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DNA-detection using nanoscale metal structures

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Jenaer Biochip Initiative

- development of robust, easy, and cost-effective nanoparticle based systems for the analysis of biomolecules
- combination of bioanalytical tests and spectroscopic methods
- realization of *point-of-care* devices
- chip-based DNA analysis with innovative detection units

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production of metal nanoparticles

Kreibig, U. and Vollmer, M., *Optical Properties of Metal Clusters*. ed. Springer, Vol. 25, 1995

- synthesized by chemical
  physical methods
- chemical reduction in lic
- Lithography, EBL...
- new enzymatic approach

Table 6.2. Methods for cluster generation

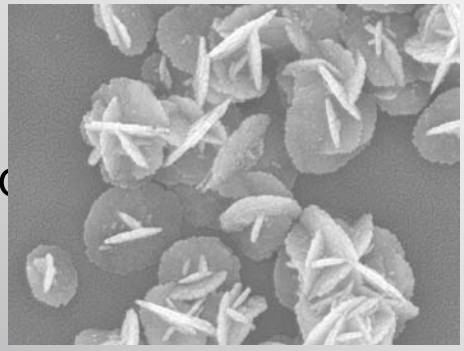
a) Condensation of atoms (supersaturation in vapor, liquids, solids)

Atoms produced by heating: resistive, laser or electron beam
sputtering: by photon, atom, molecule, or ion impact, electric pulses, electric discharges

In beams	On surfaces	In matrices
Continuous:		
• gas aggregation	• atom deposition with subsequent surface diffusion	• co-evaporation of atoms with matrix material (matrix isolation)
• adiabatic expansion (with/without carrier gas)		• diffusion in/into matrix
• field emission (liquid-metal sources)	• soft landing	• photoreduction (photographic material)
• spraying techniques		• spraying techniques into liquid matrix (solvent extraction)
Pulsed:		
• laser vaporization		• chemical reduction in liquids (with or without nuclei): colloid generation metallorganic compounds: ligand shells
• pulsed nozzles for carrier gas		
b) Dispersion of bulk material or deposition		
• sputtering	• cluster deposition from cluster beam	• co-evaporation of clusters with matrix material
• electric pulses, exploding wire	• nanocrystalline material by densification	• arc discharges in liquids
• arc discharges (Svedberg)		• pressing into porous matrix
• laser vaporization, ablation		• chemical reduction in zeolites
		• dispersion by ultrasound (emulsions)

enzymatic produced nanoparticles

- horseradish peroxidase induced particle growth
  - fast reaction and very specific
  - good reproducibility
  - stable signals
  - desert rose like structures



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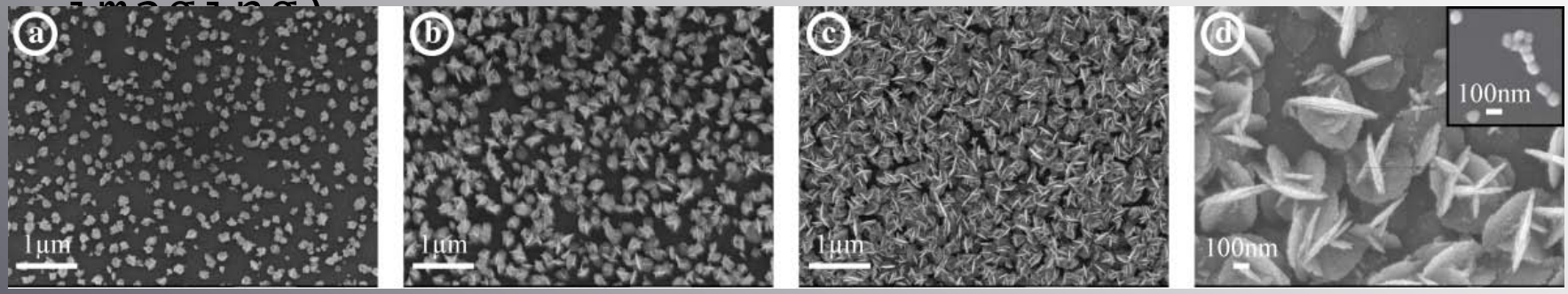
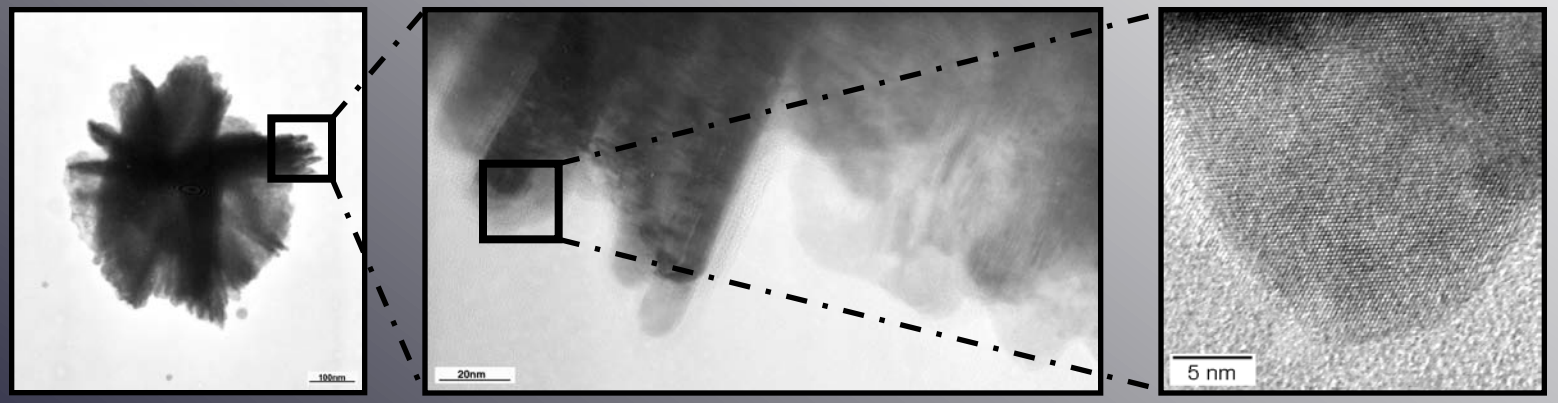
enzymatic produced nanoparticles

- particle characterization (SEM & TEM imaging)





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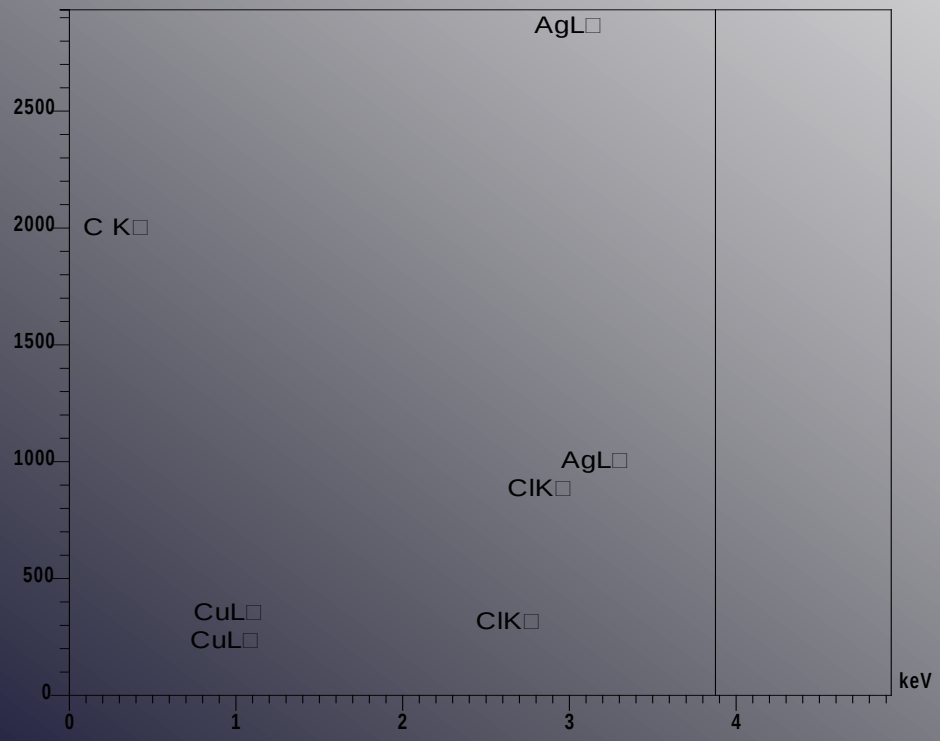
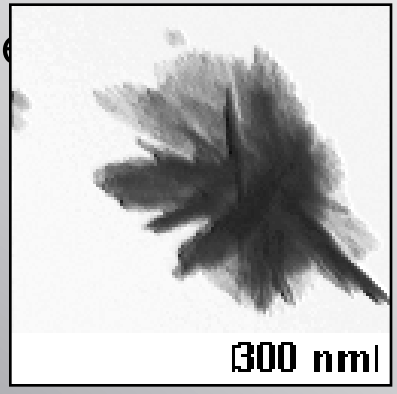
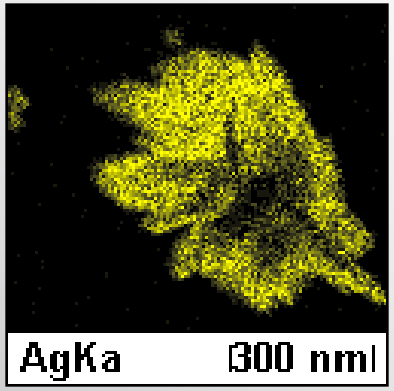
enzymatic produced nanoparticles

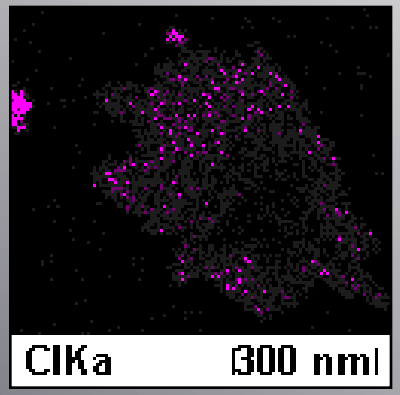
- elemental analysis - EDX mapping

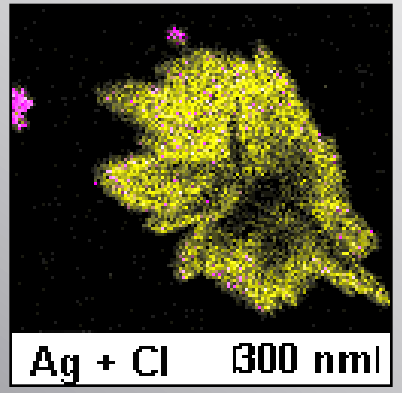
  (energy dispersive x-ray spe











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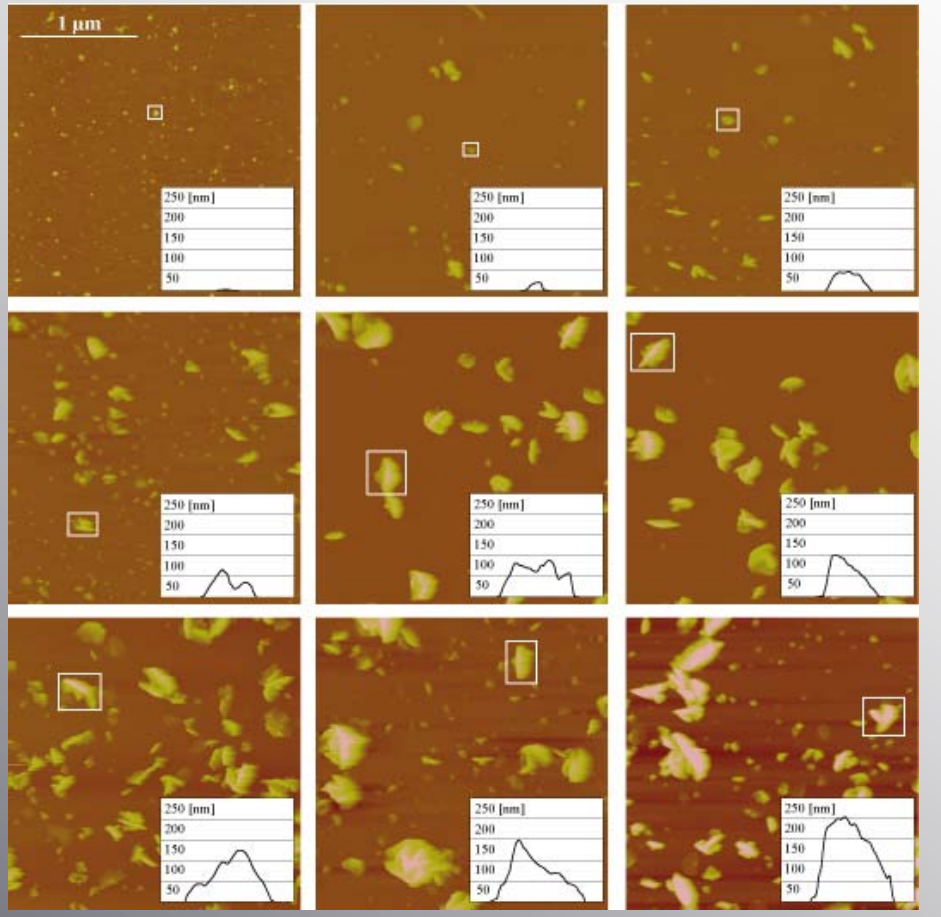
enzymatic produced nanoparticles

- growth kinetics - AF
- characterization on single nanoparticle
- stepwise reaction
- at least 30 min



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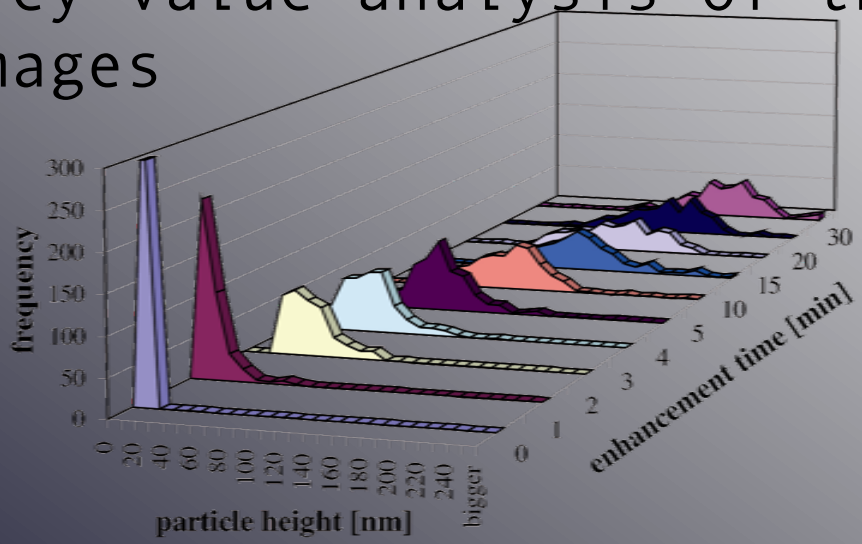
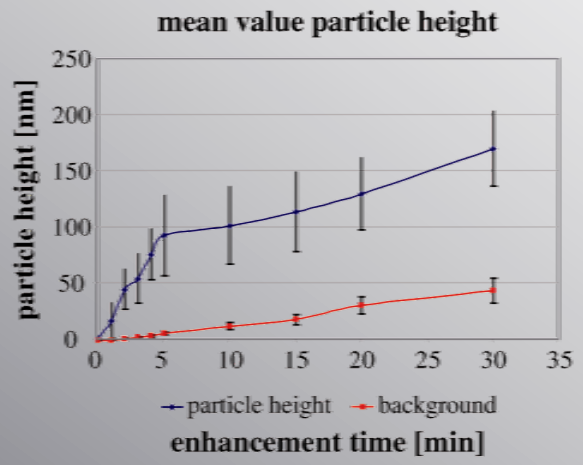
enzymatic produced nanoparticles

Schüler, T., Steinbrück, A., et al., Journal of Nanoparticle

- control of particle height by AFM (over 400 particles)
- grey value analysis of the original AFM images





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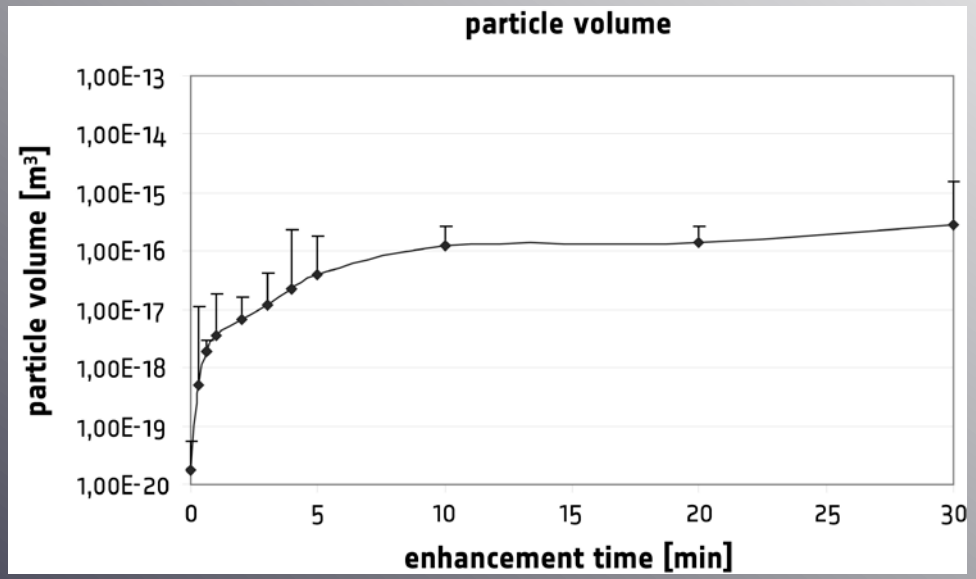
enzymatic produced nanoparticles

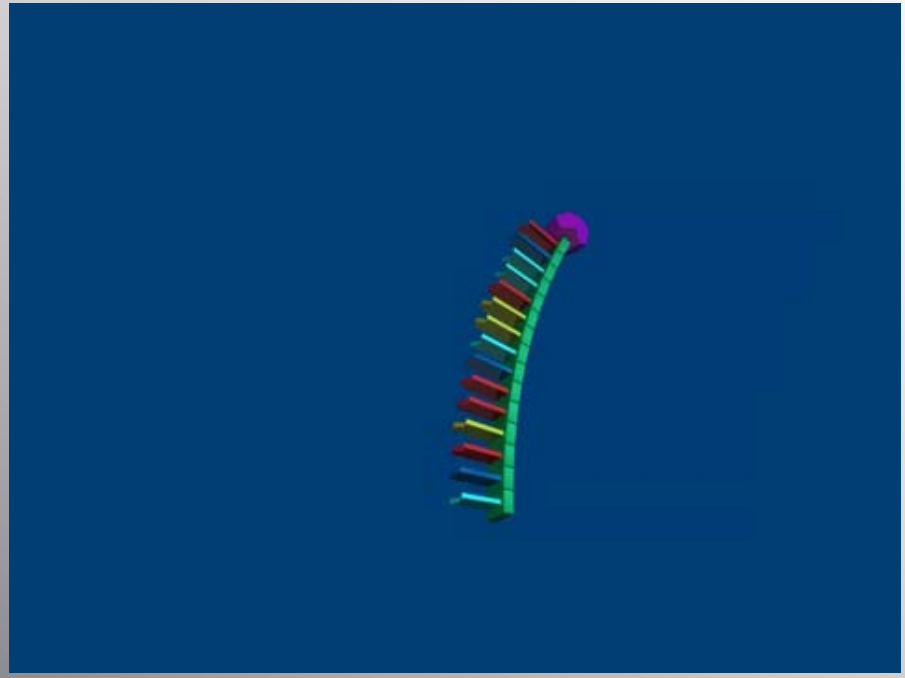
- control of particle volume
- calculation from AFM images / similar results compared to particle height



chip-based electrical DNA-detection

- principle electrical DNA-chip

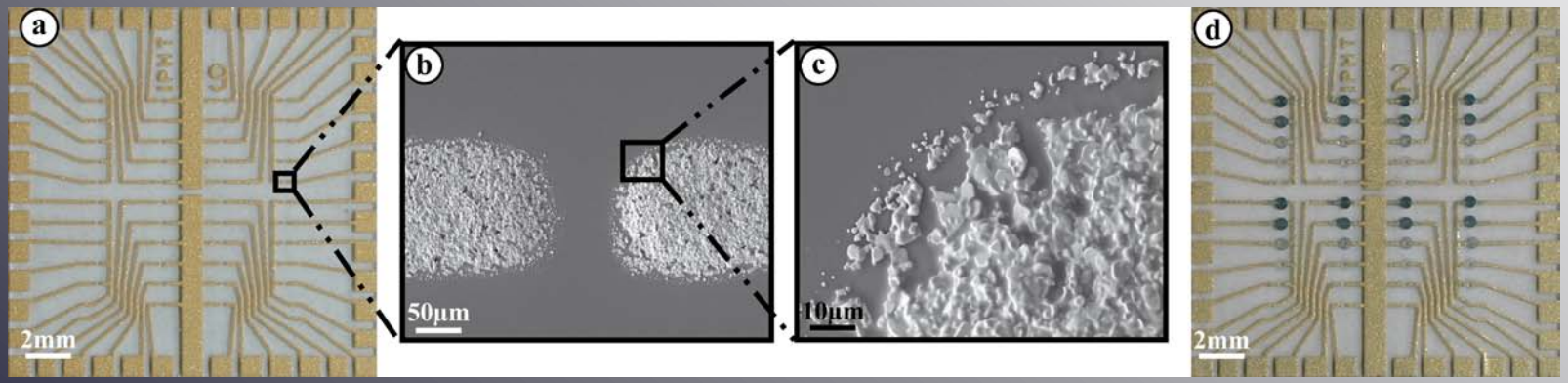
  1. immobilization of the capture-DNA
  2. hybridization of biotin labeled target-DNA
  3. binding streptavidin conjugated HRP
  4. enzymatic silver deposition



chip-based electrical DNA-detection

Schüler, T., Asmus, T., et al., Biosensors Bioelectronics (2009) **24**, 2077-84

- electrical DNA-chip with screen-printed electrodes
  - alternative substrate to photolithographic produced chips

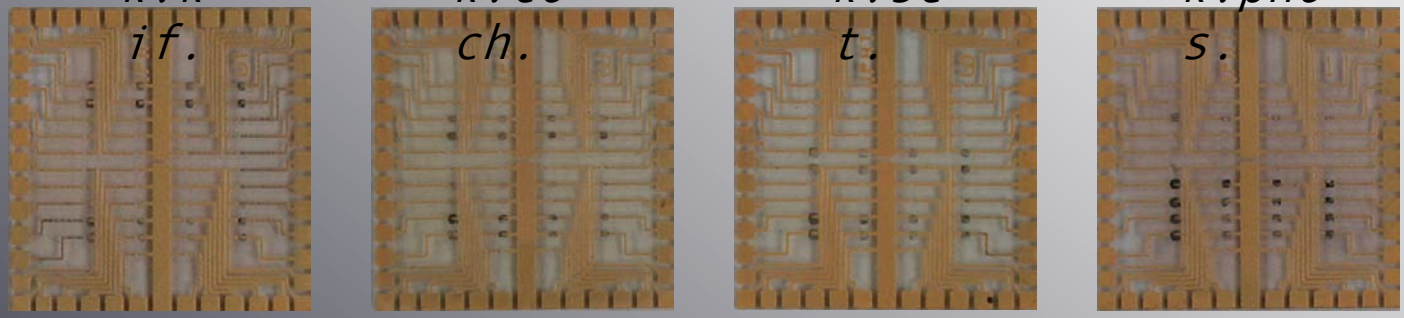


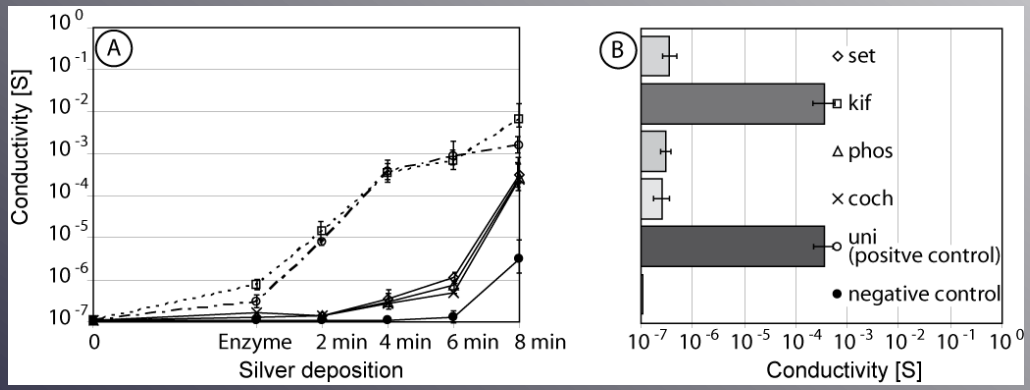
chip-based electrical DNA-detection

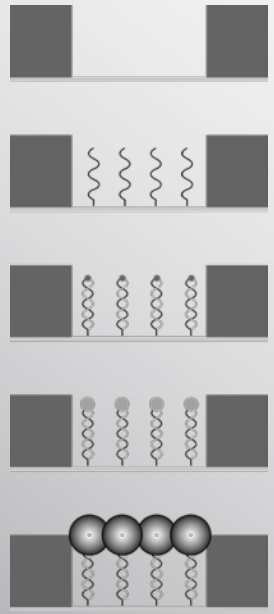
Möller, R., Schüler, T., et al., Appl Microbiol Biotechnol (2008) 77, 1181-8

- taxonomic studies of different species of *Kitasatospora*

k.kif. *k.coch.* *k.set.* *k.phos.*

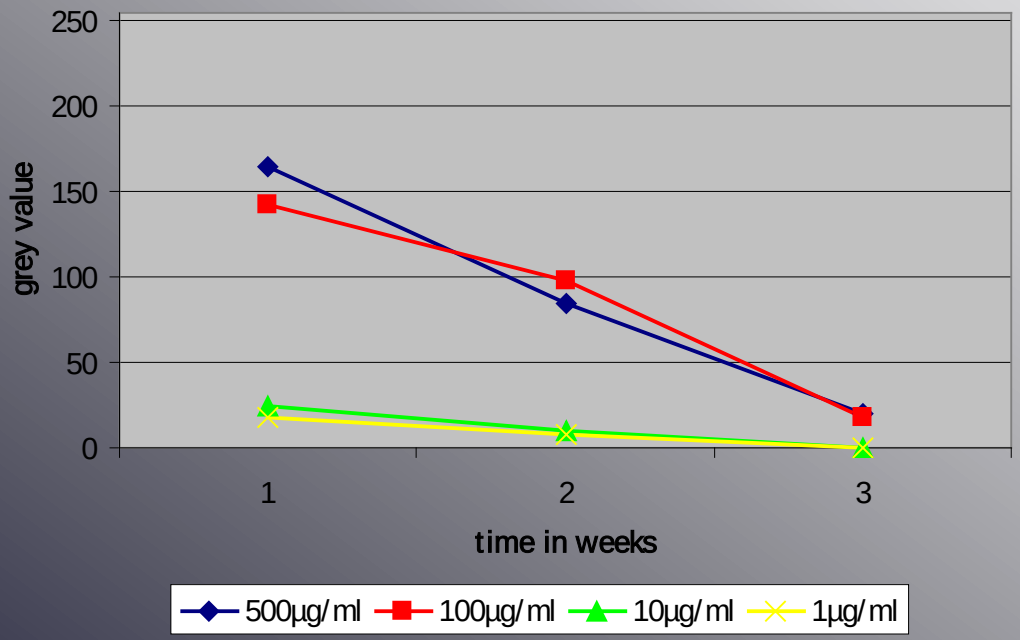


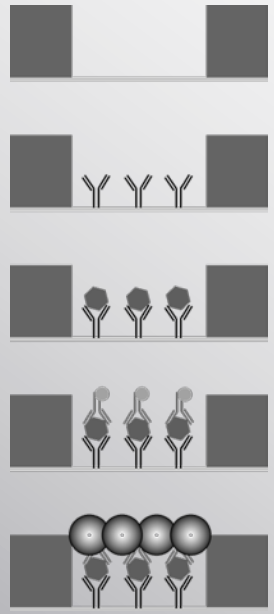




chip-based electrical DNA-detection

- protein detection (human factor H)
  - limit of detection depending on the storage time

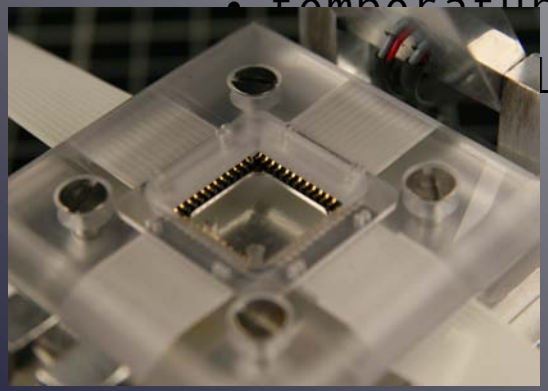
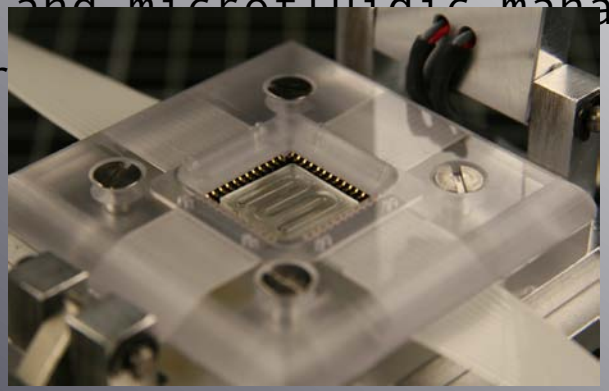
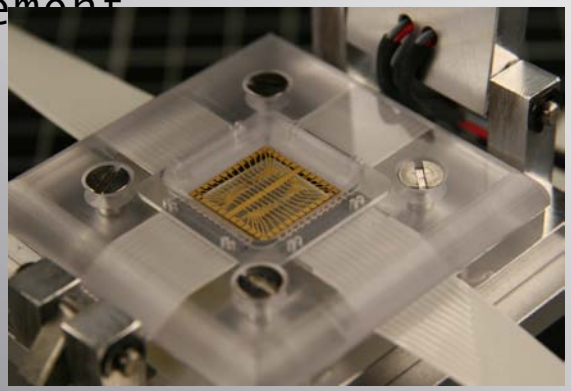




system automation

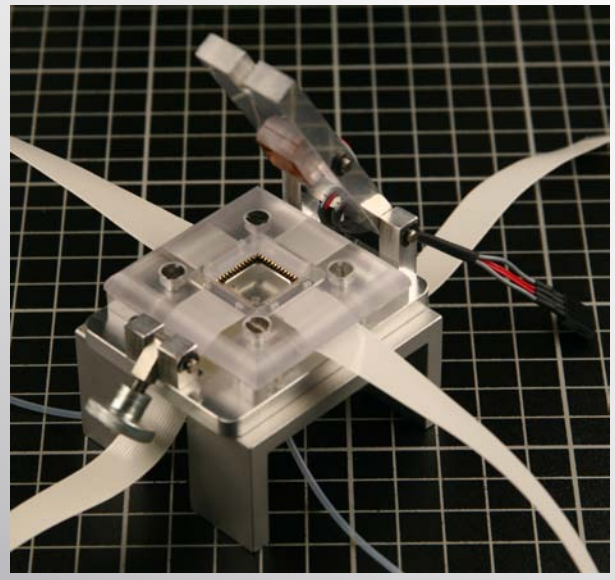
Schüler, T., Kretschmer, R., et al., Biosensors Bioelectronics (2009) **25**, 15-21

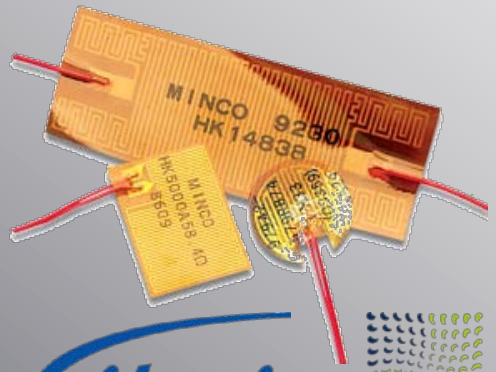
- development of a microfluidic device for the on-site testing
  - flow cell for the integration of the biochip technology
    - temperature and microfluidic management
      l r

system automation

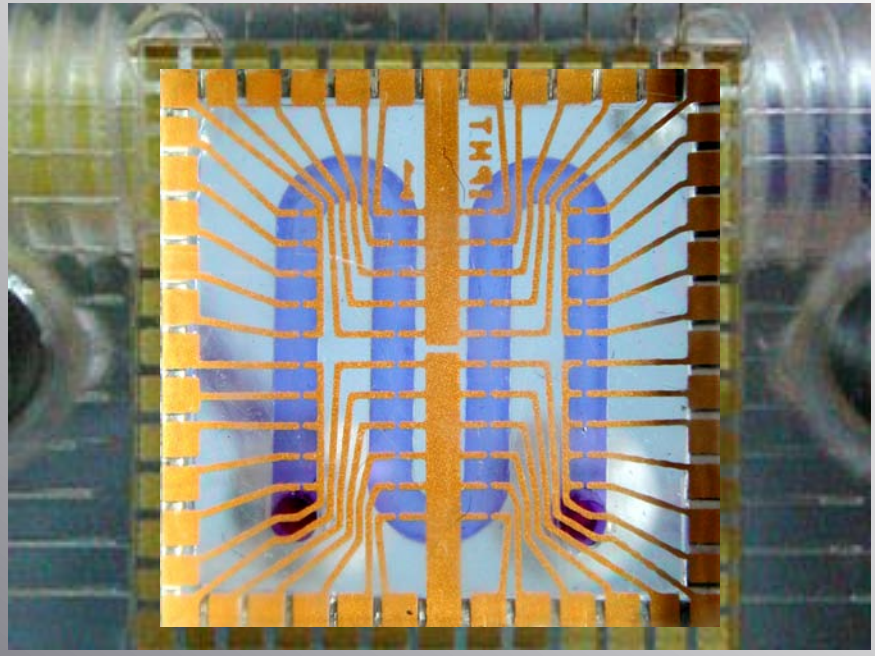
- flow cell
  - cost effective and functional
  - heating foils
  - disposable components
  - PDMS (Polydimethlysiloxane) seal with meandering structures





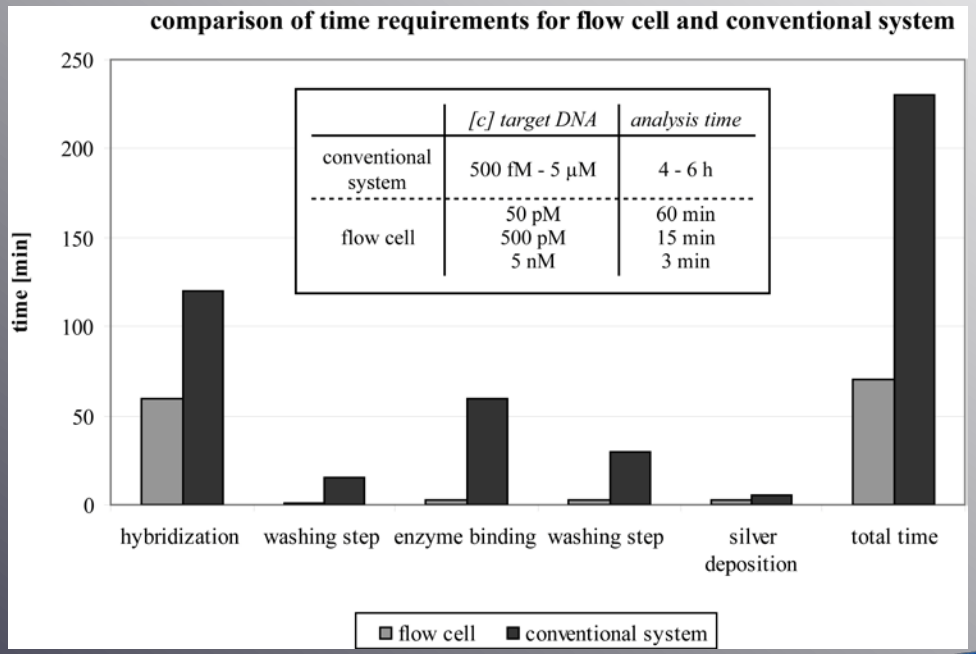
system automation

- advantages
  - active hybridization
  - fast reaction
  - non diffusion limited processes



system automation

- comparison lab-based system
  - length lab-based test ~ 4h / length flow cell test ~ 15min



system automation

- read-out device
  - Bluetooth connection for wireless data transfer
  - PDA for data evaluation and visualization

DNA-Chip Reader

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Outlook

- SERS substrates for surface enhanced Raman spectroscopy
- hydrogels to stabilize the enzyme
- polymers as alternative biochip surface
- influence on particle growth

Acknowledgement

Thank you for your attention

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