



# On the path forward to biomedical applications of natural polyfunctional compounds - humic substances

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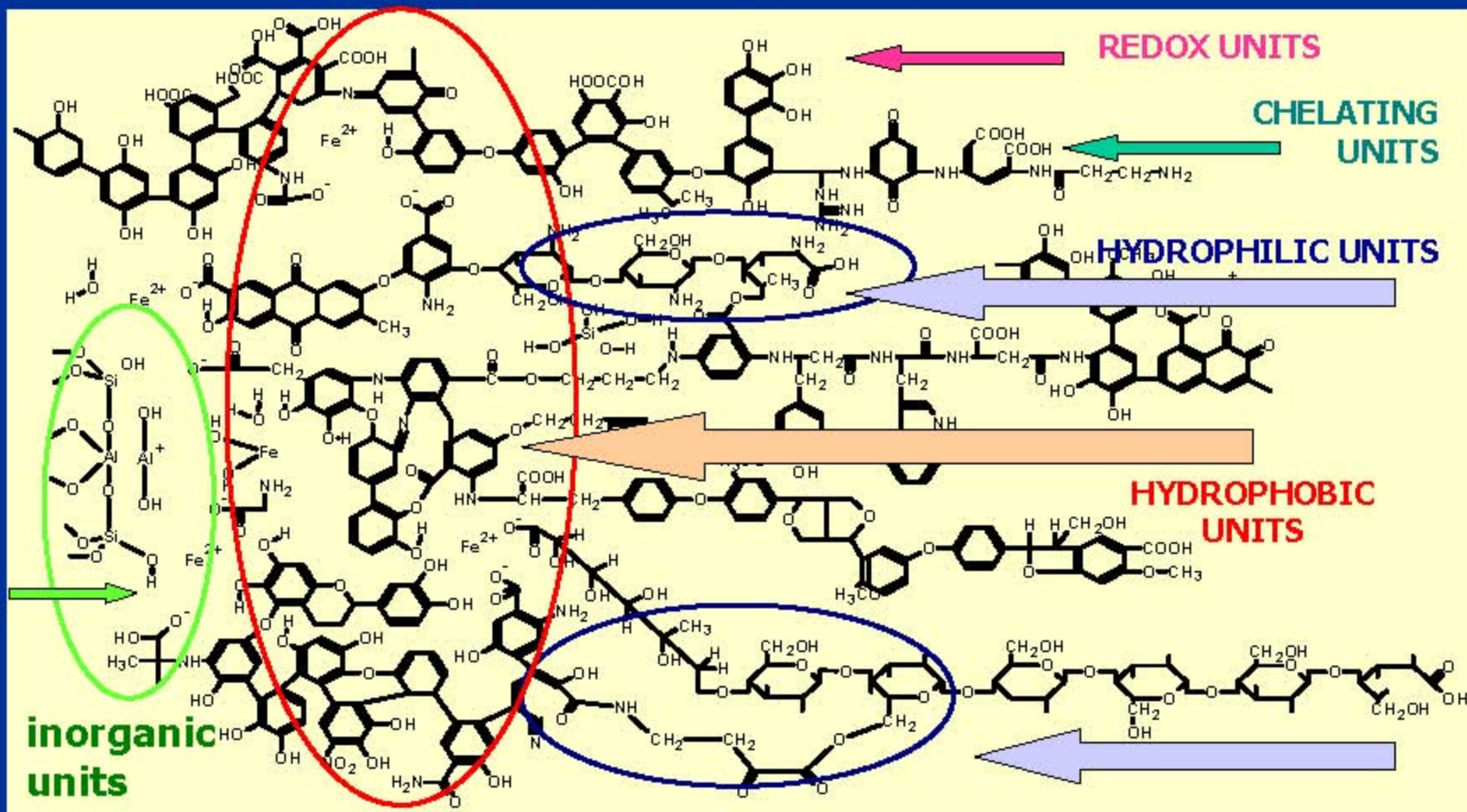
The 1<sup>st</sup> International Conference on Humic Innovative Technologies  
November 4-8, 2010, Lomonosov MSU, Moscow, Russia



**HiT2010**  
Conference

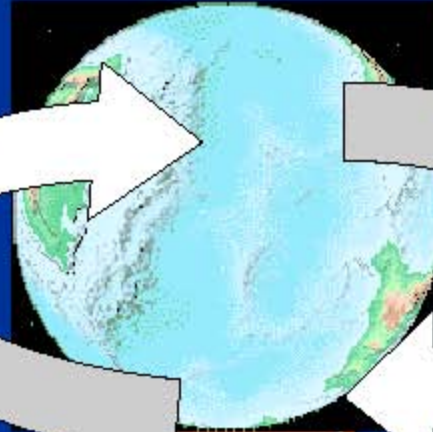


# HUMIC MOLECULES: KINGDOM OF FUNCTIONS





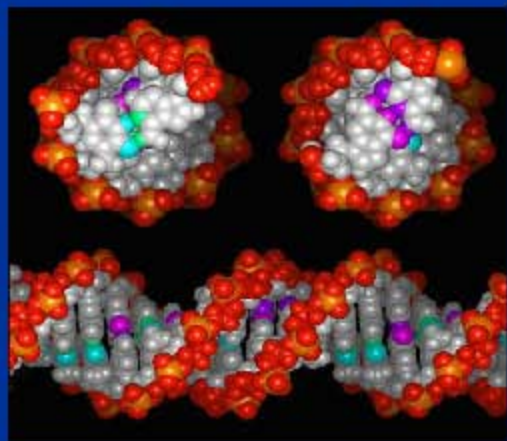
# EARTH, IN LATINE - HUMUS...



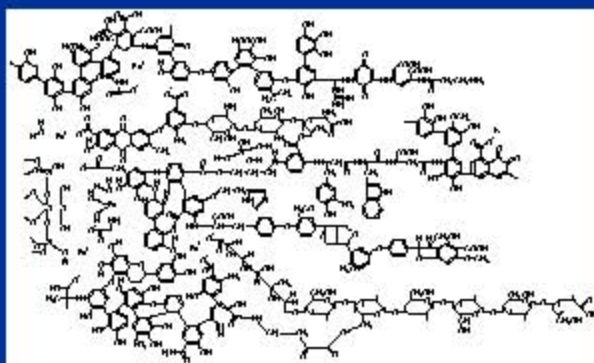
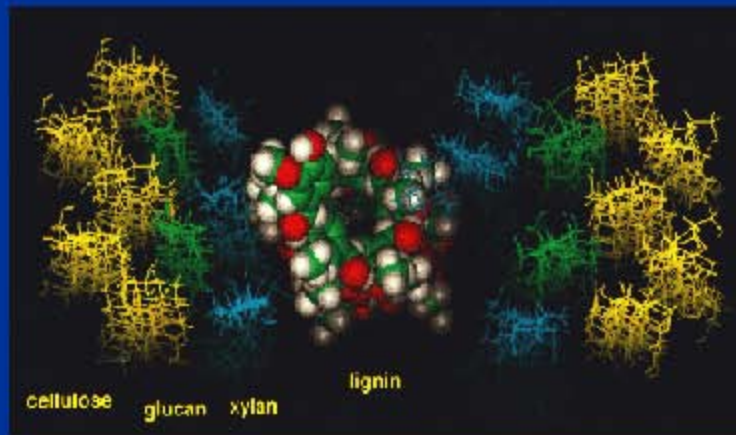
**Humus –**  
coevolution product of  
living and non-living  
matter



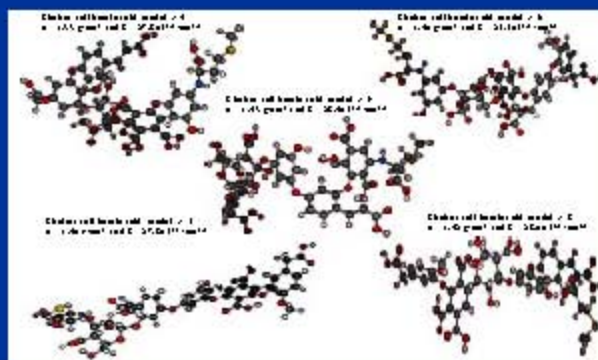
# FORMATION OF HUMICS: DECOMPOSITION OF LIVING MATTER



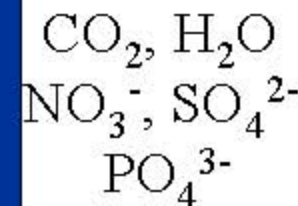
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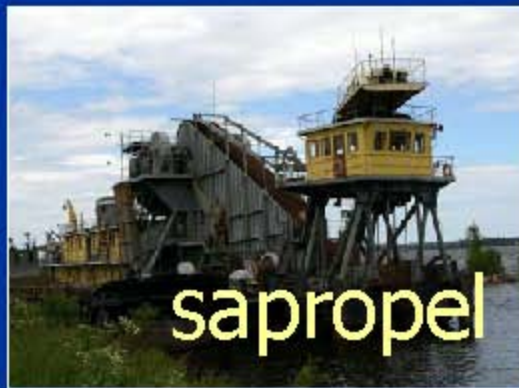


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# HUMIFIED BIOMASS

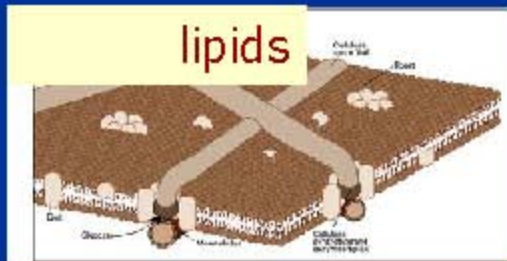


# TYPE OF BOMASS AND CONDITIONS - IMPACT ON STRUCTURE OF HUMICS



**Aromaticity**

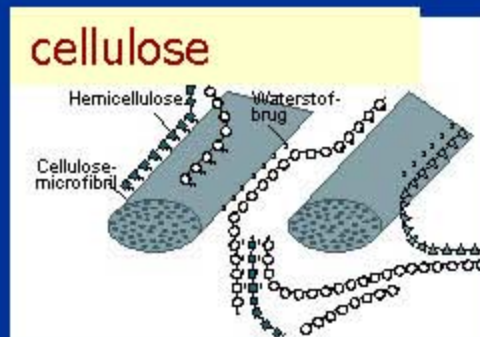
Coal



**Lipids**

Soil

Sapropel



**Sugars**

Peat

Compost

Water



## WHY HUMIC SUBSTANCES?

### UNIQUE CHEMICAL AND BIOLOGICAL PROPERTIES

- polyfunctional, extended carbon backbone, surface active
- bioadaptogenic, biocompatible, non-toxic, refractory

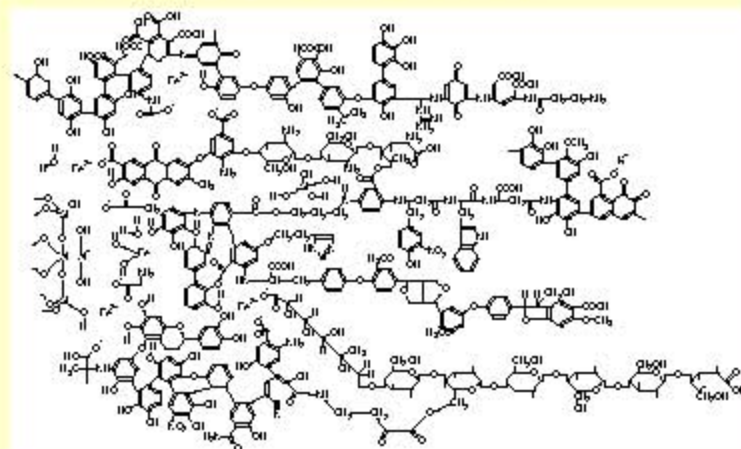
## WHAT IS A MAIN CHALLENGE?

### NATURE'S MOST COMPLEX ORGANIC MATERIALS

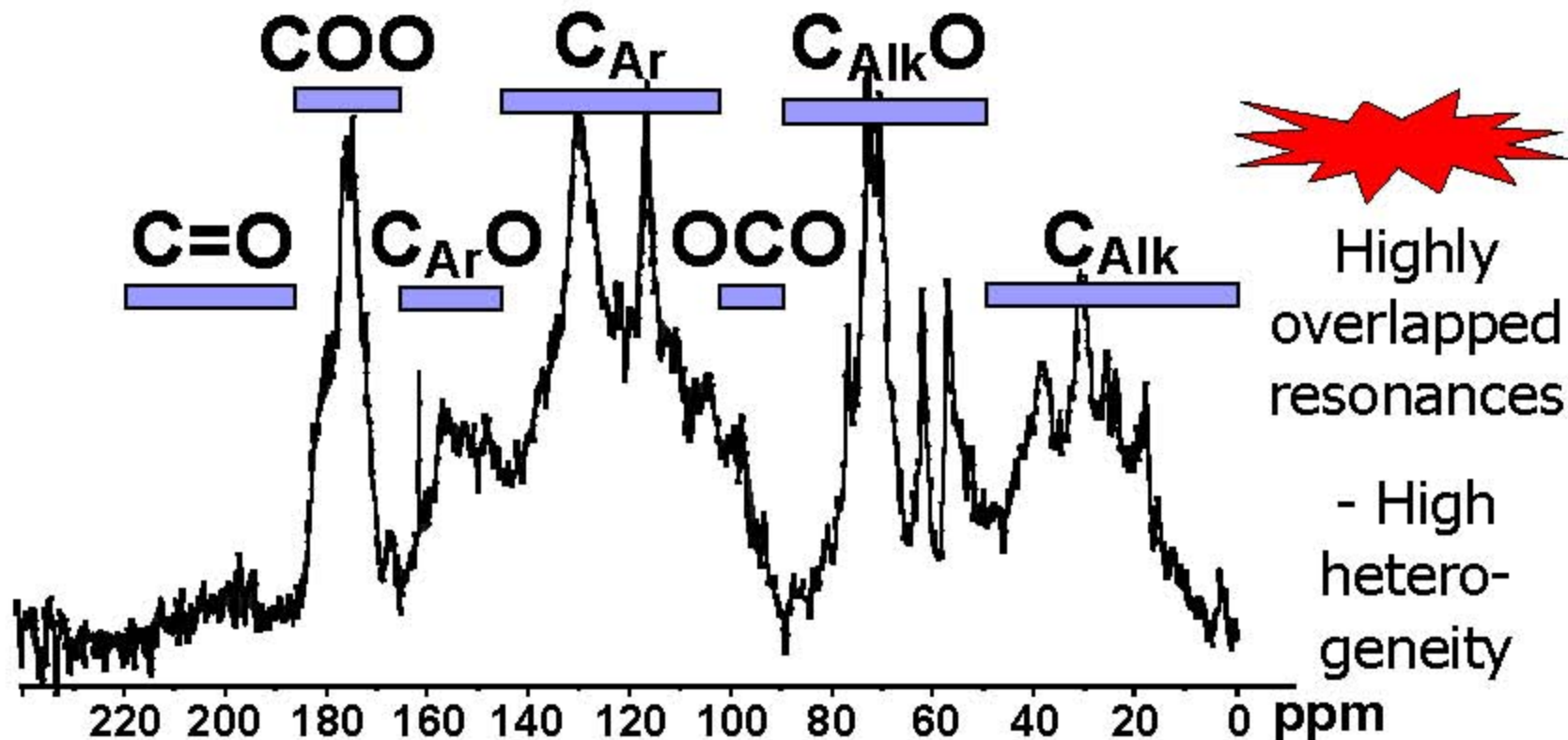
- **extreme structural heterogeneity**

translates into properties that are difficult to control

- **quality criteria are missing**



# Typical $^{13}\text{C}$ NMR Spectrum of HS

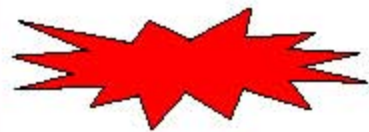


**Descriptors of structural-group composition (C, %):**

**C=O, COO, C<sub>Ar</sub>O, C<sub>Ar</sub>, OCO, C<sub>Alk</sub>O, C<sub>Alk</sub>**

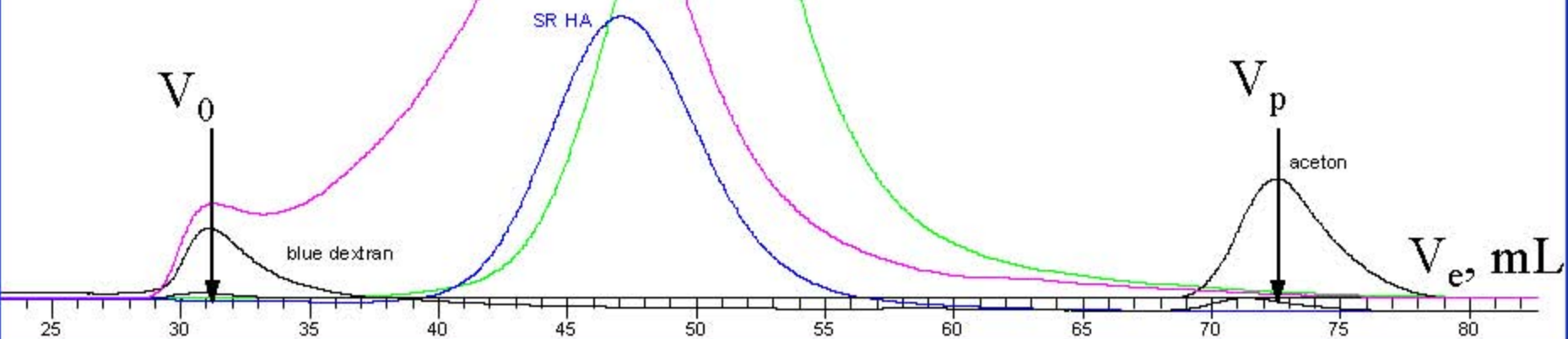


# MOLECULAR WEIGHT DISTRIBUTION OF HUMICS: HIGH POLYDISPERSITY



Broad MWD

$$\Rightarrow K_d = \frac{V_e - V_0}{V_p - V_0}$$



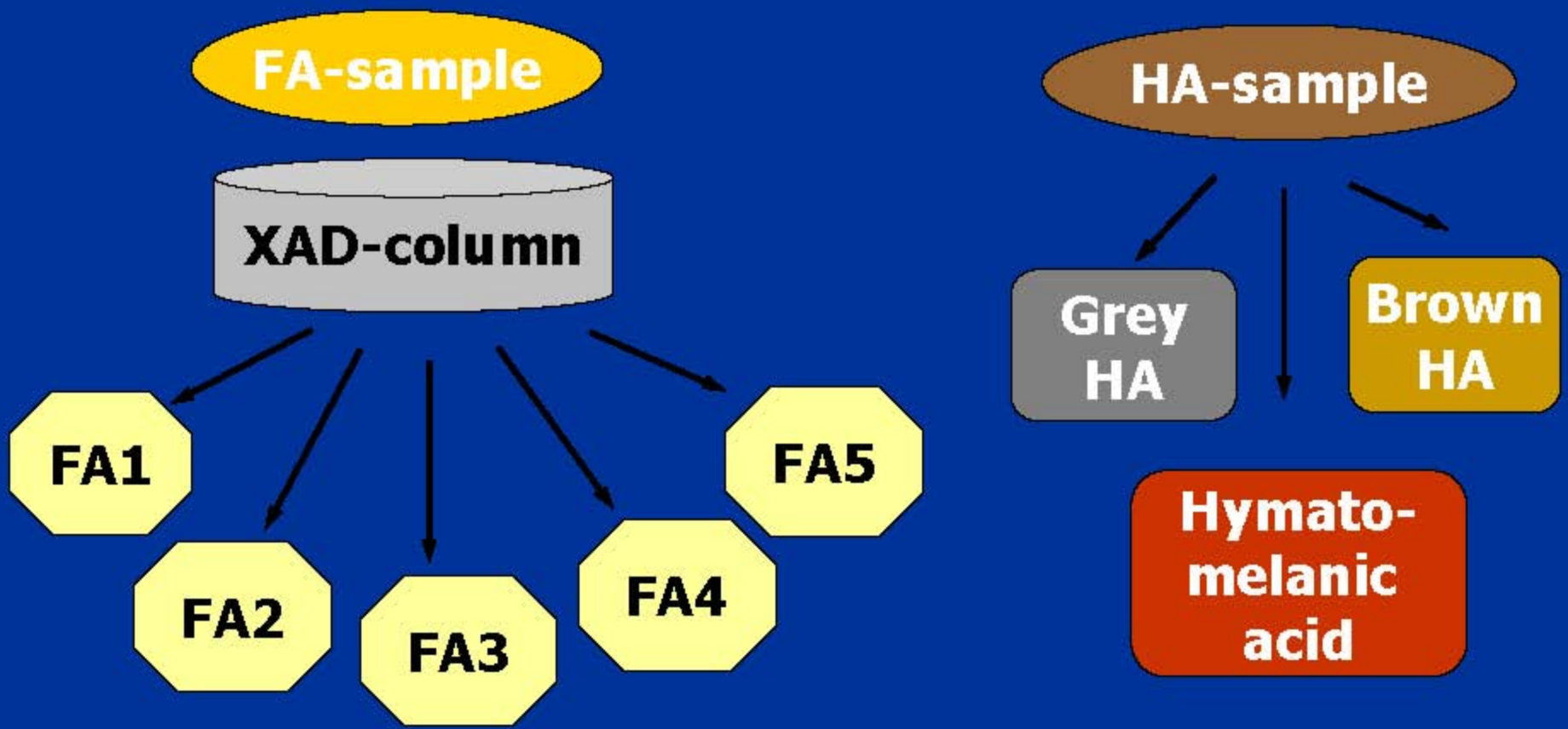
**Gel: Toyopearl HW-55S**

**Mobile phase: 0.028 M phosphate buffer, pH 6.8**

**HS concentration: 20-50 mg C/L, Detection: UV**

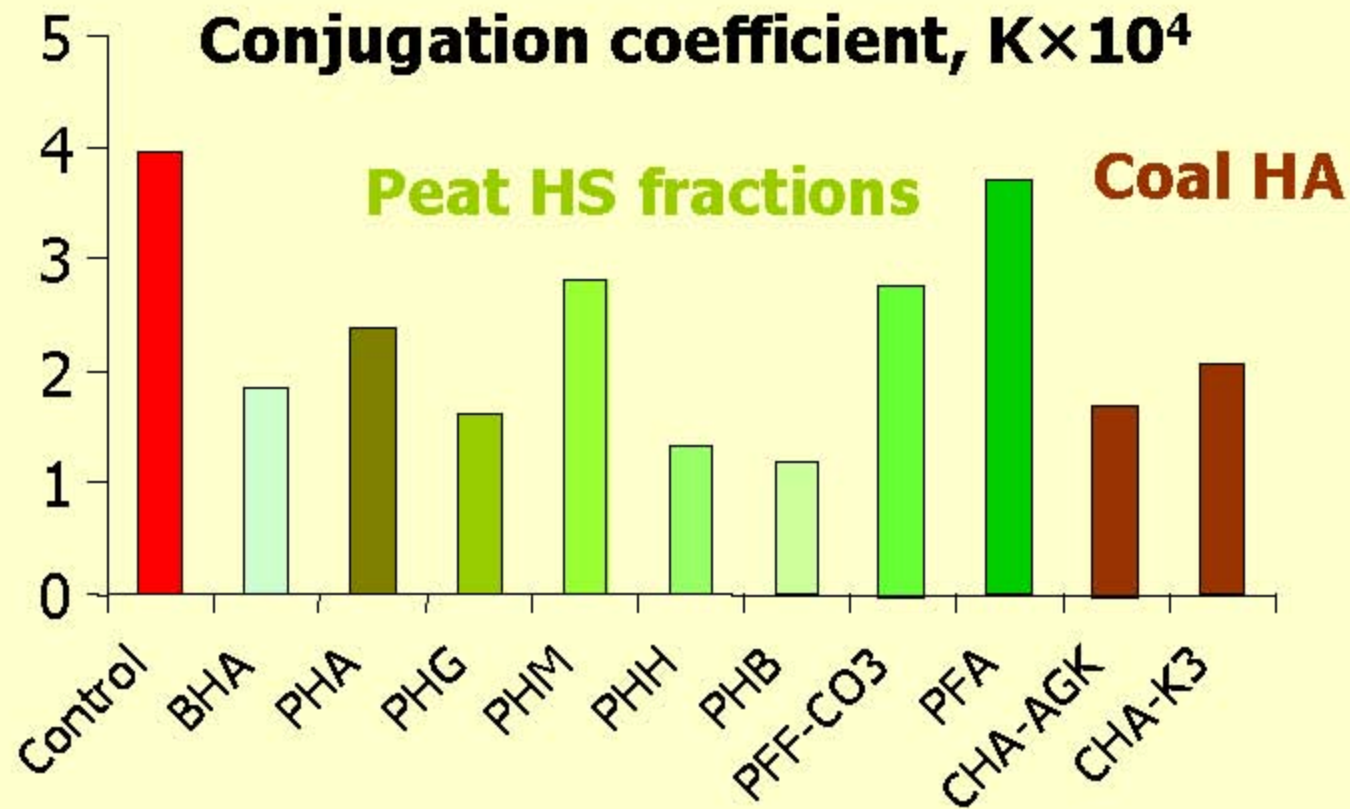


# FRACTIONATION OF HS

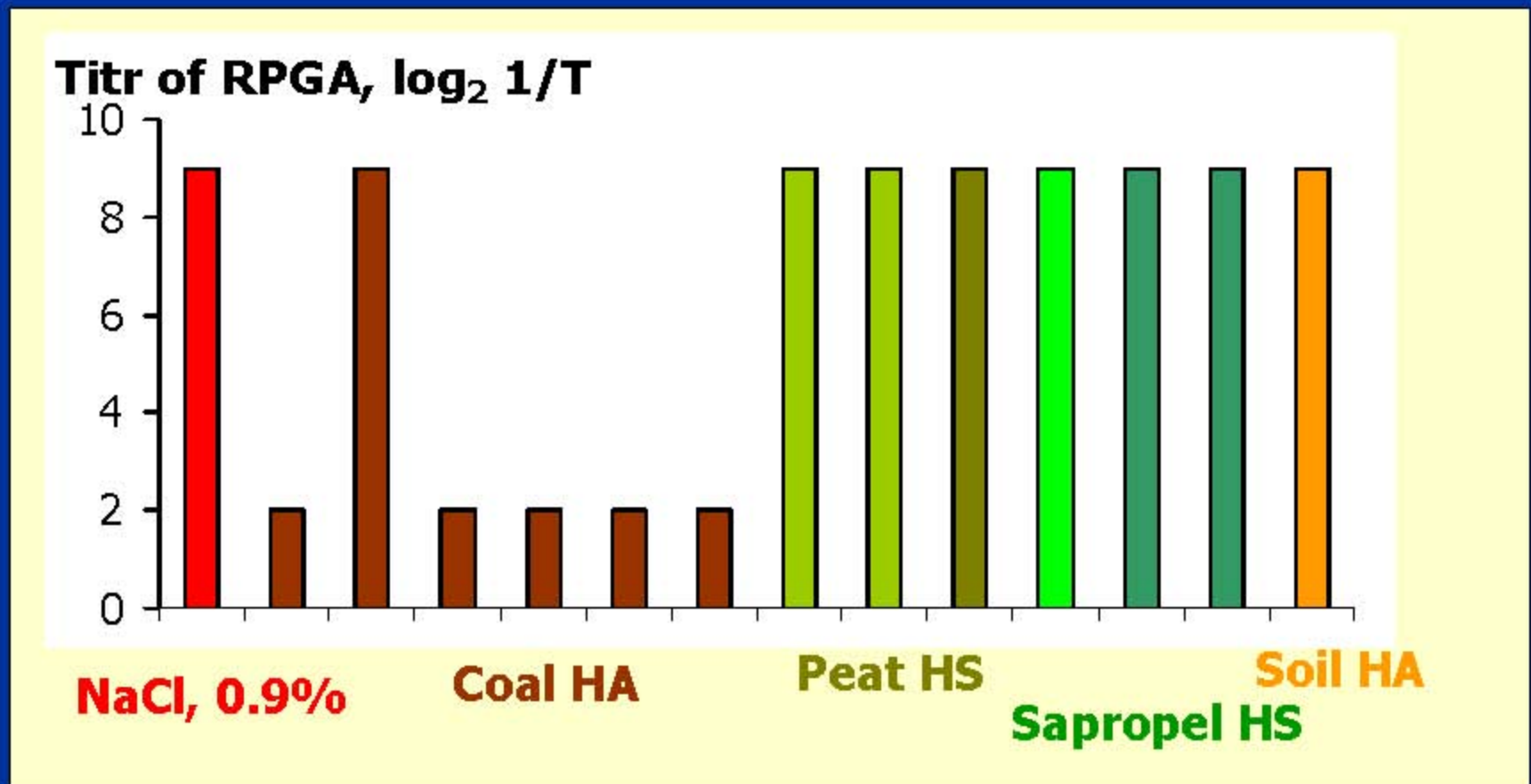




# Influence of the HS fractions on the transfer of *F*- plasmide

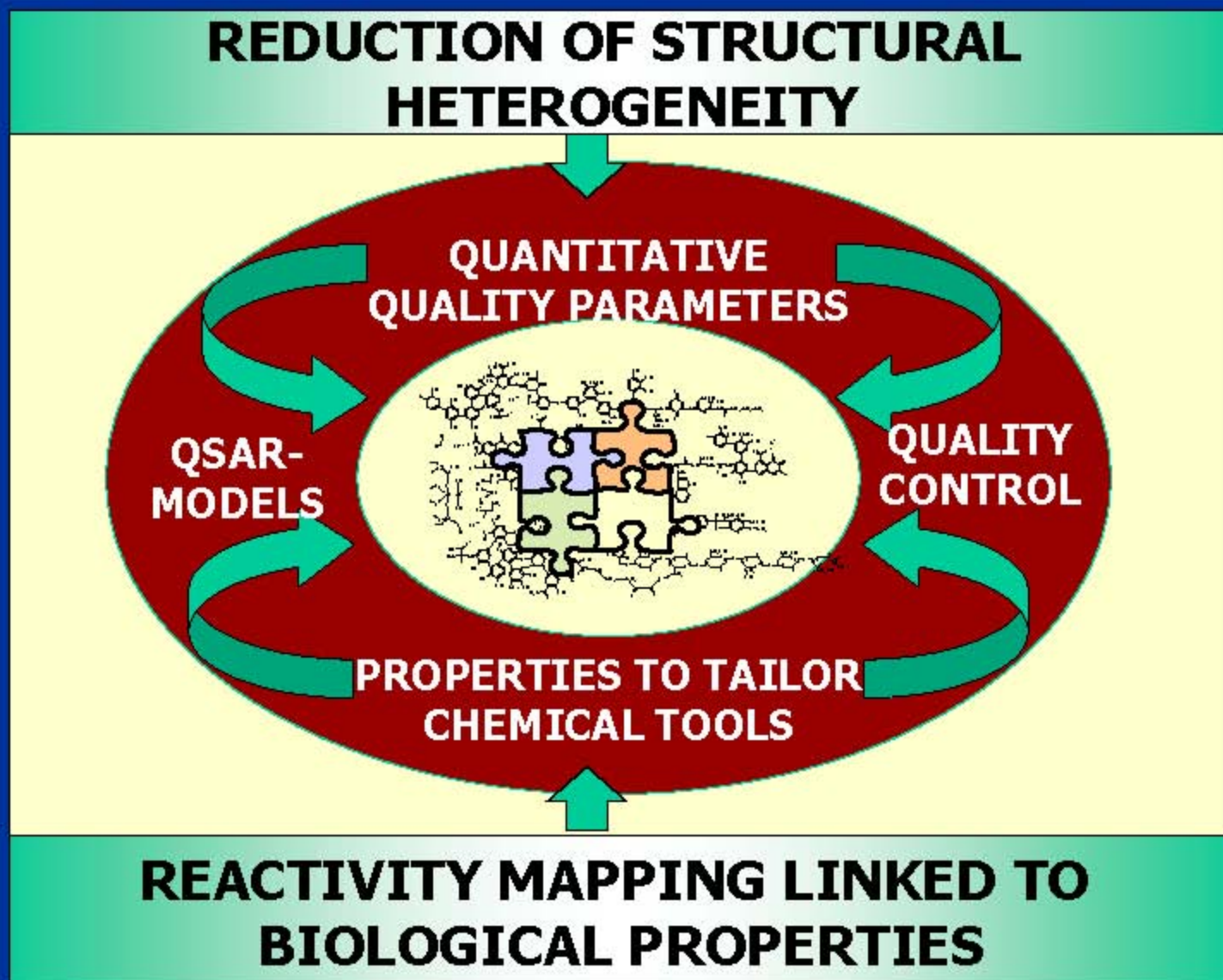


# Influence of HS fractions on sorption of endotoxin (LPS) on the erithrocytes

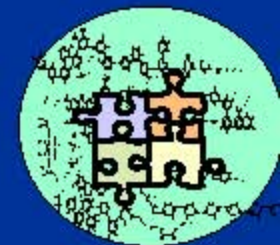




# CONCEPT OF "DESIGNER HUMICS"



# THE PROPOSED SYNTHETIC STRATEGIES



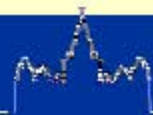
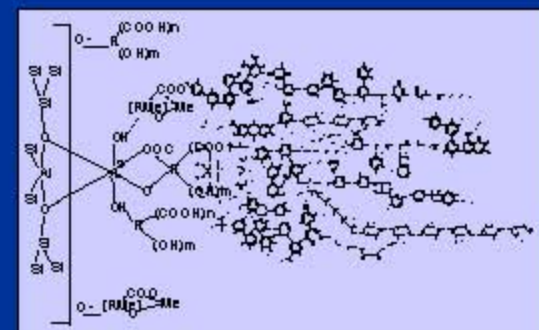
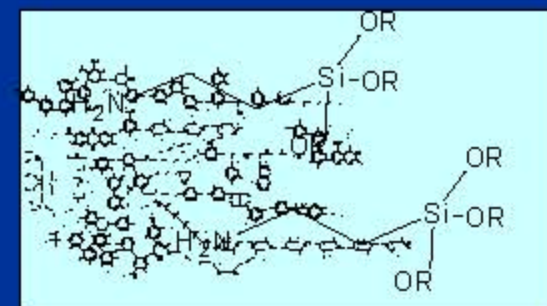
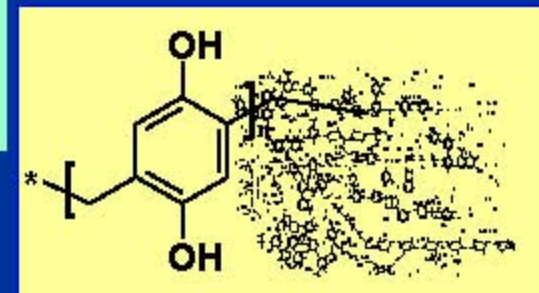
## TAILORING FUNCTIONAL MOLECULES AND MATERIALS

POLYCONDENSATION WITH DESIRED MONOMERS – HUMIC GRAFT-COPOLYMERS

DERIVATIZATION OF HUMIC MACROMOLECULES – HUMIC DERIVATIVES

## TAILORING HYBRIDE MATERIALS

IMPLANTING ONTO MINERAL SUPPORT – SYNTHESIS OF HUMIC COATINGS AND HYBRID MATERIALS



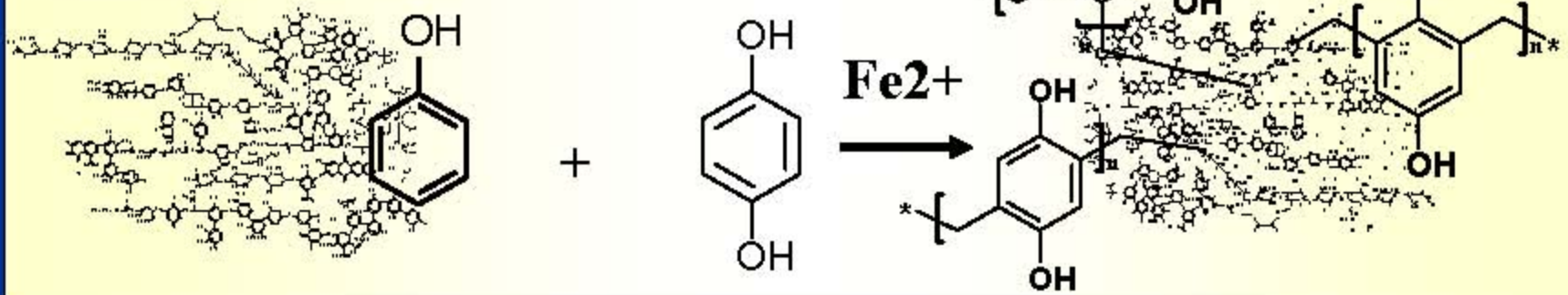


# THE PROPOSED STRATEGIES

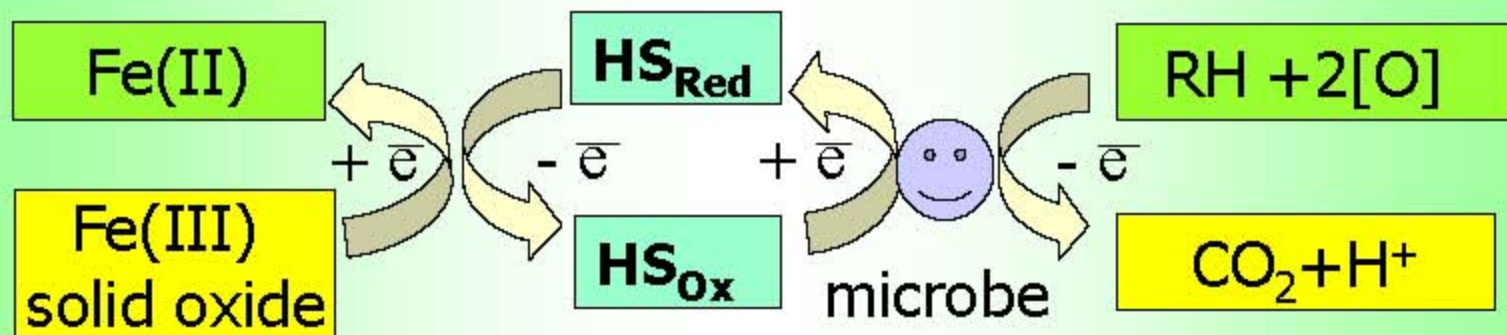


## DESIGN OF FUNCTIONAL MATERIALS

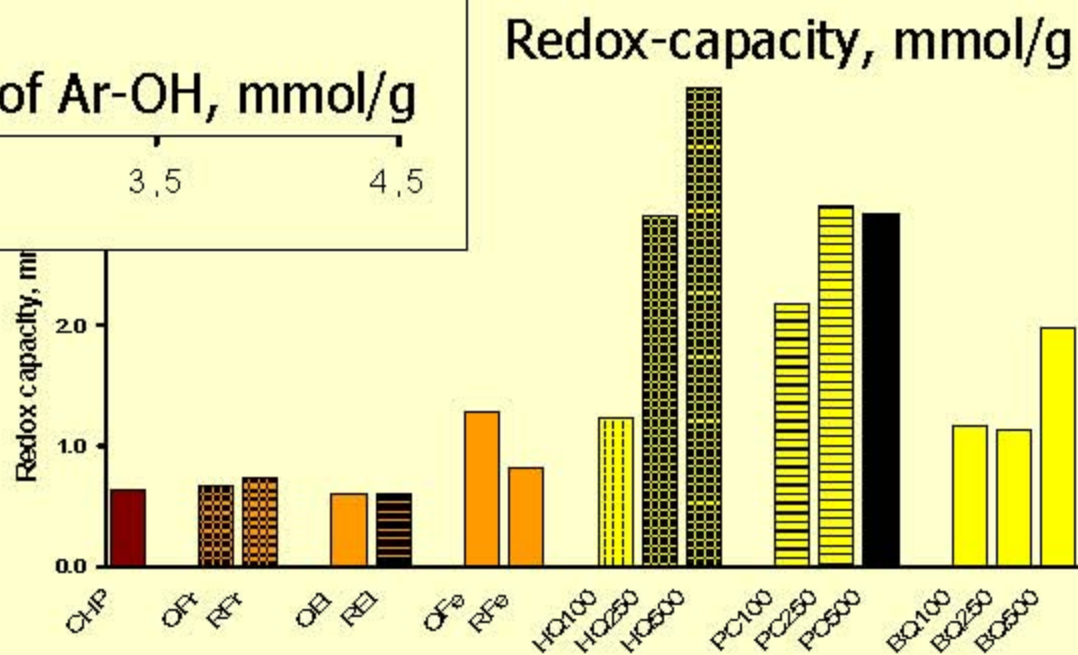
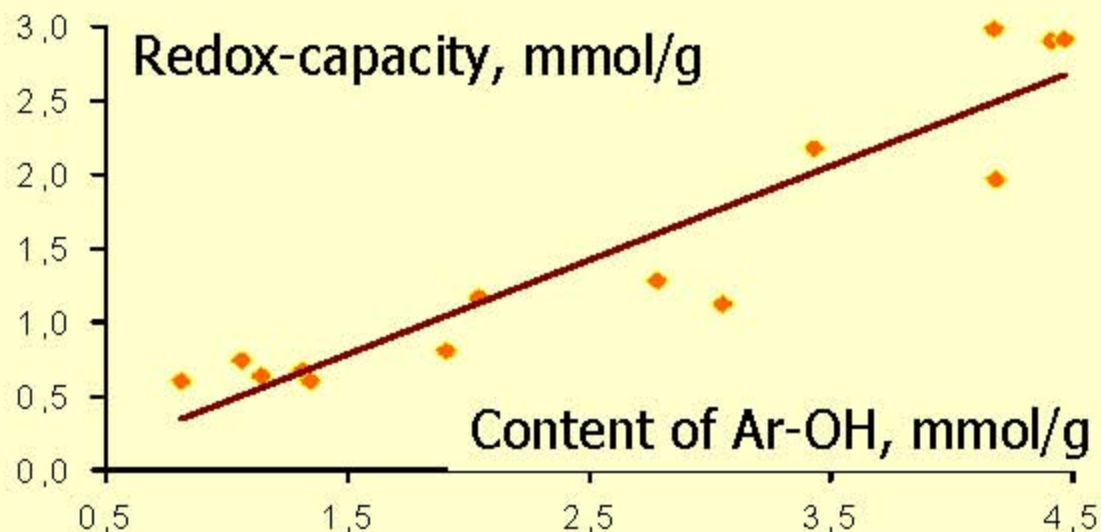
### TAILORING REDOX-ACTIVE HUMIC MATERIALS



### REDOX-MEDIATORS

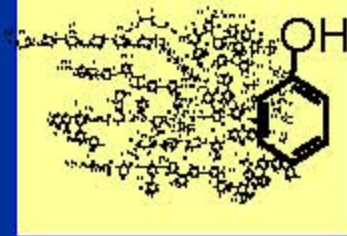


# QSAR FOR REDOX PROPERTIES

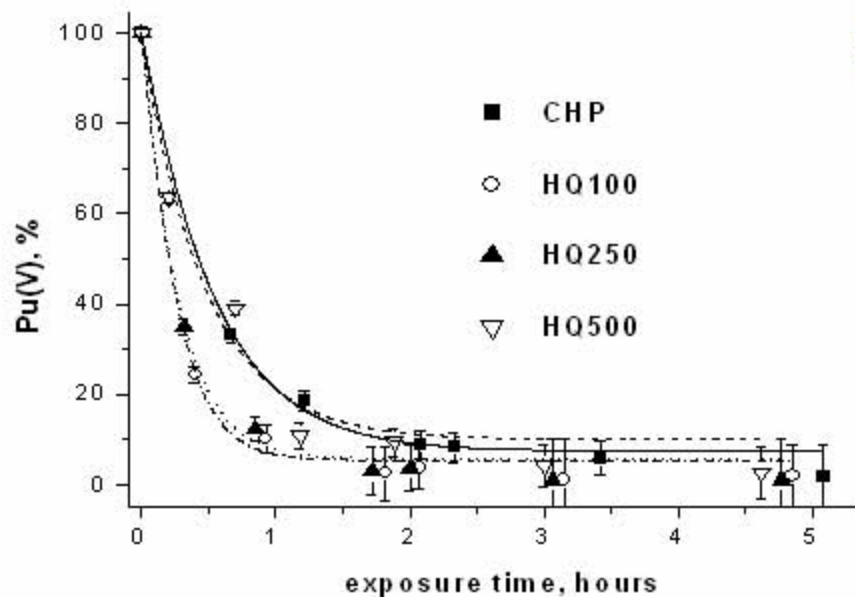




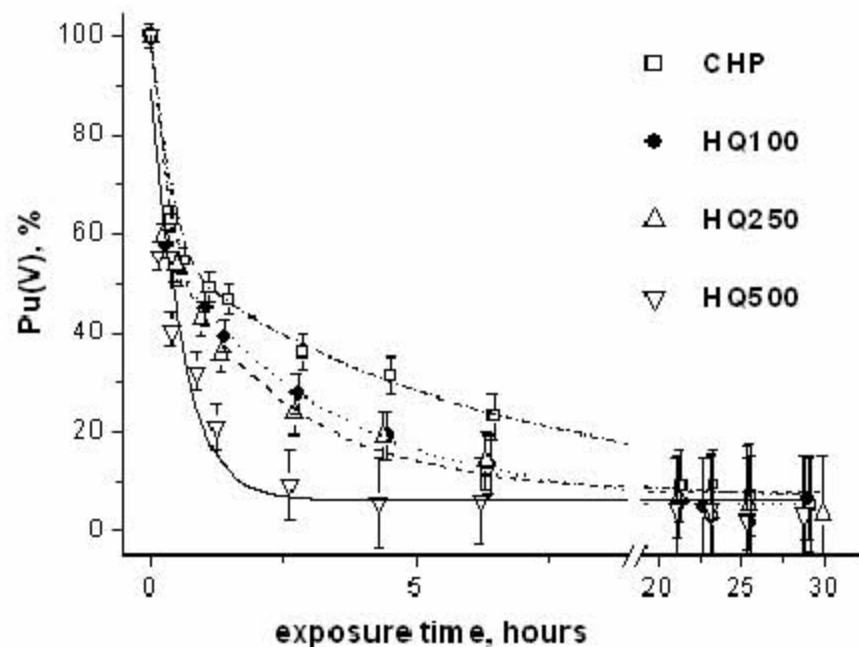
# REDUCTION OF Pu(V) BY HQ-ENRICHED HUMICS



ANOXIC CONDITIONS, pH 7.5



OXIC CONDITIONS, pH 4.5



$C_0(\text{Pu}) = 2.3 \cdot 10^{-9} \text{ M}$ ,

$C_0(\text{HS}) = 10 \text{ mg/L}$ ,  $I \sim 0 \text{ M}$

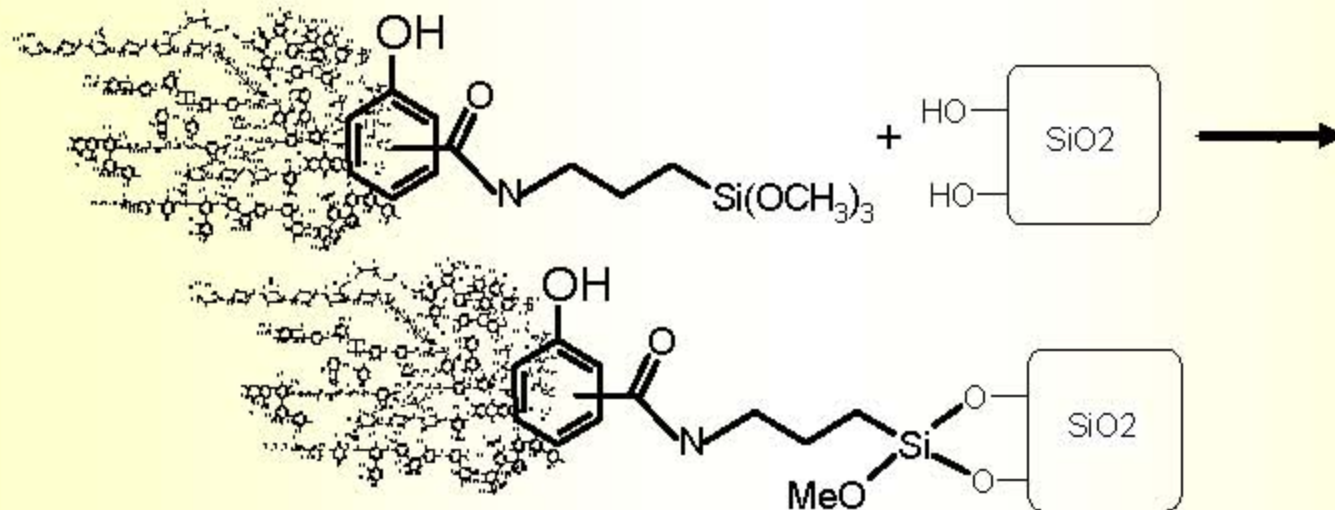


# THE PROPOSED STRATEGIES



## DESIGN OF HYBRIDE HUMIC MATERIALS

### TAILORING HUMINO-MINERAL COMPOSITES



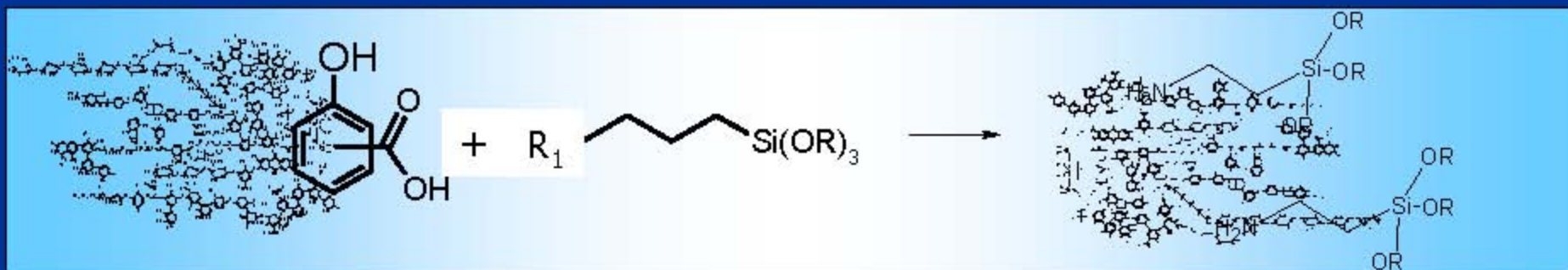
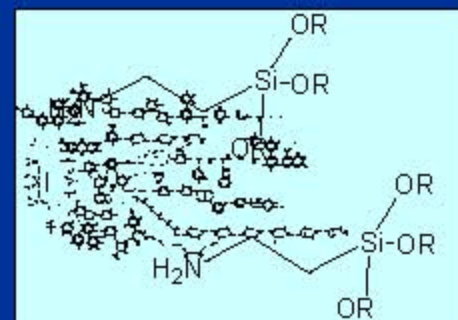
### USES IN BIOTECHNOLOGY

Scavengers - enterosorbents

Biophylic solid supports - biocompatible films



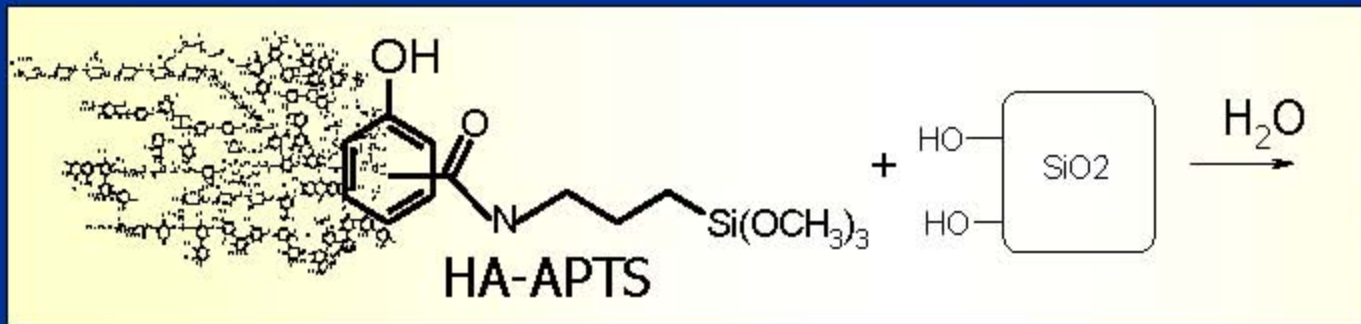
# TAILORING HUMIC DERIVATIVES WITH HIGH AFFINITY FOR MINERAL SUPPORT



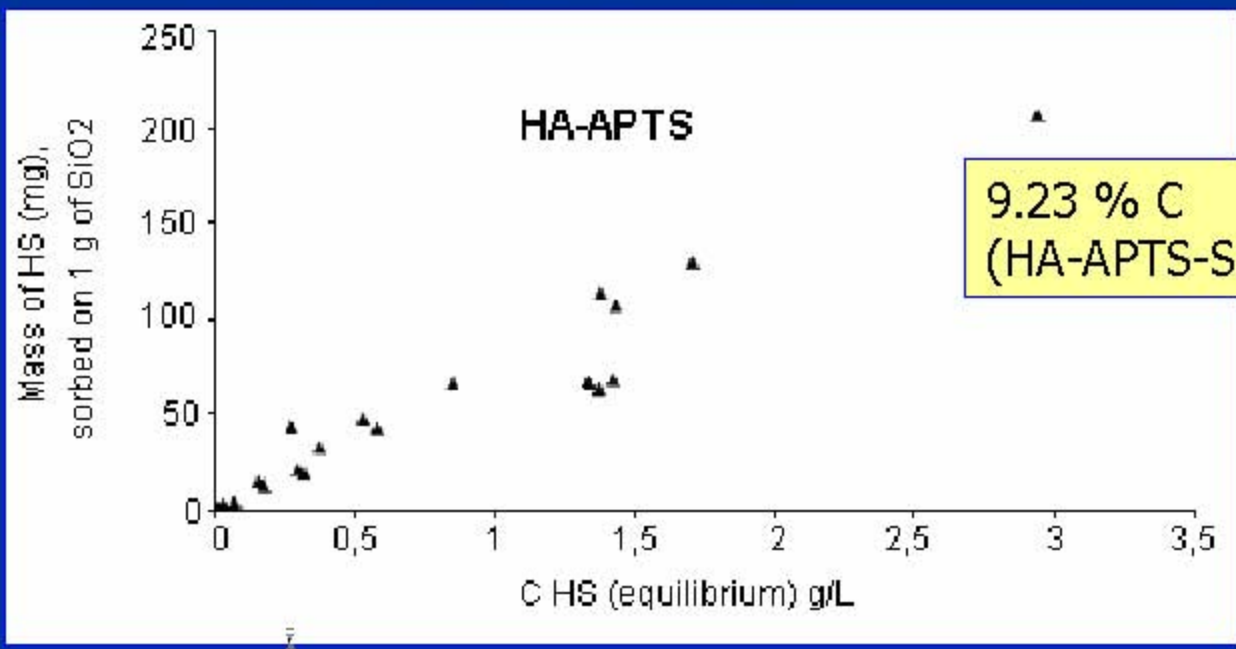
| Functionality (R <sub>1</sub> ) | Organosilane                                       | Structure   |
|---------------------------------|--|---|
| <b>Amino</b>                    | 3-aminopropyl-trialkoxysilane ( <b>APTS</b> )      | $\text{H}_2\text{N}(\text{CH}_2)_3\text{Si}(\text{OR})_3$ |
| <b>Epoxy</b>                    | 3-glycidoxypropyl-trialkoxysilane ( <b>GPTS</b> )  |   |
| <b>Isocyanate</b>               | 3-isocyanatopropyl-trialkoxysilane ( <b>IPTS</b> ) | $\text{OCN}(\text{CH}_2)_3\text{Si}(\text{OR})_3$         |



# IMMOBILIZATION OF HUMIC DERIVATIVES ON SiO<sub>2</sub>

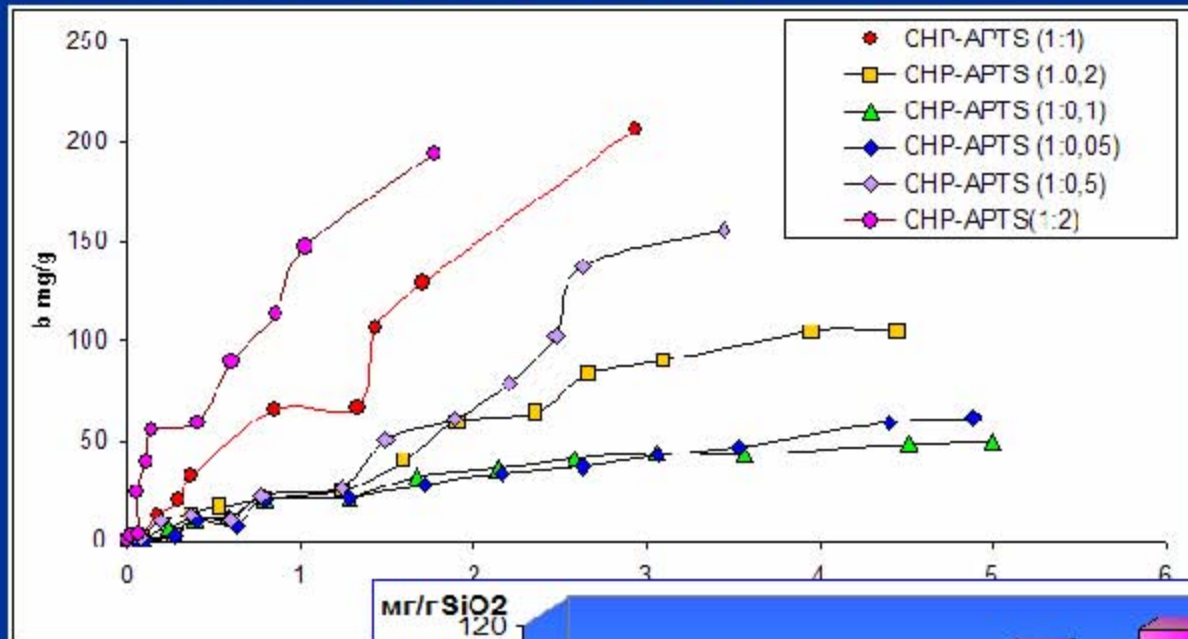


Parent HS      Modified HS

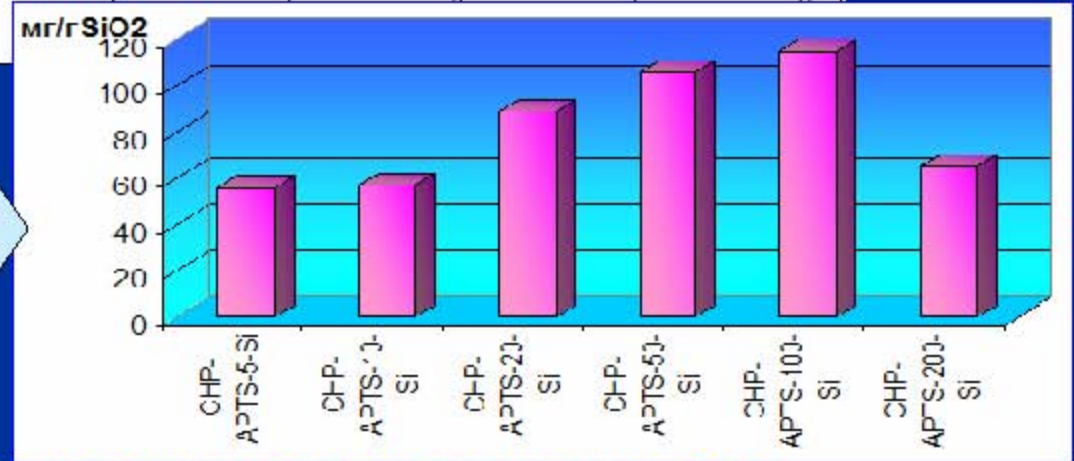




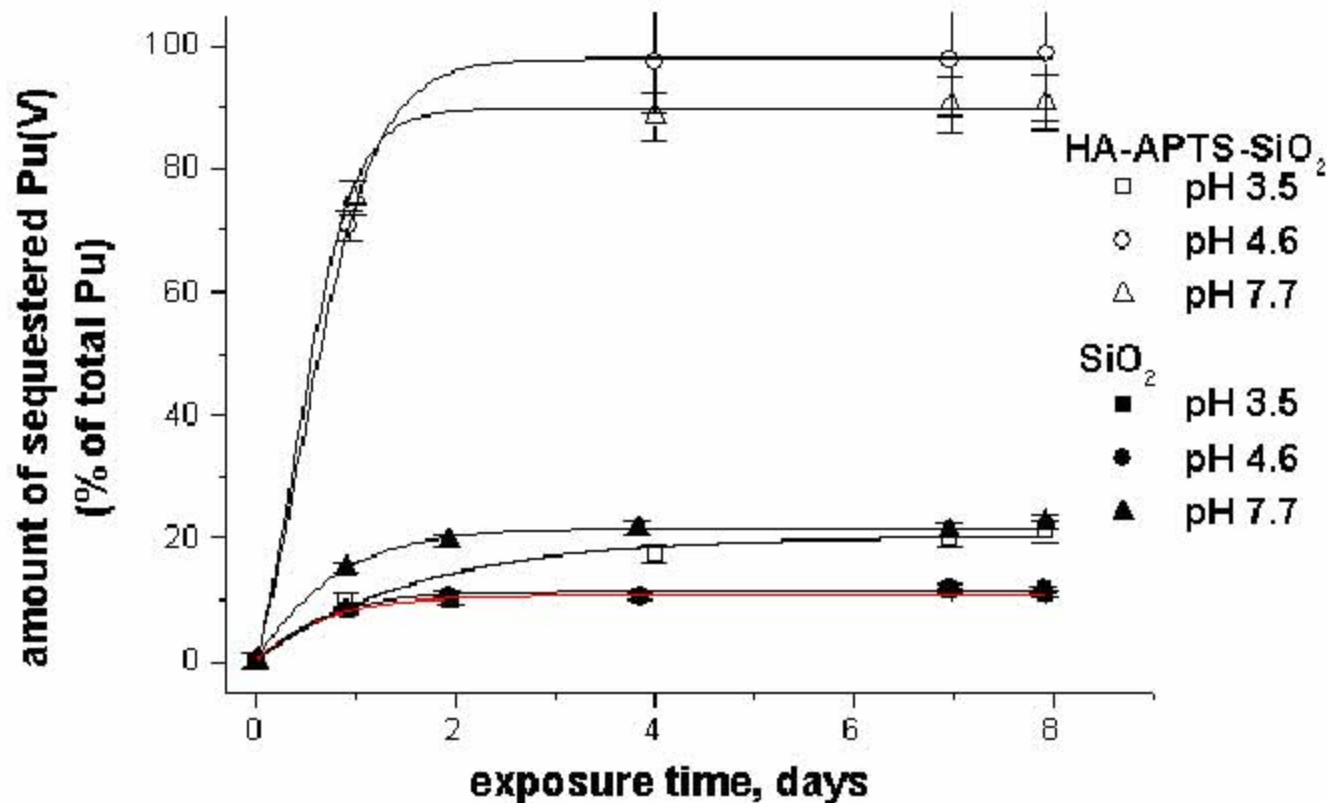
# SORPTION OF HUMIC DERIVATIVES WITH DIFFERENT MODIFICATION DEGREE ONTO SILICA GEL



Amount of HS immobilized onto silicagel, mg/g



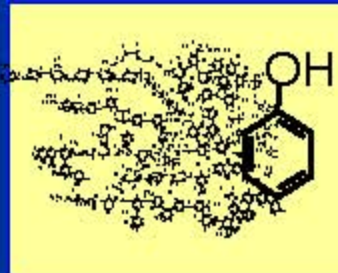
# SEQUESTRATION OF Pu(V) FROM SOLUTION



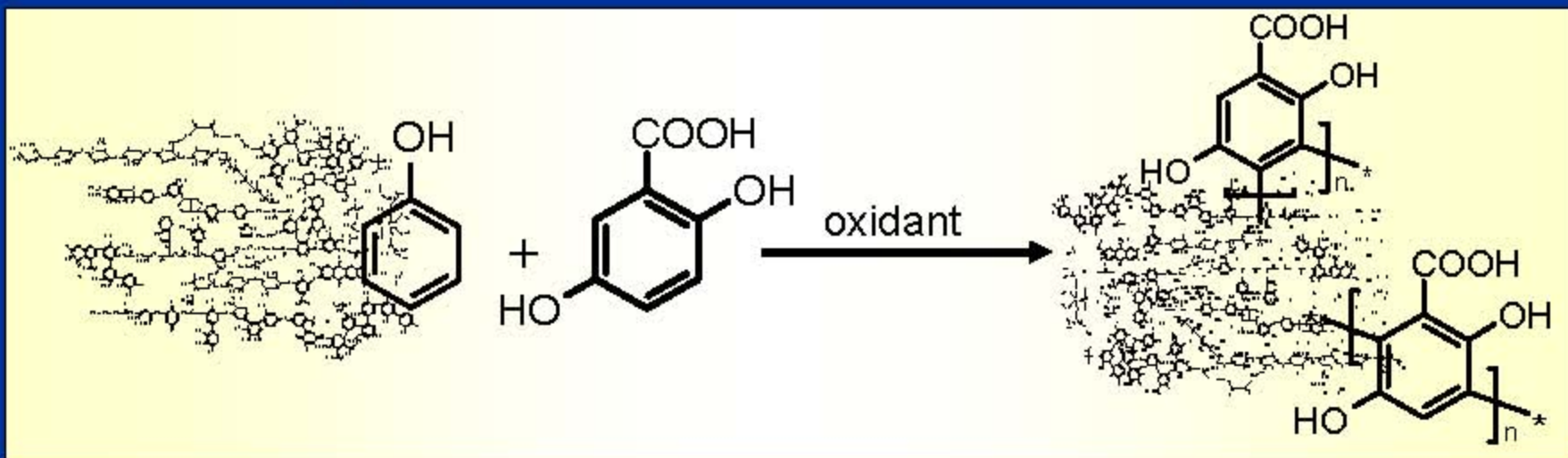
$C_{\text{tot}}(\text{Pu})=1.46 \cdot 10^{-7} \text{ M}$ ,  $C(\text{HA-APTS-SiO}_2)=0.34 \text{ g/L}$ , anoxic conditions



# TAILORING HUMICS ENHANCED COMPLEXING PROPERTIES



## OXIDATIVE QUINONE CONDENSATION



## REACTION CONDITIONS

Parent humic material: Leonardite HA (CHP, Powhumus)

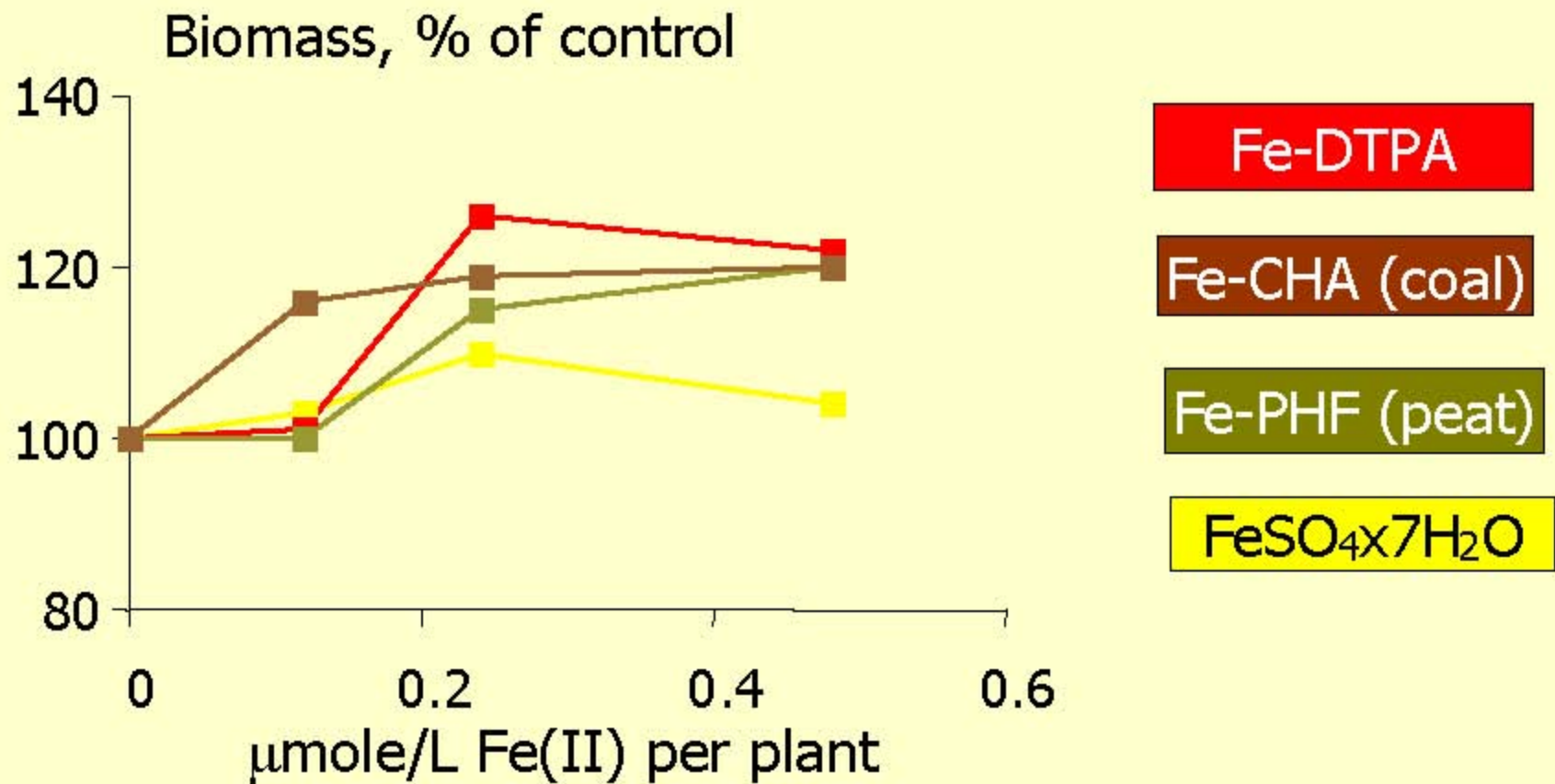
Quinonoid component: 2,5-dihydroxybenzoic acid (2,5dhba)

CHP to 2,5 dhba ratio: 1g:250 mg

oxidant: air, pH 9.5; T= 70 °C



# Fe(II)-HS complexes for correction of chlorosis of tomato plants

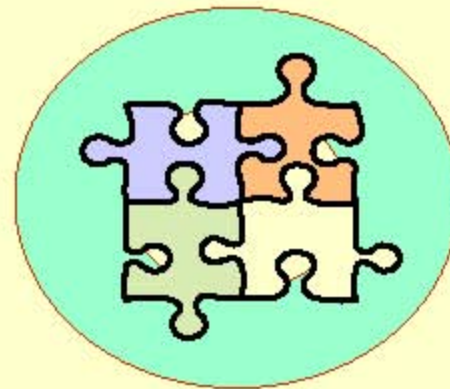




# INNOVATIVE USES IN BIOTECHNOLOGY AND BIOREMEDIATION

## BIOTECHNOLOGY, AGRICULTURE AND MEDICINE

- Enzyme carriers
- Biocompatible films
- Biopesticides
- Elicitors
- Micronutrients
- Enterosorbents
- Immunomodulators
- Antioxidants



## BIOREMEDIATION

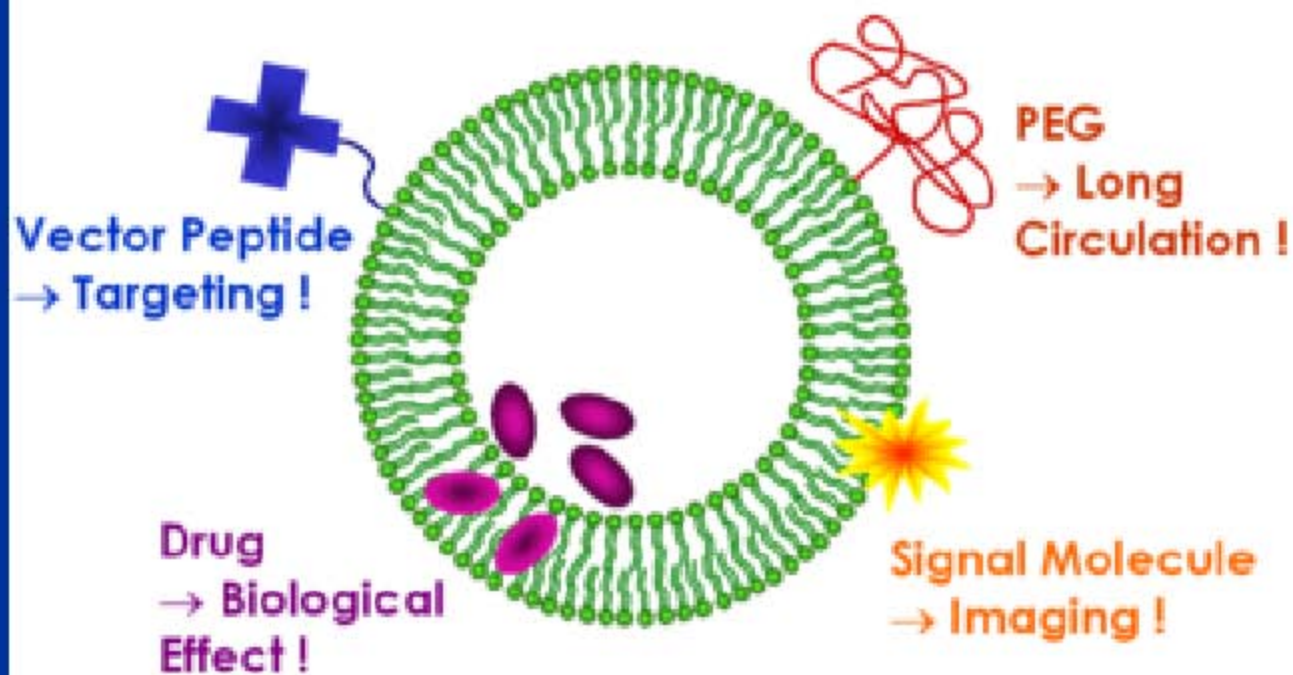
- Chelating agents
- Redox mediators
- Detoxifying agents
- Flushing agents
- Sorbents



# MULTIFUNCTIONAL THERAPEUTICS: WHAT IS THIS?

**Nanodevices** that have a core loaded with drug for **biological effect**, hydrophilic periphery for **long circulation** in body fluids, vector peptide for **targeting** and signal molecule for **imaging**

## EXAMPLE: MULTIFUNCTIONAL MICELLS AND LIPOSOMES



<http://www.fmp-berlin.de/projects/peptidelipidinteractio.html>

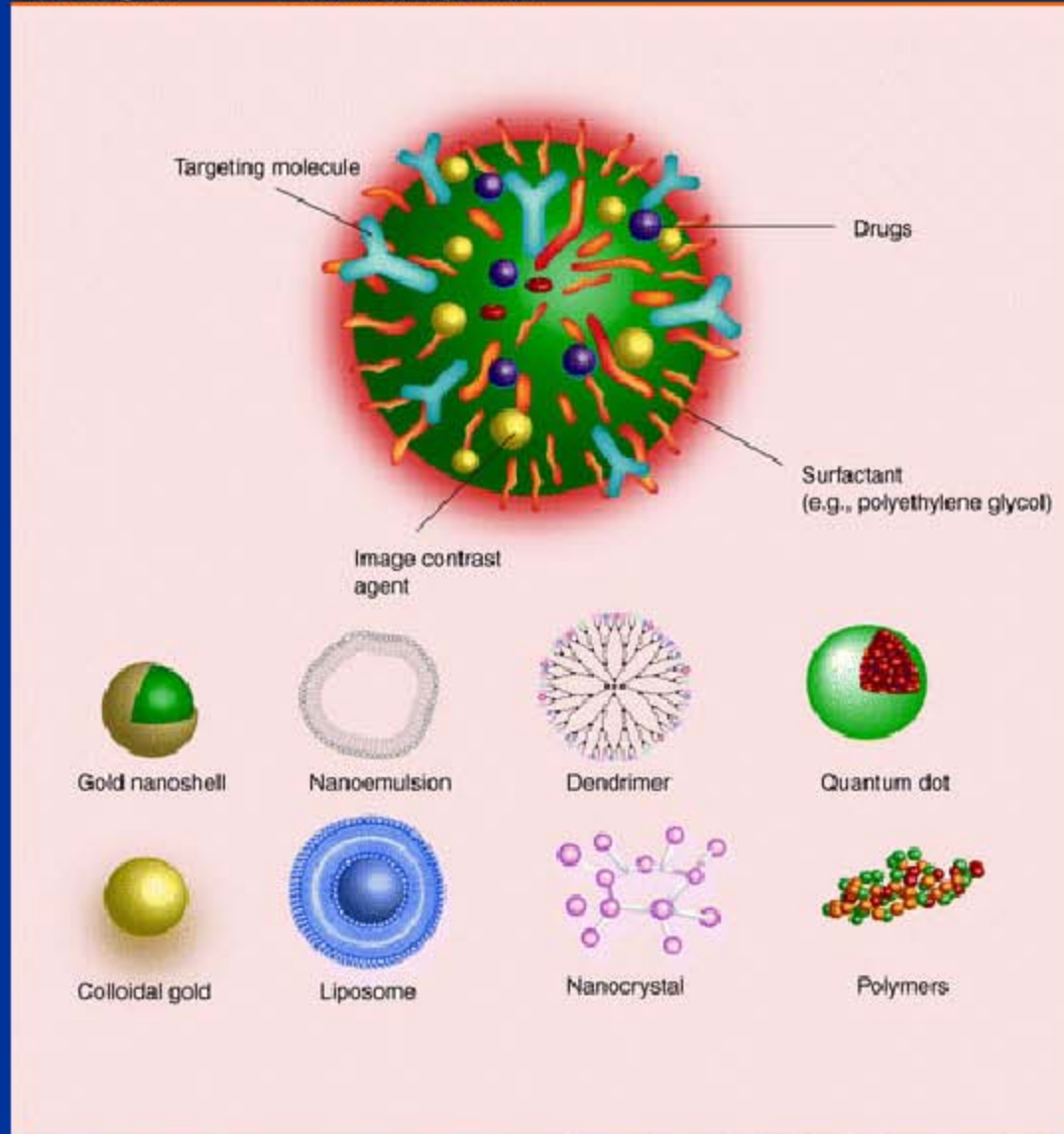




# WHAT CAN THEY BE COMPOSED OF?

Medscape

www.medscape.com



Source: Nanomedicine © 2007 Future Medicine Ltd



# ORGANIC / INORGANIC HYBRIDE THERAPEUTICS

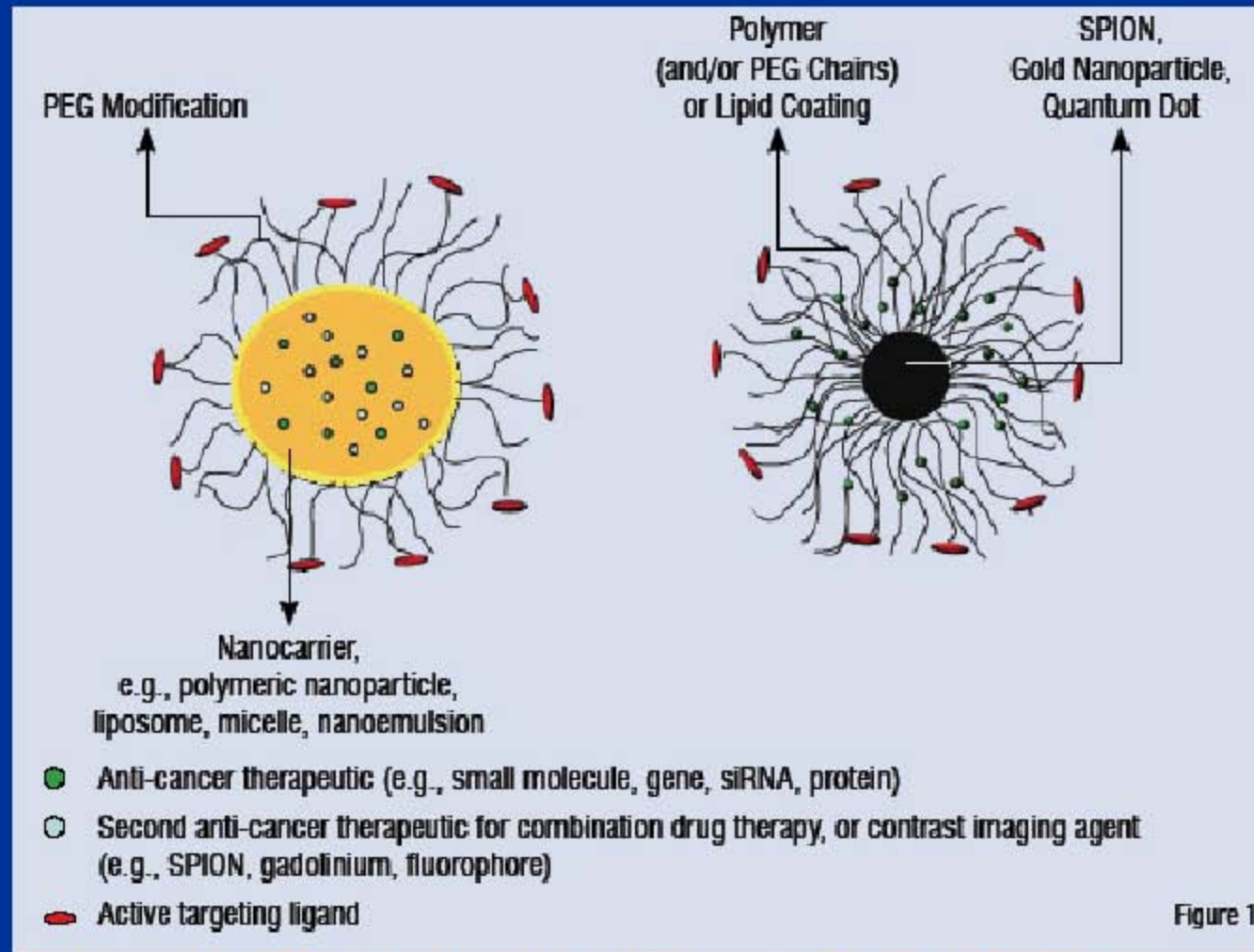


Figure 1

<http://www.natureasia.com/asia-materials/review.php?id=629>





# MULTIFUNCTIONAL THERAPEUTIC FROM DENDRIMERS

Design of a multi-functional dendrimer as cancer therapeutic

Methotrexate  
(ester-linked  
therapeutic agent)

Folic acid  
(amide-linked targeting agent)

G5-polyamidoamine  
(dendrimer platform)

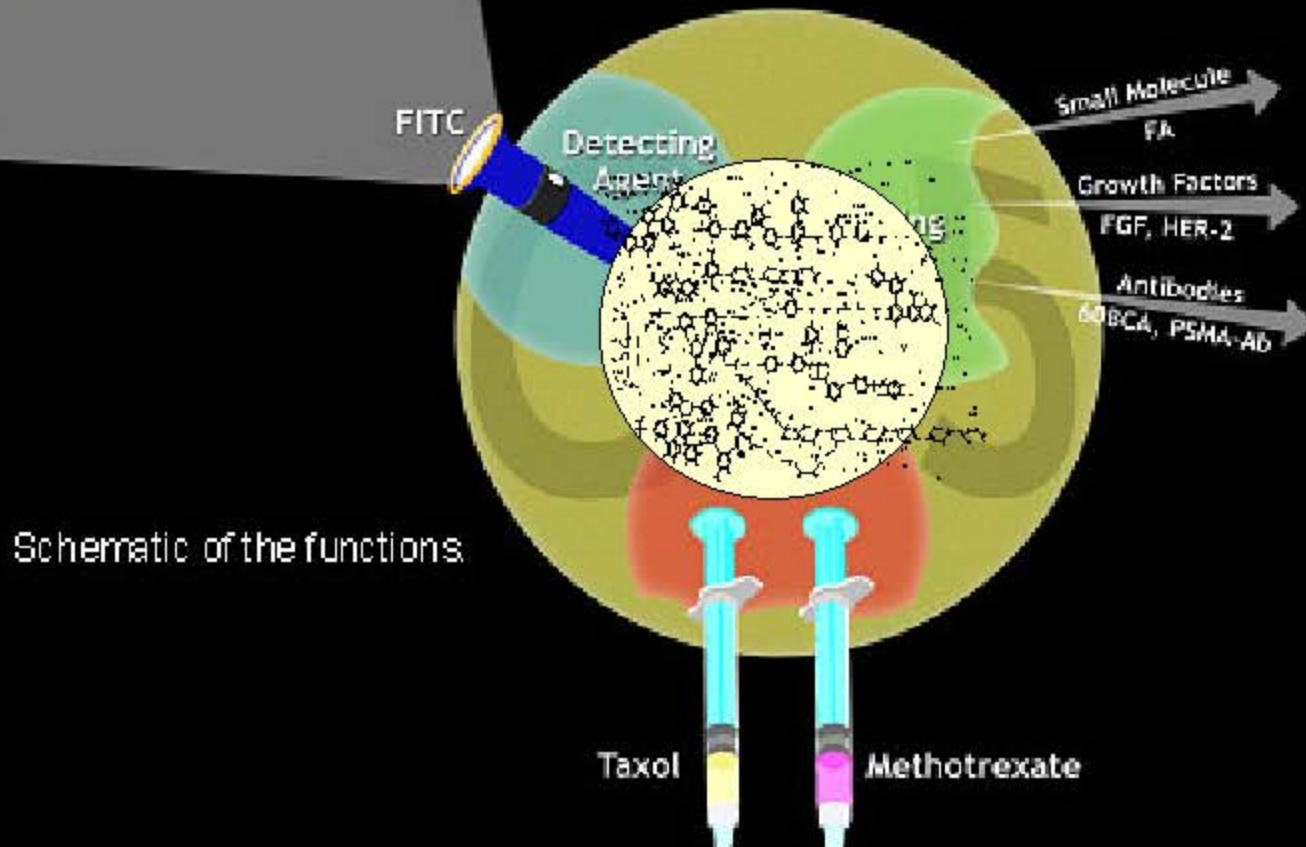
Fluorescein  
(detecting agent)

Kukowska-Latallo, Cao, Majoros, Islam, Kotlyar, East, Baker, *Cancer Research*, 2005.



# MULTIFUNCTIONAL HUMIC THERAPEUTICS

## MULTIFUNCTIONAL HUMIC THERAPEUTIC



WE ARE STILL ON THE PATH FORWARD TO...

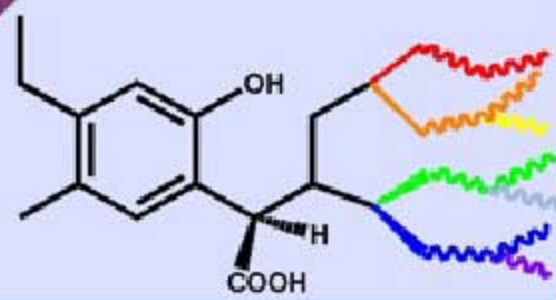


# Acknowledgements

## MGUMUS-research group



**HiT2010**  
**Conference**



**THANK YOU VERY MUCH!**

**СПАСИБО БОЛЬШОЕ!**

