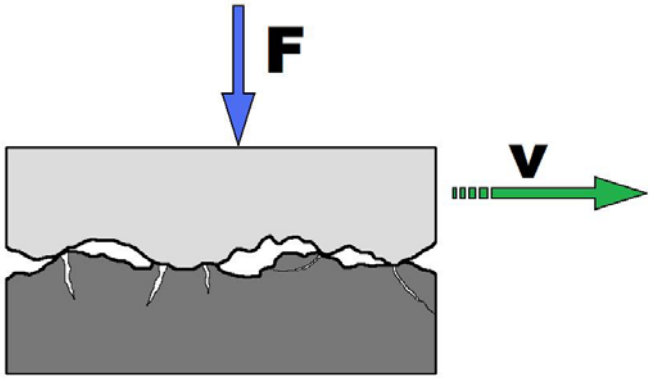


E-modulus of different material categories



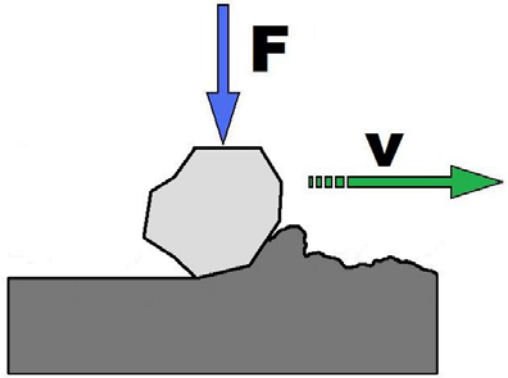
Main Wear Mechanisms

Surface fatigue wear



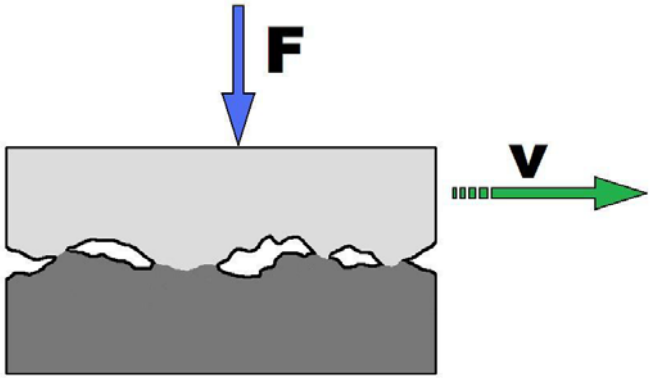
Crack initiation and propagation

Abrasion wear



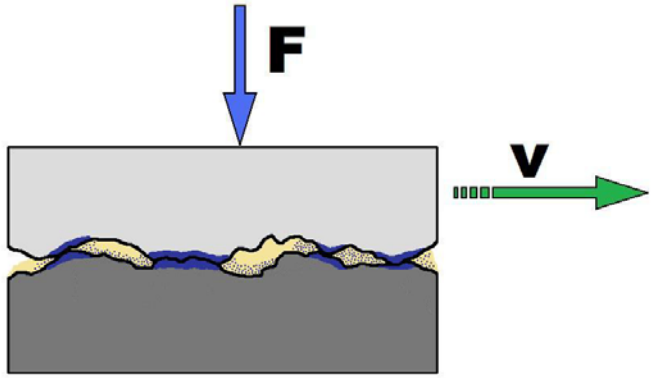
Scratch formation and plastic flow

Adhesive wear



Material transfer, cold-welding junctions

Tribo-chemical wear



Formation and removal of reaction products (e.g., particles)