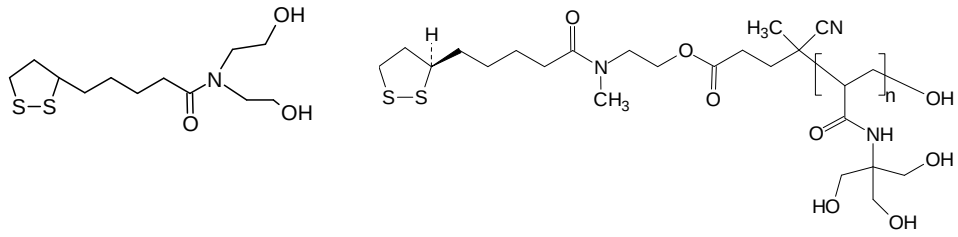
MOLECULAR SENSORS

We develop molecular sensors for various detection methods (i.e. both sensing surfaces and devices). The sensing surfaces are based on molecule specific layers composed of self-assembled receptor molecules or synthetic receptors. The surfaces are designed to have a low non-specific binding of interfering molecules. Molecular and device simulations are used to predict the binding but also to design the sensing phenomena.

The research topics include:

- **Molecule specific sensing elements**
  - Synthesis of molecules with various functional groups and/or repellent properties



  - Synthesis of nanoparticles

- **Molecule specific sensing surfaces**
  - Self-assembled monolayers (SAMs) and non-fouling monolayers

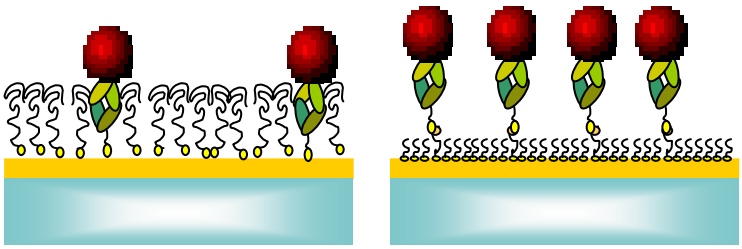
  - Immobilisation of receptor molecules

    Antibodies are mostly adsorbed on the sensor surface or covalently coupled via functional groups that are not site-specific. The lack of control over the orientation of antibodies limits the proportion of available binding sites, whereas site-specific immobilisation leads to higher activity. Our approach has been to couple antibody Fab´-fragments covalently directly onto gold and to block the space in between the fragments with a non-ionic hydrophilic polymer of N-[tris(hydroxy-methyl)methyl]-acrylamide.[1-3] The polymer possesses low non-specific binding and can be covalently attached onto the gold surface by disulfide anchors. The immobilisation method has been demonstrated for

antibody fragments specific of human IgG, C reactive protein, Helicobacter pylori and morphine.

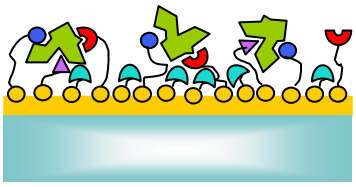
The immobilisation method is generic and can be used for coupling any antibody in an oriented manner to the sensor surface. There are several advantages with the method:

1. It is simple and easy to perform in only a few steps.
2. The site-directed orientation of the antibodies ensures a high specific binding of antigen with a minimum amount of antibody needed for immobilisation.
3. The non-specific binding is extremely low due to the repellent polymer.
4. A membrane-like environment is provided by the polymeric host matrix that protects the antibodies from unfolding.
5. The layer is reasonable stable, and can be regenerated for repeated use.



- <u>Synthetic receptors</u>

In a novel concept we use building blocks composed of lipoate derivatives to produce synthetic receptors based on imprinted self-assembled monolayers (i-SAMs). The lipoate derivatives are screened by molecular dynamics studies and the most promising candidates are synthesized. The compounds used so far carry a disulphide moiety on one side for anchoring to the gold surface and a variable functional group on the carboxylic acid side for complexation with the template. After self-assembly, the template is washed out of the self-assembled film, and “footprints” may be formed in the layer, which allow rebinding of the template.[4] Synthetic receptors composed of an imprinted self-assembled monolayer exhibit the same binding response to the antigen, morphine as a site-specific oriented antibody monolayer. A similar binding curve could be obtained as that for binding of morphine to an antibody Fab´ fragment/polymer layer – indicating that synthetic receptors produced are comparable to those of antibody layers. Concentrations down to 0.1 ng/ml have been measured with surface plasmon resonance.



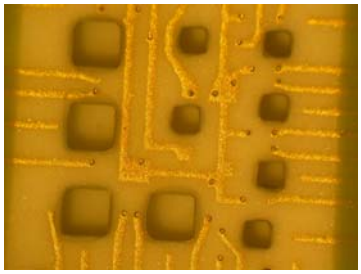
- Single-stranded DNA surfaces

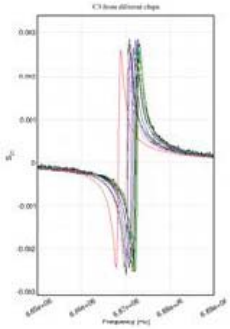
  Thiol modified single-stranded DNA (SH-ssDNA) and blocking agents of various lipoate derivatives or polymers have been co-adsorbed on gold from the same solution or post-treated with the blocking agents.[5] The lowest non-complementary binding and the highest complementary binding of DNA are obtained with a layer assembled from a binary solution of SH-ssDNA and a lipoate blocking agent.

➢ **Sensitive detection methods and devices** (optic, acoustic, electrochemical, thermal)

- Microacoustic sensors

  We are developing molecule specific sensors based on microsystems technologies (MEMS, microacoustic resonators) especially for measuring specific phenomena occurring in liquid environment. The technology provides intrinsic capability for integration and production of array type sensor systems, as well as compatibility with batch processing technologies. Compared with the existing biosensor solutions, our microacoustic sensors have several potential advantages related to their beneficial novel acoustic mode (Patent 2005).[6] The potential application areas cover a wide range of demands e.g. from medical diagnostic to the monitoring of chemical, biological and environmental risks.





- Surface enhanced fluorescence

  We are developing sophisticated approaches for measuring surface restricted fluorescence phenomena. The surface based detection methods under development provide attractive options to perform fast direct tests with very high surface-sensitivity.[7]

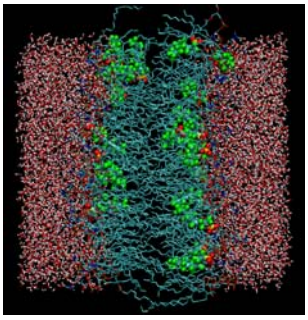
- Surface plasmon resonance (SPR)

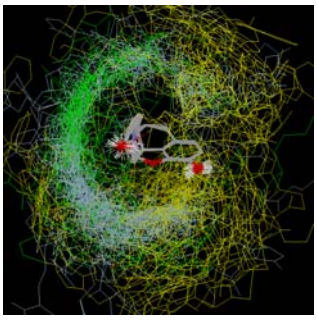
  VTT has a long history in developing and utilizing SPR technology for characterization of (molecule specific) surfaces. In 2006 the SPR technology developed at VTT was transferred to BioNavis Ltd. to take over and further evolve the technology.[8]

➢ Computational simulations and modelling

- Molecular simulations

  Molecular simulations are used to predict the structures and properties of different molecules and molecular assemblies as well as the binding phenomena of molecular sensors. [4, 9-10]





- Device modelling and simulations

  The design and development of the sensing devices (transducers), as well as the sensing phenomena, are supported by different computational methods. The methods typically used to optimize the device performance include finite element methods, equivalent circuits and analytical models.

➢ Sensor electronics

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