Technical conditions:

Description of device usage:

System for measurements of interaction of biomolecules in real-time mode. It is able to measure hydrodynamic friction to determine the absolute size and shape of interacting molecules using high frequency dynamic electrical switching mode. It is able to measure real-time kinetics of interactions independently of the size of molecules through changes in the local environment by enhancing the fluorescence of molecules. The device includes a temperature-controlled automatic sample dispenser, a temperature controlled biochip environment for the measurement itself, and two independent probing fluorescence channels. The device is fully programmable and computer-controlled; it also includes an automated system for conjugation of biomolecules to DNAs controlled by computer station.

Technical specifications:

Sensing of interactions		*Technical parameters offered by the supplier **
Limit of detection LOD	10 fM	YES
Dissociation constant K_D	At least in the range from 50 fM to 1 mM K_D measurements from kinetics and titration	YES
Association rate constant kON	At least in the range of 1E3 – 1E8 $M^{-1}s^{-1}$	YES
Dissociation rate constant kOFF	At least in the range of 1E-6 – 1E0 s^{-1}	YES
Analysis		*Technical parameters offered by the supplier **
Determination of Molecule Size	Hydrodynamic Protein Diameter (D_H, Stokes radii on chip) 1 nm < D_H < 14 nm (8 kDa – ~500 kDa)	YES
Determination of Molecule Shape	Conformational changes (qualitative and quantitative if $\Delta D_H \geq 0.1$ nm)	YES
Temperature control of measurements	Measurement at constant temperatures Measurement in temperature gradients	YES
Detection of Melting point – Range	At least in the range of 8°C to 75°C	YES
Melting point - Ramp speed	$\Delta T/\Delta t$ at least up to 10°C/min	YES
Melting temperature – Accuracy	At least ΔT_M ~ 0.5°C	YES
Melting curve analysis (TM) & small-molecule induced changes in thermal stability	Measurable	YES
Multiple binding	Detection of avidity, cooperativity	YES

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	Measurements of two different analytes on the same detection spot via dual-colour detection	
Determination of Thermodynamic Parameters	ΔG, ΔH, ΔS	YES
Equilibrium binding energies	Van't Hoff analysis 8°-75°C	YES
Transition state energies	Eyring analysis 8°-75°C	YES
Software package for analysis and design of automatic measurements	2 licences, free upgrade for 2 years	YES
Sample and Liquid handling		***Technical parameters offered by the supplier ****
Number of flow channels	At least 4 flow channels	YES
Number of electrodes	At least 20	YES
Electrode material	Gold	YES
Electrode diameter	Maximum 120 µm	YES
Conjugation method	Coupling to DNA oligos	YES
Flow channel height	Maximum 60 µm	YES
Minimal sample volume	At least from 10 µL to maximum 50 µl	YES
Pumps	2 pumps installed: syringe and peristaltic	YES
Pump Rate	At least in the range from 1 to 4000 µL / min	YES
Pump Capacity	At least 5 mL (syringe) and NA (peristaltic)	YES
Temperature Range (flow channel)	8°C – 70°C (low flow rates) 10°C – 40°C	YES
Ramp speed (flow channel)	up to 10°C / min	YES
Autosampler capacity	36 × 1.5 mL vials & 12 × 10.0 mL vials or 96 well plate & 6 x 10.0 mL & 6 x 1.5 mL	YES
Autosampler Temperature	At least in the range from 10°C – 40°C (at 20°C ambient temp. and rel. humidity < 25%)	YES
Tubing material	PEEK, Radel	YES
Measurement mode		***Technical parameters offered by the supplier ****
Detection principle	Time-correlated single photon counting of electrically actuated fluorescent DNA levers	YES
Time-resolved switching at high frequencies	1 kHz – 1 MHz, square wave	YES
Low-frequency switching	0.1 Hz – 4 Hz, square wave	YES
Voltage sweep Staircase	ΔV > 1 mV	YES
Constant voltage	± 1 mV	YES
Voltage range	± 1 V	YES

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Sampling rate	1 Hz – max. 5 Hz	YES
Substrate material	Glass	YES
Counter electrode	Indium tin oxide (ITO)	YES
Regeneration		***Technical parameters offered by the supplier ****
Regeneration method	Oligonucleotide denaturation & hybridization	YES
Standard conditions	Denaturation at pH 13-14, hybridization with 100 – 500 nM oligo	YES
Regeneration cycle duration	Max. 8 min	YES
Analyte molecules		***Technical parameters offered by the supplier ****
Proteins	Protein-protein Protein-DNA or Protein-RNA Protein-small molecule Protein-peptides	YES
Antibodies	Antigen-Antibodies Bispecific analysis Biparatopic, triparatopic antibodies	YES
Nucleic acids	DNA, RNA, LNA, PNA with single-nucleotide mismatch sensitivity DNA Origamis Structural RNA	YES
Small molecules	DNA binding (intercalation) Protein-Small molecules	YES
Chemical modifications and/or size	Proteins or nucleic acids which cause changes in conformation or charge	YES
Cell-like structures	Virus-like particles, liposomes and lipid vesicles	YES

* Supplier will indicate YES / NO. If the supplier complements the minimum required technical parameters NE, this is the reason for excluding the tenderer from further participation in the procurement procedure.

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switchSENSE®

Multi-parameter biophysical analysis of molecular interactions

k_{ON} | k_{OFF} | K_D | IC_{50} | D_H | T_M | ΔG | ΔH | ΔS | k_{CAT} | K_M | U

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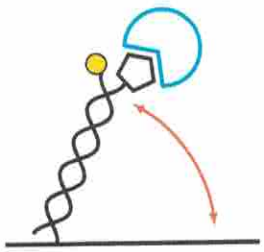
switchSENSE®

switchSENSE® technology utilizes a novel electro-switchable biosurface to provide researchers and commercial laboratories the ability to characterize interactions between molecules in real-time.
This technology is unlike existing methodologies in that it combines high sensitivity kinetics with structural information on size, shape and conformation providing a new depth and understanding of the interaction.

Studies are performed on a re-usable biochip, generated using familiar coupling and hybridization methods. Within this biochip, DNA levers are embedded onto a series of gold electrodes. These nanolevers serve either as target for molecular interactions themselves, or hold other interaction partners. To characterize interactions, the DRX instrument is used to bring about deliberate movement of these nanolevers by altering the voltage across the gold surface. When interactions occur, these movements are affected and in turn, used in the calculation of kinetic and biophysical information.

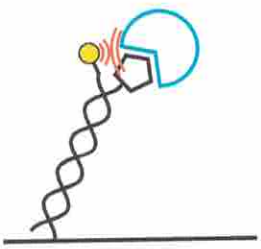
Measurement Modes

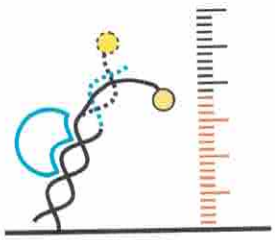


switchSENSE® combines three measurement modes:

The high frequency dynamic electrical switching mode probes the hydrodynamic friction and serves to analyze the size and shape of biomolecules.

The fluorescence proximity sensing mode reveals the binding of molecules in real-time through changes in the dye`s local environment.





The molecular ruler mode utilizes a long-ranged energy transfer to gauge the height of the fluorophore above the surface with sub nanometer accuracy.

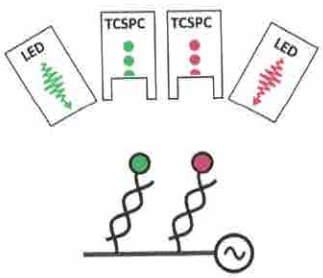
www.dynamic-biosensors.com/switchsense/

Dual-Color

The DRX² instrument is the first biosensor to offer the analysis of two molecular probes on the same detection spot.

Each sensor spot carries two lever sequences, one with a red tag, and one with a green tag. The instrument tracks the movement and position of the different levers separately and simultaneously. The two levers can either be in 1:1 ratio at ~50 nm separation or users can readily define ratio and surface density.

DRX²



Schematic of a dual-color **switch**SENSE® experiment

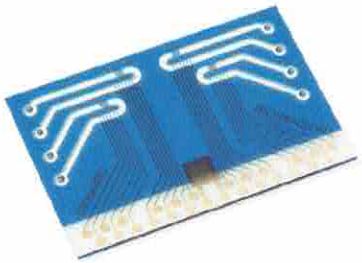
Biochips

switchSENSE® biochips are designed for flexibility and adaptability featuring 20 microelectrodes, arranged in 4 separate on-chip flow channels for maintenance-free operation.

The microelectrode surfaces are supplied with electrically switchable ready-to-use DNA nanolevers. A number of different conjugation protocols and kits are available to functionalize the nanolever layers with molecules of interest.

The biochip may be regenerated many times using automated routines and can be configured in three levels of multiplexing, allowing the use of up to 6 different capture molecules in parallel in each flow channel.

www.dynamic-biosensors.com/biochips/



switchSENSE® Biochip

DRX Series Instruments

Single DRX and dual-color DRX² analyzers are electro-optical instruments specifically designed for automated **switch**SENSE® measurements. Instruments feature automated liquid handling and temperature control.

www.dynamic-biosensors.com/instruments/

DRX Instrument

Data Generation

switchSENSE® Technology can be used to generate the following data:

Binding Kinetics
Binding Affinity
Protein Diameter
Conformational Change
Nuclease & Polymerase Activity
Bispecific Binders & Avidity
Melting & Thermodynamics
Multimers & Aggregation

Performance Specifications

Limit of detection 10fM
Dissociation constant 50fM – 1mM
Association rate constant 1E3 – 1E8/Ms
Dissociation rate constant 1E-6 – 1E0/s
Hydrodynamic diameter accuracy of 0.1nm
Temperature 8° – 75°C (chip),
10° – 40°C (autosampler)

switchSENSE® is a proprietary measurement technology by Dynamic Biosensors GmbH. Instruments and biochips are engineered and manufactured in Germany.

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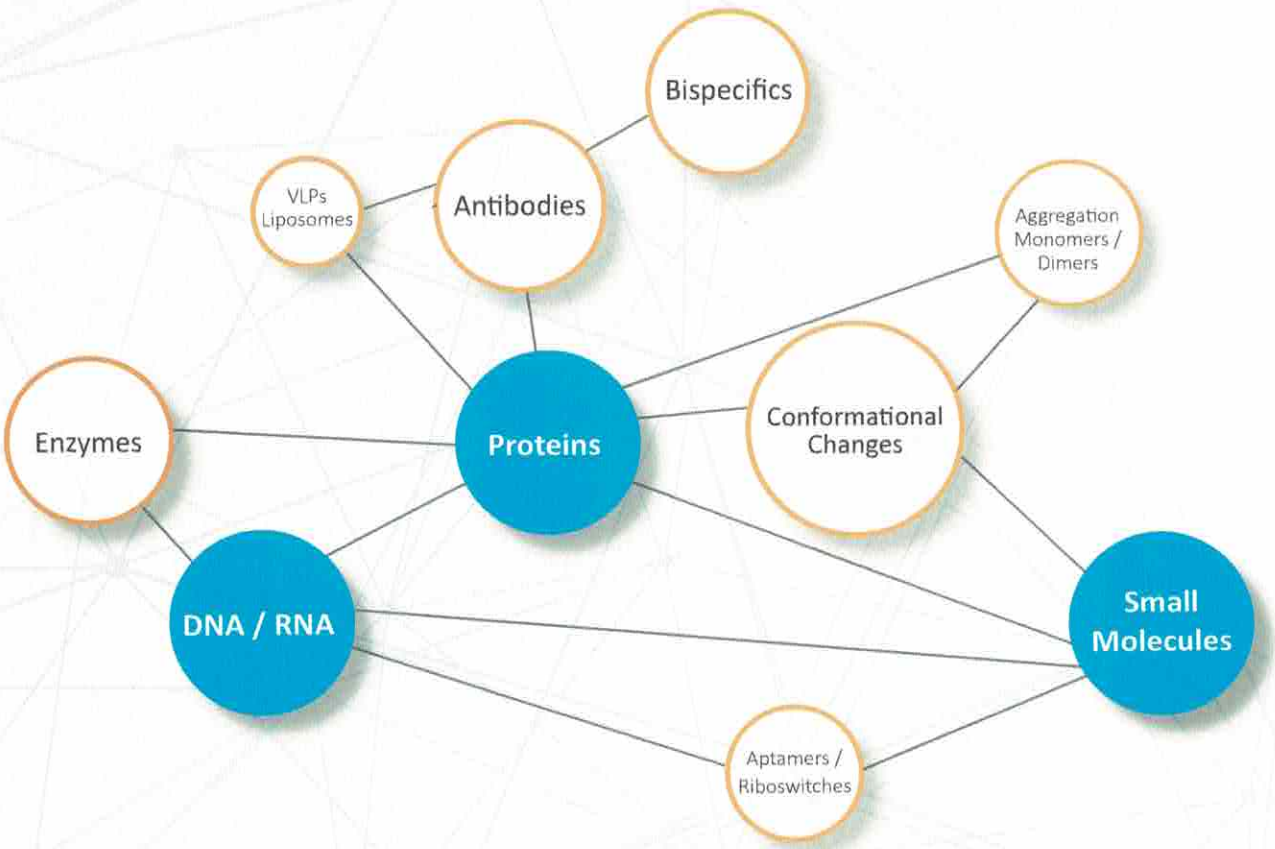
R. Strasser

Research Areas

switchSENSE® is used in a wide range of research areas from early discovery stages within leading academic groups to drug development programs at large pharma companies.



„**switch**SENSE® allows us to measure affinity and kinetics of DNA-binding proteins which we are unable to analyze with any other method."

Michael Schraeml, PhD, Head of Protein and Enzyme Technologies
Roche Diagnostics GmbH – Penzberg, Germany

For a list of recent publications please visit **www.dynamic-biosensors.com/literature/**

Contact **info@dynamic-biosensors.com** to speak to our application team about methodologies or to arrange a demonstration.

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DRX²

TECHNICAL SPECIFICATIONS

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switchSENSE® analyzer DRX² instrument

Dual color detection

Sensing | Analysis | Sample and Liquid Handling
Measurement Modes | Regeneration | Analyte Molecules

SENSING

Limit of detection LOD	10 fM
Dissociation constant K_D	50 fM – 1 mM K_D measurements from kinetics and titration
Association rate constant k_{ON}	1E3 – 1E8 $M^{-1}s^{-1}$
Dissociation rate constant k_{OFF}	1E-6 – 1E0 s^{-1}

ANALYSIS

Size	Hydrodynamic (Stokes) protein diameter D_H 1 nm < D_H < 14 nm (corresponding to app. 8 kDa – 500 kDa)
Conformation & structure	Changes in conformation or folding of proteins or nucleic acids. Qualitative results as changes in switching speed and quantitative results as D_H changes if $\Delta D_H \geq 0.1$ nm.
Temperature control	Measurement at constant temperatures 8°C – 75°C Measurement in temperature gradients 8°C – 75°C Temperature ramp $\Delta T/\Delta t$ up to 10°C/min
Melting curve analysis, T_M measurement	8°C < T_M < 75°C Melting temperature accuracy ΔT_M < 0.5°C Small molecules induced T_M changes measurable
Multiple binding sites	Quantitation of avidity, cooperativity Measurements of two different analytes on the same detection spot via dual-color detection

Thermodynamic parameters	ΔG, ΔH, ΔS
Equilibrium binding energies	Van't Hoff analysis 8°-75°C
Transition state energies	Eyring analysis 8°-75°C

SAMPLE and LIQUID HANDLING

Number of flow channels	4 flow channels per chip
Number of electrodes	20
Electrode material	Gold
Electrode diameter	120 µm
Conjugation method	Coupling to DNA oligos with amine-reactive, thiol-reactive, or click chemistries
Ligand capture	His-tag, Strep-tag, Biotin, Fc-capture, GFP, GST, ...
Flow channel height	60 µm
Minimal sample volume	10 µL – 50 µl (depending on measurement mode)
Pumps	2 pumps installed: syringe and peristaltic
Pump rate	1 – 4000 µL / min
Pump capacity	Syringe: 5 mL; peristaltic: continuous
Autosampler capacity	36 × 1.5 mL vials & 12 × 10.0 mL vials or 96 well plate & 6 x 10.0 mL & 6 x 1.5 mL
Autosampler temperature	10°C – 40°C (at 20°C ambient temp. and rel. humidity < 25%)
Tubing material	PEEK, Radel

MEASUREMENT MODES

Detection principle	Time-correlated single photon counting of electrically actuated fluorescent DNA levers. Simultaneous excitation and detection of two fluorescence colors on one measurement spot.
Dual color detection	Green (525 – 575 nm) and red (650 – 685 nm) fluorescence channels
Time-resolved switching at high frequencies	1 kHz – 1 MHz, square wave
Low-frequency switching	0.1 Hz – 4 Hz, square wave
Voltage sweep staircase	ΔV > 1 mV
Constant voltage	± 1 mV
Voltage range	± 1 V

Sampling rate	1 Hz – 10 Hz
Substrate material	Glass
Counter electrode	Indium tin oxide (ITO)

REGENERATION

Regeneration method	Oligonucleotide denaturation & hybridization (when using covalent coupling) or tag-dependent regeneration procedures
Standard conditions	Denaturation at pH 13-14, hybridization with 100 – 500 nM oligo
Regeneration cycle duration	<8 min

ANALYTE MOLECULES

Proteins	Protein-protein Protein-DNA or protein-RNA Protein-small molecule Protein-peptides
Antibodies	Antigen-antibody Bispecific analysis Biparatopic, triparatopic antibodies
Nucleic acids	DNA, RNA, LNA, PNA with single-nucleotide mismatch sensitivity DNA origamis Folded RNA structures
Small molecules	DNA binding (intercalation, groove binding) Protein-small molecules
Chemical modifications and/or size	Proteins or nucleic acids, which cause changes in conformation or charge
Cell-like structures	Virus-like particles, liposomes and lipid vesicles

OPERATING PARAMETERS

Power supply	50-60 Hz 100-120 VAC / 220-240 VAC
Max. current	6.5 A at 100 VAC
Fuses	2x 8A T
Operating temperature	< 15-28°
Operating rel. humidity	< 70%
Noise	< 40 dB
Altitude	< 2000 m

Instrument Freight Information

Weight	130 kg / 290 lb
Dimensions	60 x 60 x 60 cm / 23" x 23" x 23"

Directives & Certifications

European CE Directives	2006/95/EC Low Voltage Directive Tested according to standard EN 61010-1 2004/108/EC Electromagnetic Compatibility Directive Tested according to the following standards EN 61326-1: 2006 EN 61000-6-2: 2005 EN 61000-6-4: 2007 / A1: 2011 EN 61000-3-2: 2006 + A1 + A2 EN 61000-3-3: 2008
ISO	Dynamic Biosensors GmbH is certified according to **ISO 9001:2015** and **ISO 14001:2015**
North America – NRTL	UL 61010-1, 3rd Ed. CAN/CSA-C22.2 No. 61010-1-12, 3rd Ed.

Dynamic Biosensors GmbH is the sole owner of the proprietary **switch**SENSE® technology for characterization of molecular interactions. **switch**SENSE® technology is protected by 22 patents in Europe, USA and Japan and is available world-wide exclusively through Dynamic Biosensors GmbH.

Selected patents are: EP2622093B1, EP1588755B1, EP2042861A3, EP2192401B1, EP1588755B1, EP14000670.1, WO2014114665A1, US9164055B2, US2005069932A1, US8445262B2, US8309365B2, US8945944B2, US8568966B2, US5942397A, DE102007005472B4.

Contact

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Germany

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San Diego, CA 92126
USA

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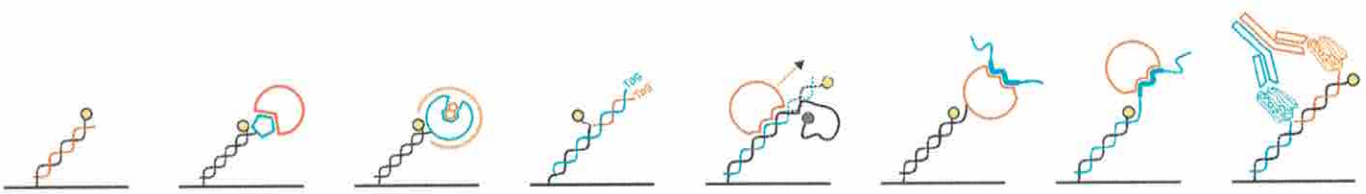
Technical Support
Phone: +49 89 89 74 544 66
Email: support@dynamic-biosensors.com



switchSENSE® is a proprietary measurement technology by Dynamic Biosensors GmbH.
Instruments and biochips are engineered and manufactured in Germany.

Munich DE I San Diego, CA USA I Warszawa, PL I Tokyo JP I Singapore SG

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82152 Martinsried/Planegg · Germany

Dynamic Biosensors GmbH
Lochhamer Str. 15
82152 Martinsried/Planegg
Germany

Dr. Ralf Strasser
strasser@dynamic-biosensors.com
T: +49 (0)89 89 74 544 – 15

Martinsried, 12. March 2019

POWER OF ATTORNEY

Dear Sir/Madam,

Acting on behalf of Dynamic Biosensors GmbH, NIF 14313181651, with its seat in Lochhamerstrasse 15, 82152 Martinsried, Germany (the "Company"), I Ralf Strasser, Passport no. 10801826, living in Steinpilzweg 3a, 81377, Munich, Germany, hereby grant a power of attorney to

Dr. Daisylea de Souza Paiva

Passport n. YC764298, living in Karlstrasse 100, 80335, Munich, Germany to represent the Company in the tender procedure: "Přístroj pro měření interakce biomolekul v reálném čase".

This power of attorney includes in particular the right to sign the contract related to the tender specified above. The power of attorney is valid until further notice.

Ours sincerely,

Dynamic Biosensors GmbH
Lochhamer Str. 15
D-82152 Martinsried/Planegg
Tel. +49 (0)89 / 89 74 544-0
www.dynamic-biosensors.com

ppa. Ralf Strasser

Ralf Strasser, PhD
Head of Biochemistry

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