

## HELIX®: NEXT-GENERATION MODULAR BIOSENSOR FOR INTERACTION AND CONFORMATION ANALYSIS

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SwitchSENSE® is an automated, fluorescence-based biosensor chip technology that employs electrically actuated DNA nanolevers for the real-time measurement of binding kinetics ( $k_a$ ,  $k_d$ ) and affinities (with  $K_D$  values down to the fM range).

Fluorescent dyes located on the biosensor surface detect the interaction of ligand and analyte molecules in different ways. The fluorescence proximity sensing mode detects the binding of molecules in real-time through changes in the dye's local environment. Association and dissociation of analyte molecules can be observed in real-time. In addition, the high frequency dynamic electrical switching mode probes the hydrodynamic friction of analyte molecules and serves to determine the size and shape of biomolecules. When analytes bind to oscillating DNA nanolevers on the sensor spots, the nanolever movement is slowed by the additional friction imposed by the analyte, thereby revealing its size changes. The unique use of two different fluorophores makes it possible to monitor two independent signals from two interactions at the same time and on the same sensor spot. It also enables fluorescence resonance energy transfer (FRET) experiments, for binding and conformation analyses that require the resolution of intra-molecular distance changes with sub-nanometer resolution. The DNA-encoded anchor sequences present in the biochip surface allow the immobilization of a wide range of different molecules or even a combination of different molecules in varying ratios and densities. This technology is unlike existing methodologies in that it combines high sensitivity real-time kinetics with structural information on size, shape and conformation, providing a new depth and understanding of the interaction.

The seminar will highlight the broad range of applications of the switchSENSE® technology that is supported by the next generation heliX® biosensor:

DNA/RNA binders' analysis:

- A multichannel optical detection system to multiplex several binding reactions into one measurement
- Screening and hits validation inducing aptamer folding

Conformational changes analysis:

- Comparing the hydrodynamic friction of different ligands with DNA origamis - Screening and ranking of small molecule inducing conformational changes by de novo real-time conformation referencing

For coming in 2022: measuring kinetics directly on cells