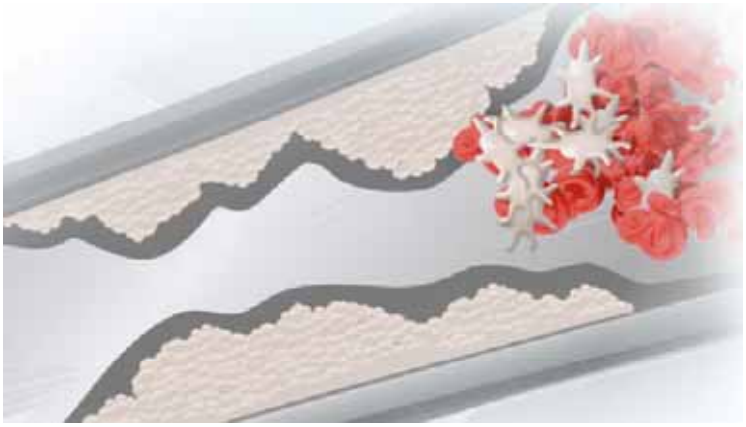
Antithrombogenic coating with SiC



MB - JASS 09
Kathrin Lorenz
Flavius Deleanu

Max Schaldach - Stiftungsprofessur
Biomedizinische Technik MSBT

Antithrombogenic coating

Outline:

- → **Blood** composition
- → **Fibrinogen/Fibrin**
- → **Proteins**
- → **Coagulation** cascade
- → Avoidance of the **electron transfer**
- → Coating with **α-SiC:H**
- → **PECVD**
- → **Quality** of the α-SiC:H- layer

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Antithrombogenic coating

Major **challenge** for today's **stent development**:

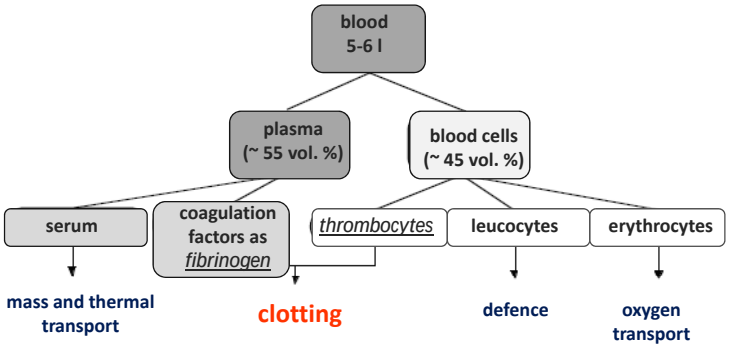
reduction of acute and subacute **closure** as well as **restenosis**

Problem:

implant materials lead to the formation of a **thrombus**, respectively a clot. This can lead to a **failure** of the **implant**.

Antithrombogenic coating

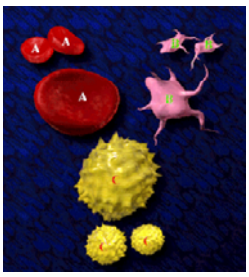
Blood composition



Antithrombogenic coating

Appearance:

- **Red cells**: $5*10^6$ /ml (= erythrocytes)
- **White cells**: $7*10^3$/ml (= leucocytes)
- **Plateles**: $3*10^5$/ml (=thrombocytes)



Plasma composition:

water - 90%, **proteins** - 7%, **inorganic c.**(Na^+, K^+, Mg^{2+}, Ca^{2+}, PO_4^{3-}…) - 1%, **organic c.**(urea, fats, cholesterol, glucose…) -2% of plasma volume

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Antithrombogenic coating

The accumulation of a thrombus is a **blood- plasmatic coagulation cascade** of biochemical processes

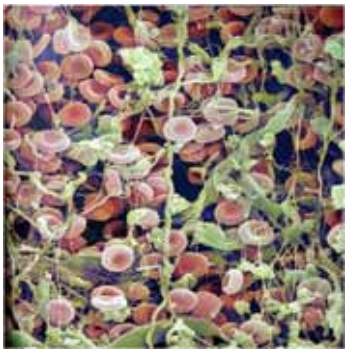

Figure left: microscopic view on a thrombus

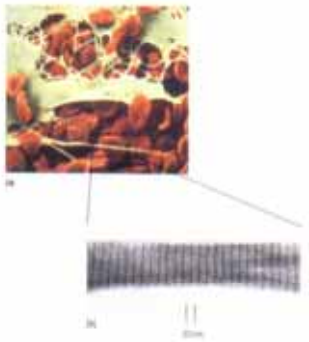

Figure right: electronic micrography of a fibrin section

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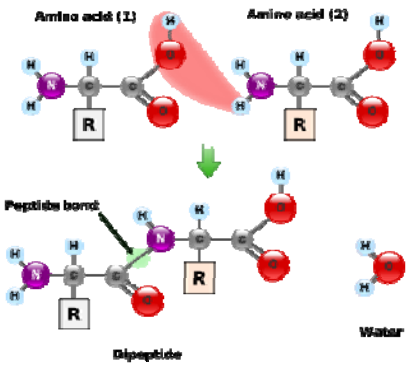
Antithrombogenic coating

Starting point of the thrombus formation is an **electron transfer** form the **fibrinogen** to the **solid**:

Figure: model of fibrinogen:
- Consisting of ~ **3000 amino acids; ~ 50 nm length**
- Arranged in **2 sets of 3 peptide chains** (α, β, γ)

Antithrombogenic coating

What are **proteins**?

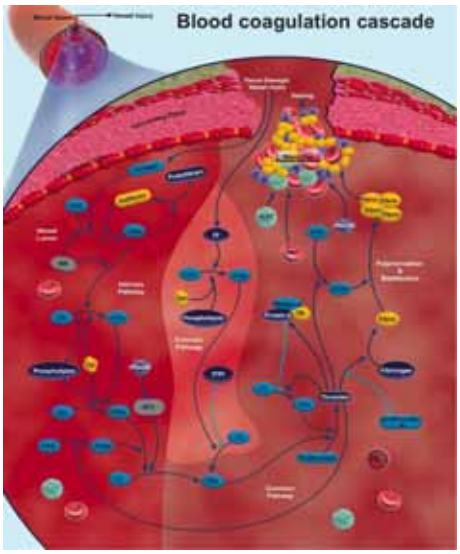


→consist of amino-acids

→ 21 different amino-acids

→ peptides = amino-acid-chains

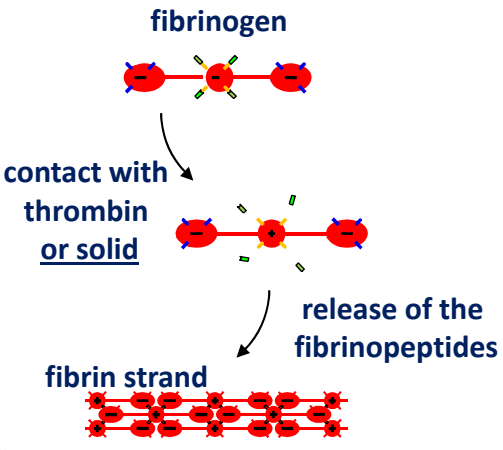
Antithrombogenic coating



Coagulation cascade for the case of a vessel damage (**blood-stopping**):

→ Numerous proteins catalyze various steps in the cascade

Activation of Fibrinogen



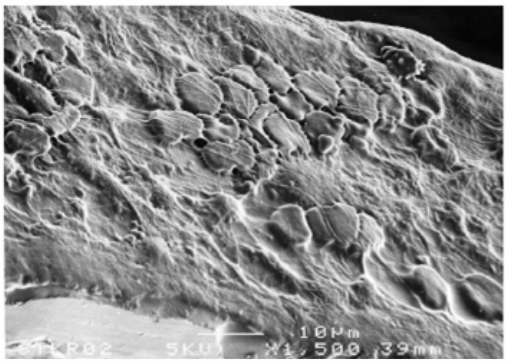
Electron transfer leads to **release** of **fibrin- peptides:**

→**new charge** distribution of fibrin

→ **attraction** between fibrin-monomers

→formation of a **strand**

Antithrombogenic coating



Scanning electron micrography (1500x):
→**Dense layer** of blood proteins and formed elements covered by **fibrin- strands** already **after 1 day**!

Antithrombogenic coating

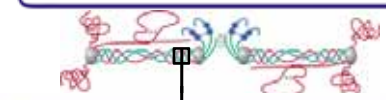
Hypothesis of the physical process:

→ **Contact activation** of fibrinogen takes place with an **electron transfer**

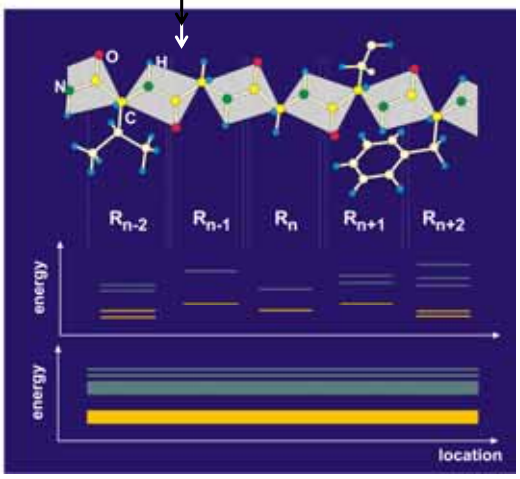
→ Proteins like fibrinogen have an electronic **structure** similar to that of **amorphous semiconductors**

→ **Contact activation** is determined by the **electronic properties** of the macromolecule and the material

Antithrombogenic coating



fibrinogen

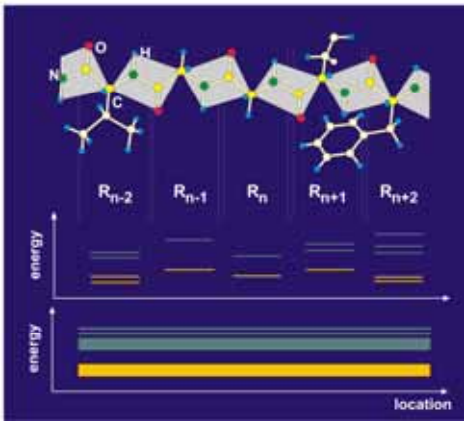


The **amino acids** in the peptide chains:

electronic structure similar to atoms

electronic states

Antithrombogenic coating

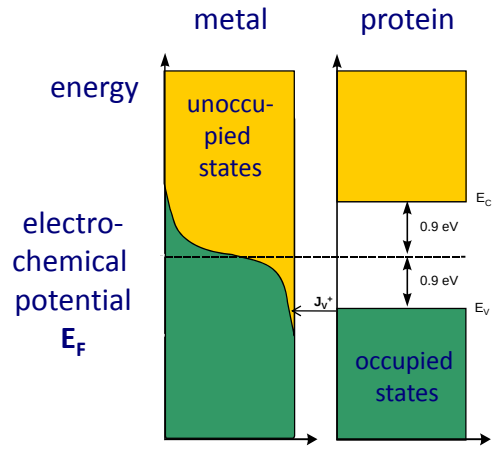


Energy level determined by the **type** of specific side **chain**

Electronic **interaction** of chains → higher and lower **density of states** in the macromolecule

Electronic states occupied up to **Fermi level E_F** → region of **low density**

Activation of Proteins on Solid Surface

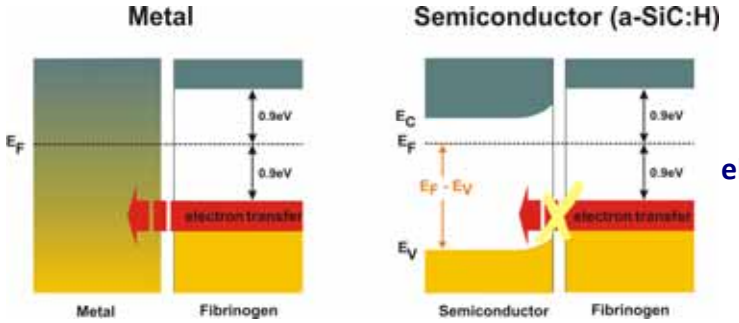


transfer current:

$$j_p^+ = C \int_{-\infty}^{E_V^+} T(E) n^{red}(E) p^{ox}(E) dE$$

n = # occupied states
p = # unoccupied states

Antithrombogenicity

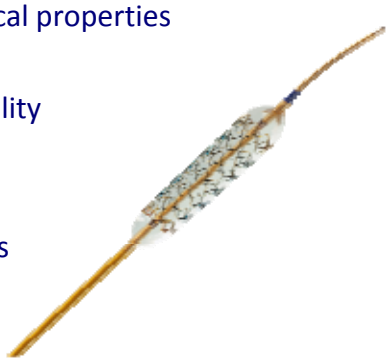


How can you **avoid electron transfer** from **fibrinogen to the solid**?

Solid: **no empty electronic states** at the transfer level (deeper than 0,9 eV below Fermi's level E_F)
Preventing charging of the interface (band- bending): conductivity must be higher than 10^{-3} S/cm

Material selection – Hybrid concept

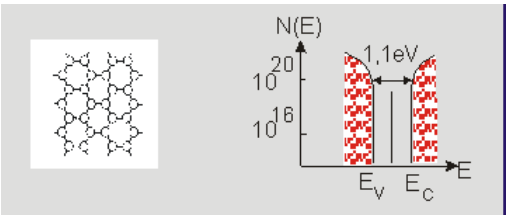
- **Bulk material**: mechanical stability, plastic deformation, longitudinal flexibility
  - → **316 L** show superior mechanical properties
    but…
    poor hemo- and biocompatibility
- **Surface**: non-activating
  - → has to fulfill critical parameters
  - → **Semiconductor** is chosen



Material selection - Semiconductor

- **Density of states** in band gap

c-Si

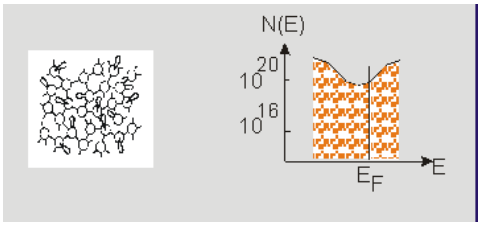


→E_{crit} = 0,55 eV
→ crystalline layer → easy chipping of

Material selection - Semiconductor

- **Density of states** in band gap

a-Si

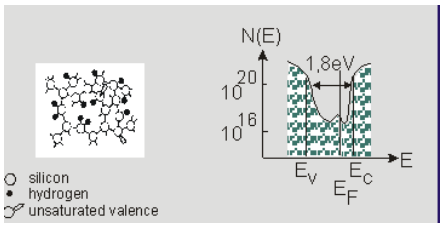


→Good mechanical properties
→No band gap

Material selection - Semiconductor

- **Density of states** in band gap

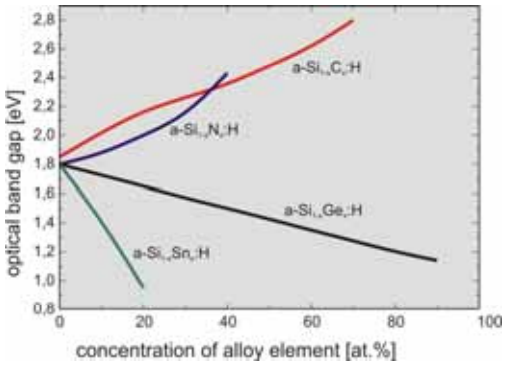
a-Si:H



→**Saturation** of the **dangling bonds** with **H**
to create a band gap

Material selection - Semiconductor

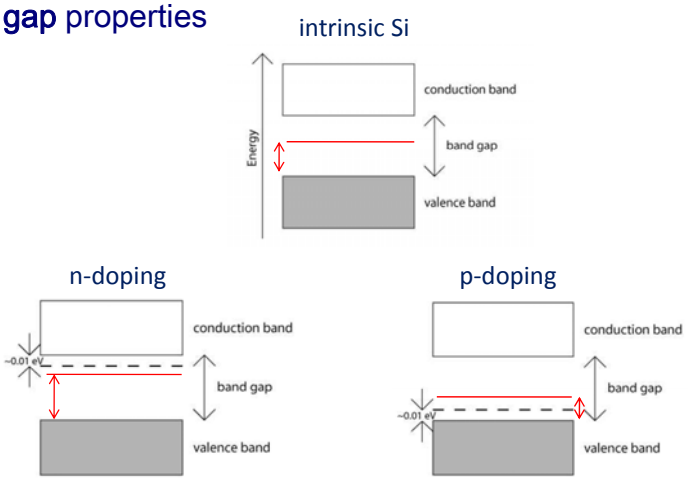
- **Band gap** properties



→ Alloying with **C** to **increase** the **band gap**

Material selection - Semiconductor

- **Band gap** properties

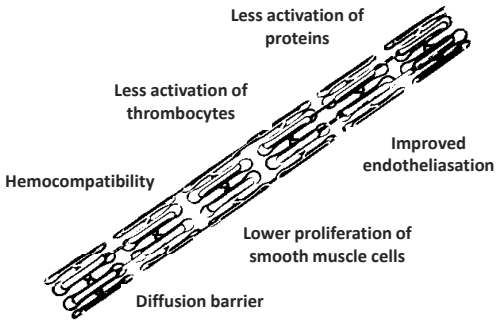


→ **Doping** with **P** (n) to shift the **fermi level** and to **increase** E_{crit}

a-SiC:H

Material of choice:

amorphous hydrogen-rich phosphorous-doped silicon carbide (**a-SiC:H**)



Stent production

316L tube
(1.6mm diameter)

laser cutting

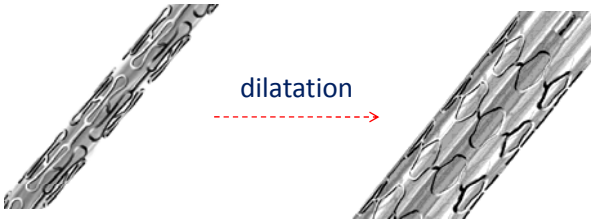
mordant

bare stent

Stent production

annealing

Optimization of mechanical properties



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Stent production

Electro-polishing

Minimization of surface roughness

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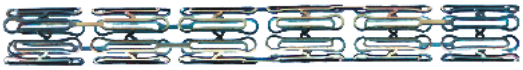
Stent production

Galvanic gold plating → Improvement of x-ray visibility

→ Coating with antithrombogenic a-SiC:H



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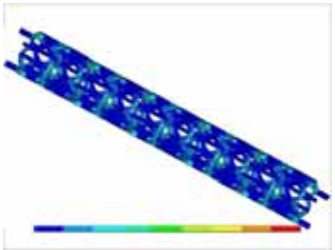
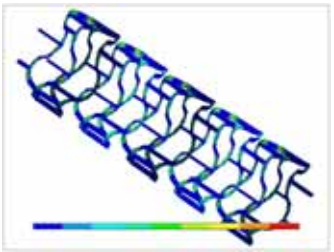
a-SiC:H

- How **realize** an a-SiC:H-coating?
- **Thickness** of layer?
- Can we achieve a **good adhesion**? Layer has to withstand mechanical stresses during dilatation (40 % strain)!





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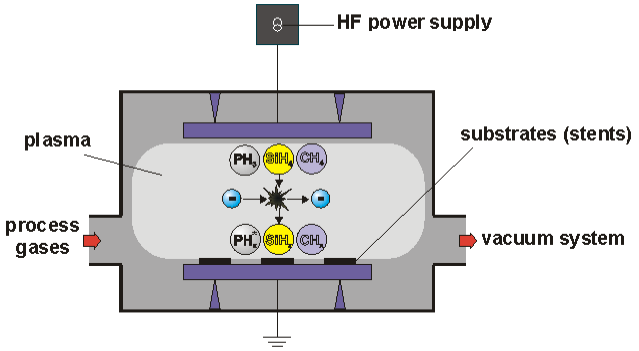
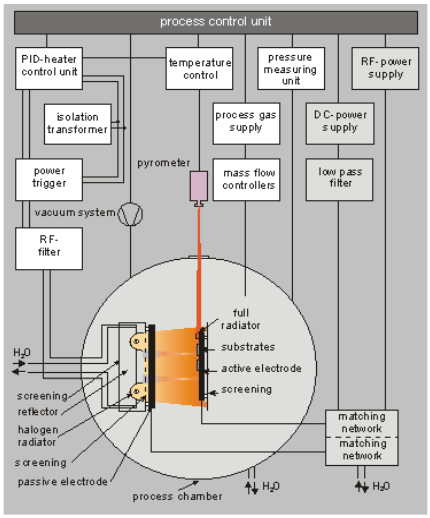
Coating: PECVD process

Pretreatment: cleaning and surface activation (**plasma etching)**



Process gases: silane (SiH_4), methane (CH_4), phosphine (PH_5)

PECVD process

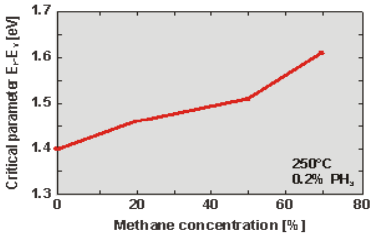


Capacitive coupled plasma (13,56 MHz)

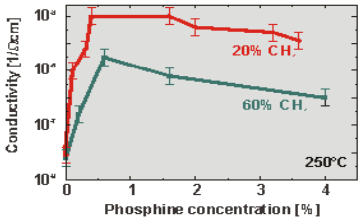
P = 0,16 W/cm²
p = 0,1 mbar
T_{subst} = 250 °C
T = 2,5 h

Calibration of process

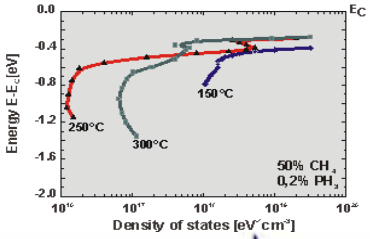
Critical parameter



Conductivity



Density of states



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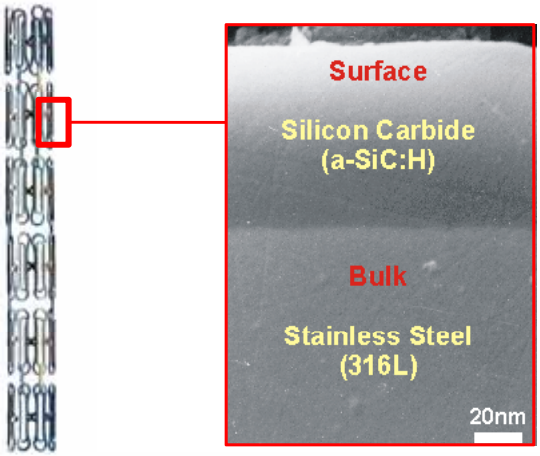
Coated layer



a-SiC:H coating

- amorphous
- phosphore-doped
- hydrogen rich
- thickness ~ 100 nm

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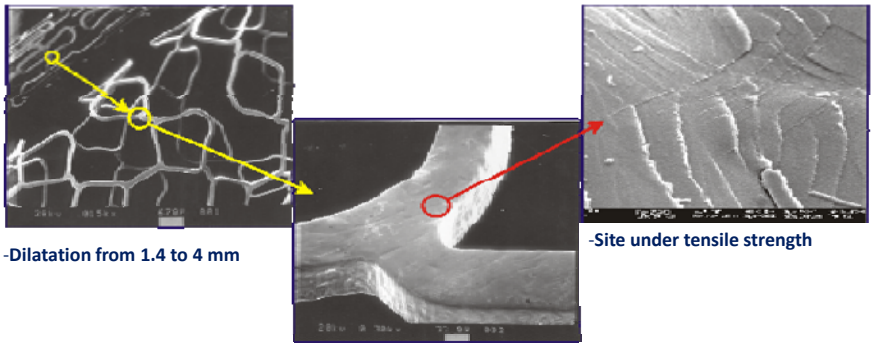
Adherence under tensile strength



-Dilatation from 1.4 to 4 mm

-Site under tensile strength

→ **Tight connection between a-SiC:H coating and stent body**

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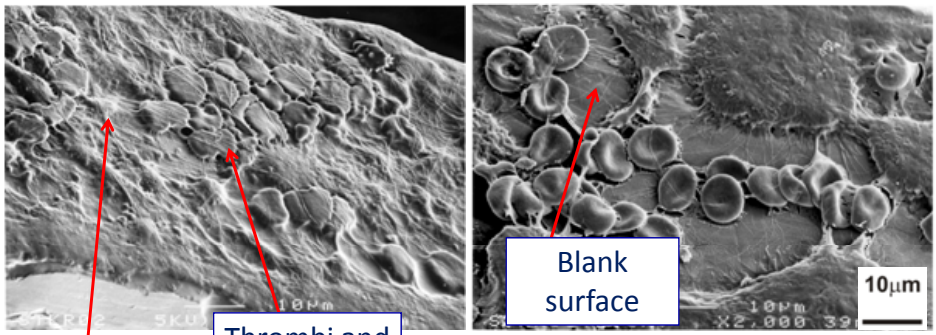
Hemocompatibility of Silicon Carbide Coating

Stainless Steel (316L) **Silicon Carbide (a-SiC:H)**

1 day in contact with blood



SEM images

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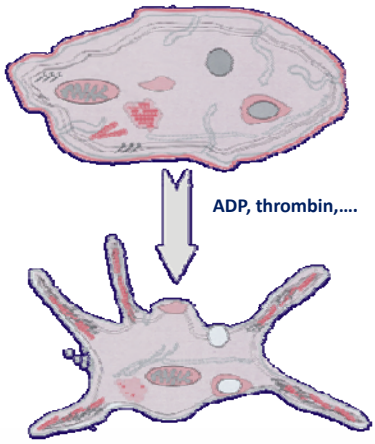
Activation of cells



Resting thrombocyte

Activated state

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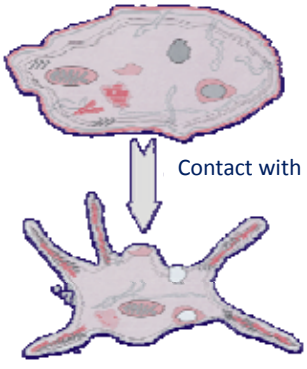
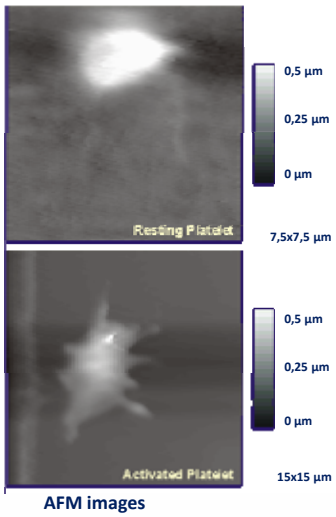
Improvement of cell interaction

Silicon Carbide (a-SiC:H)



Stainless steel (316 L)



AFM images

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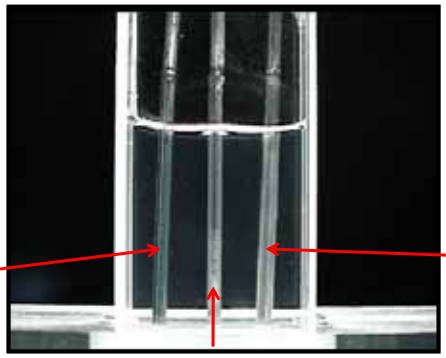
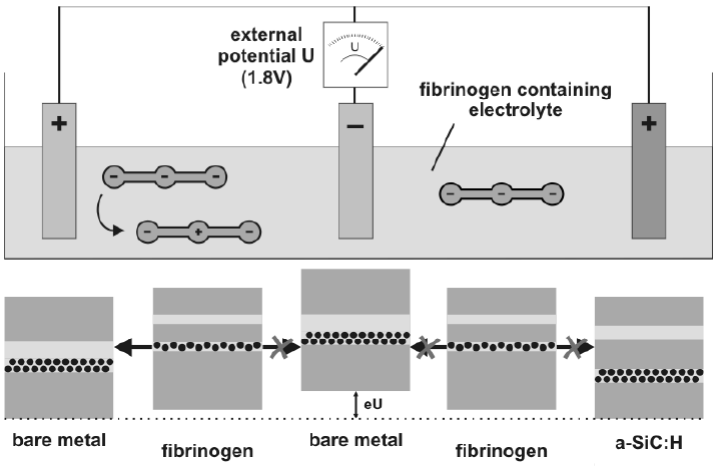
Experimental Setup

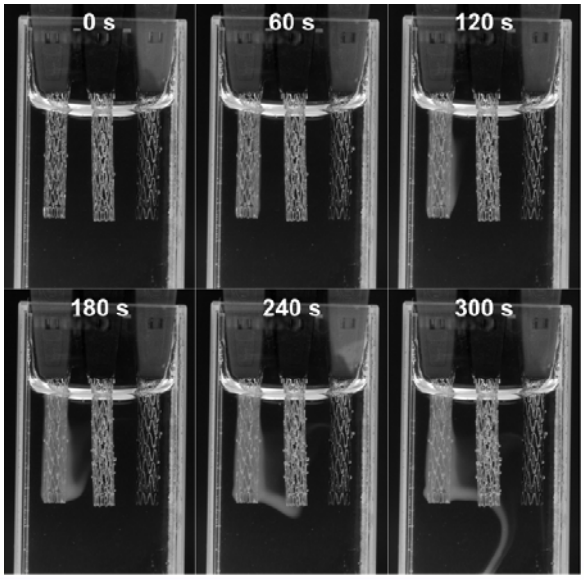
- Electrolyte with **fibrinogen** (physiological concentration 4 g/l)
- 3 electrodes



Experiment – Electronic Model



Experiment



→ Verification of the electronic model

→ No fibrin formation at the coated stent