Functional assays for membrane protein on nanostructured supports (ASMENA)

EU 7th Framework

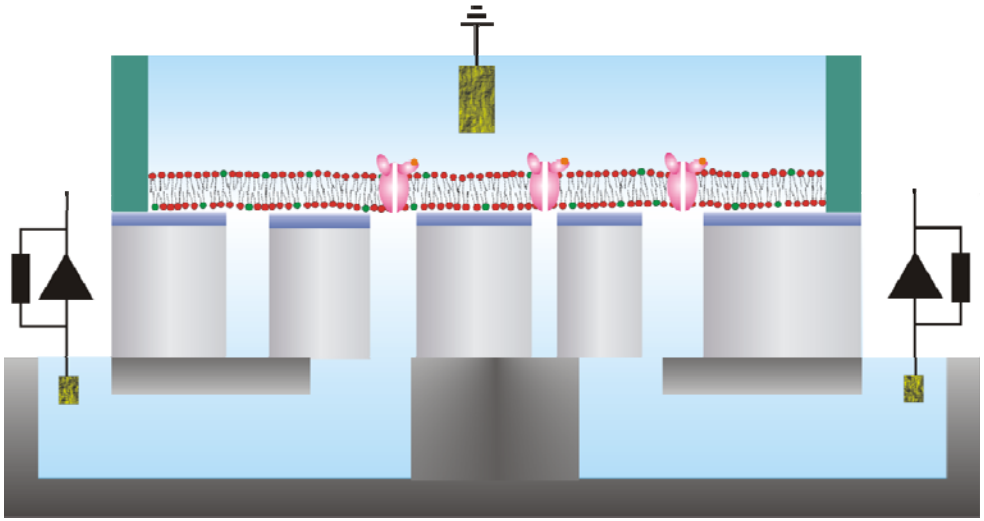
Nanosciences, nanotechnologies, materials & new production technologies (NMP)

FP7-NMP-ASMENA

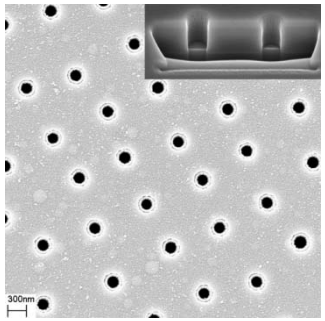
ASMENA objectives

The main ASMENA objectives can be summarized as generating the scientific and technological know-how to achieve:

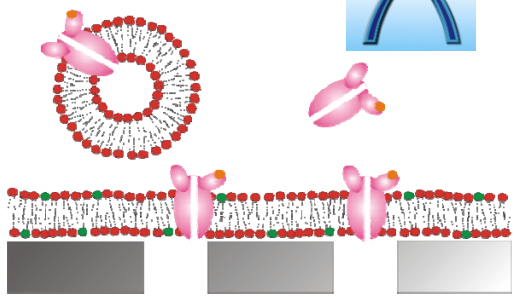
1. an electrochemical sensor platform for ion channel/transporter drug screening/analytical profiling
2. a local surface plasmon resonance sensor platform for aquaporin (possibly also ion channel) drug screening/analytical profiling
3. a membrane protein functionalized waveguide sensor platform for drug screening/analytical profiling based on self-assembled proteolipid membranes and label-free sensing.



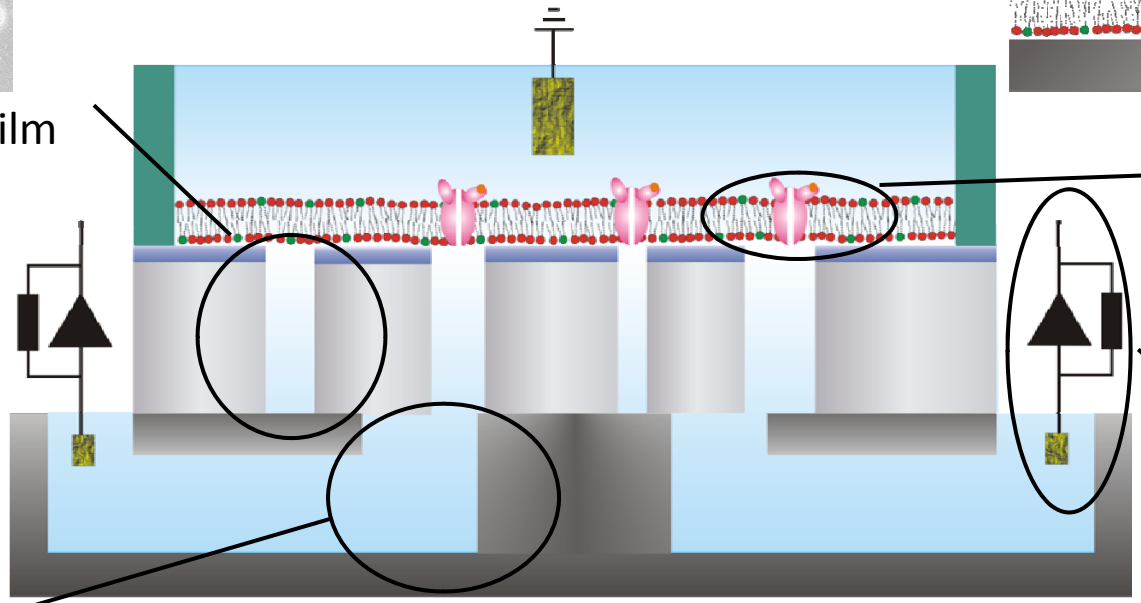
Concept - Nanopore-spanning membrane sensing



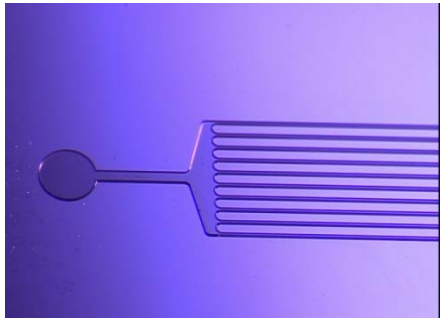
Nanoscale porous film



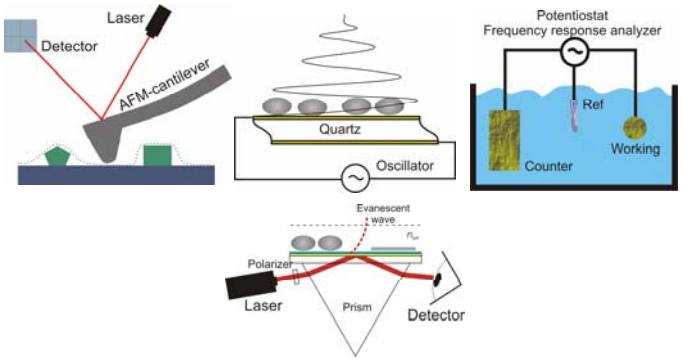
Self-assembly of biomembrane



Microfluidics



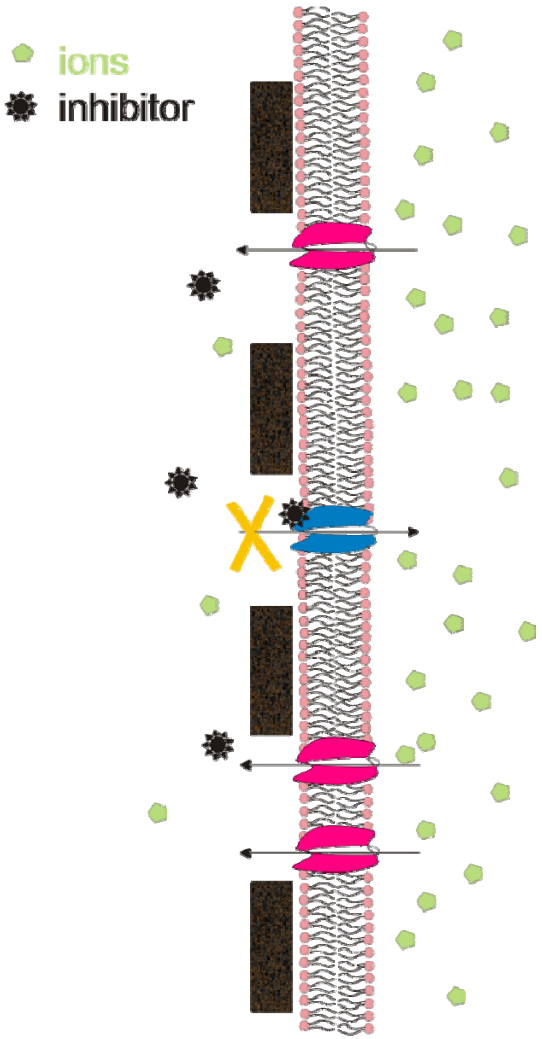
Sensing techniques



Key concepts

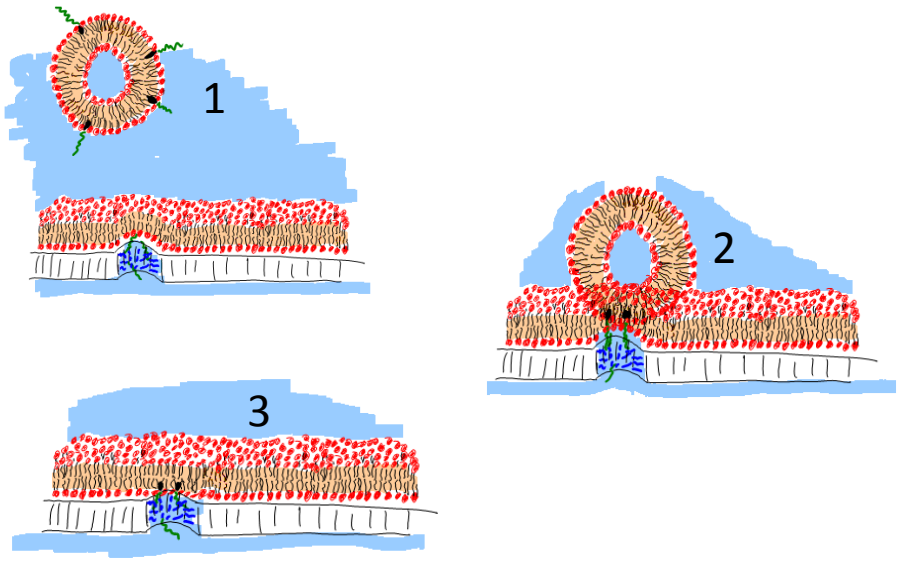
- nanoscale topographical features, specifically nanopores, to enhance stability of the bilayer and sensitivity of measurement integrated in a sensor chip format (WP1)
- nanoscale surface modifications allowing directed self-assembly of desired proteolipid structures on the chip (WP2)
- self-assembly of proteolipid membranes onto the nano-sized sensor structures from proteoliposomes to achieve a simple and robust preparation suitable for commercial applications. (WP3)
- affinity assays based on high-density membrane protein comprising lipid membrane-functionalized nanostructures on waveguides (WP4)
- insertion of membrane protein drug targets into the free-standing membranes for functional measurements (WP5)
- assays for quantitatively measuring membrane protein functionality for drug candidate screening and analytical profiling (WP6)

Why *nanopore*-spanning membranes?

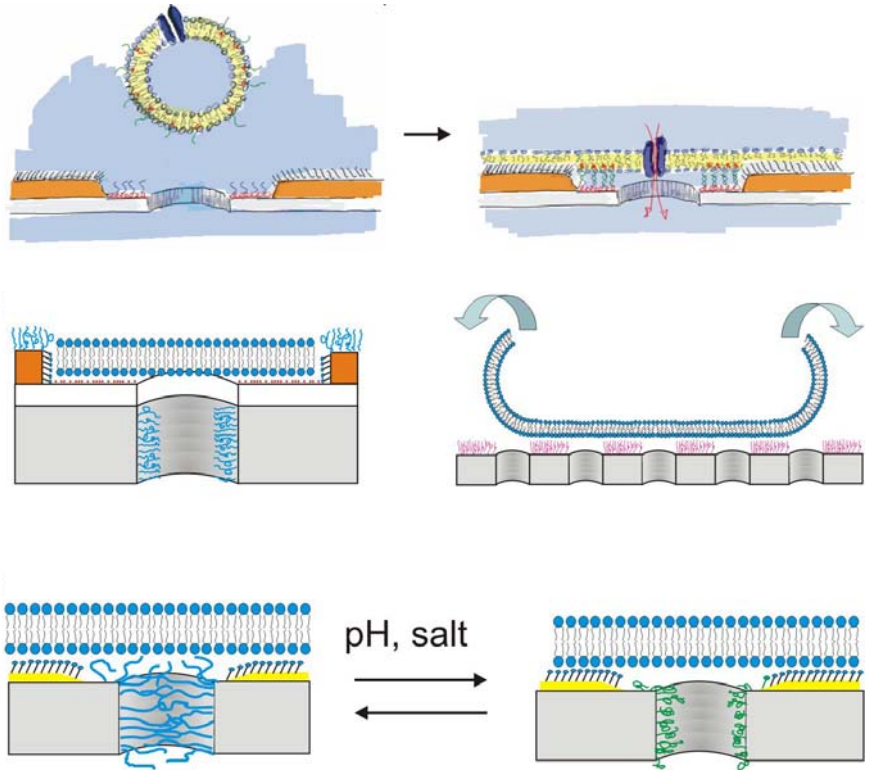


- *multiple* sensing techniques for screening of receptor *function*
- *access* to both sides of the bilayer
- *mobility* of lipids and integrated proteins
- space for *integration* of membrane proteins with sensor support in native-like environment
- mechanical *stability* for multi-day measurements
- miniaturized *array* readout
- microfluidics for *low sample consumption*

Concept – self-assembly of spanning membrane



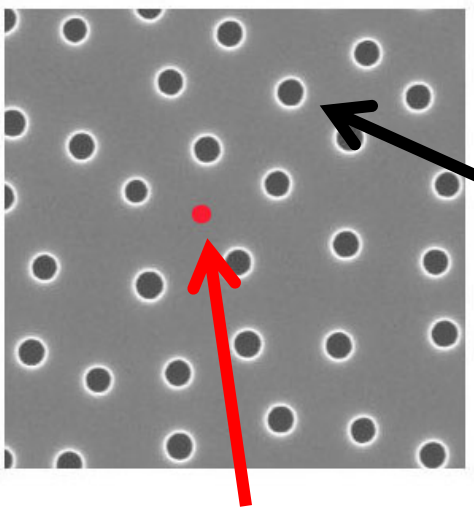
Major challenge is the low-cost formation of nanopore-spanning proteolipid membranes



- Main focus is on targeted fusion of proteoliposomes into a supported lipid bilayer
- Targeting and controlled nanopore sensor function to be achieved by specific polymer-surface chemistry

Concept - LSPR

Specific chemistry for assembling protoliposomes into LSPR active pores

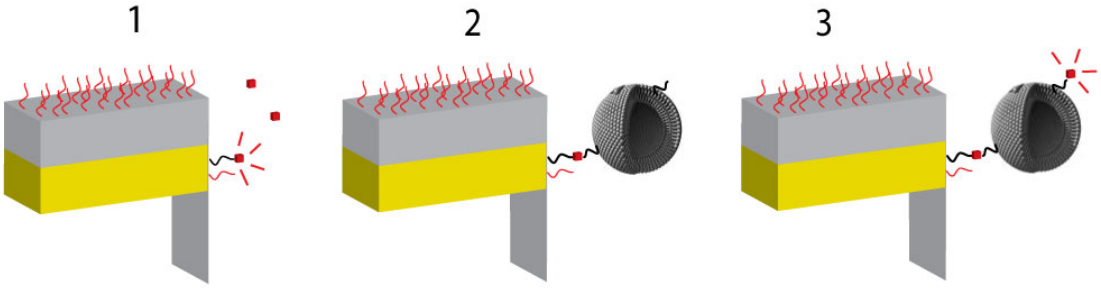


~10 % coverage of pores and liposomes

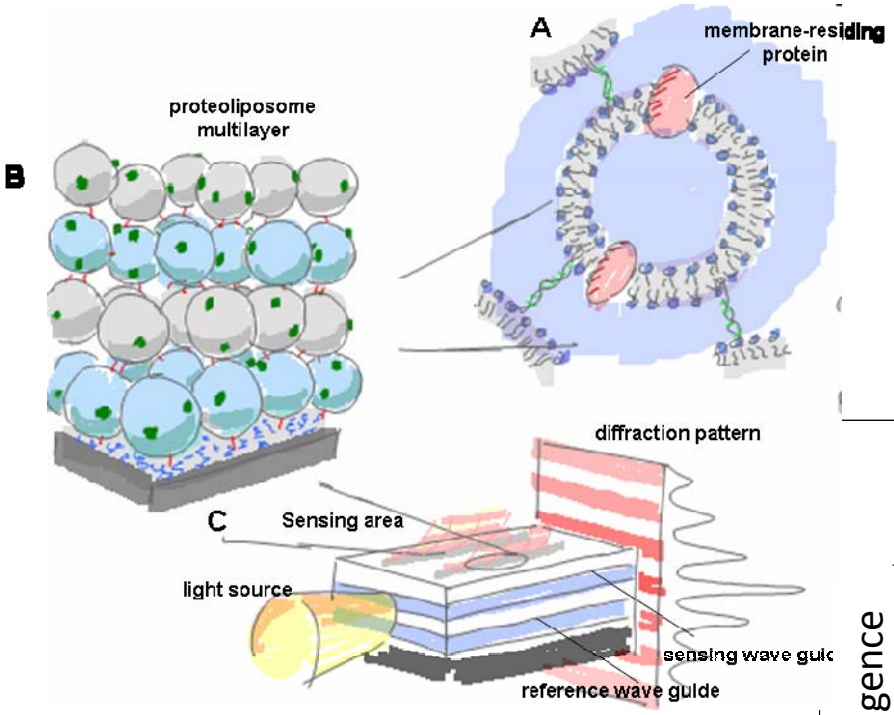
<0.1 % non-specific coverage of liposomes

Advantages:

- High sensitivity (Biacore level)
- Membrane proteins in native and reconstituted natural environment
- Low cost
- Miniaturization and microscopic array readout
- Rapid sample exchange
- Renewable chips

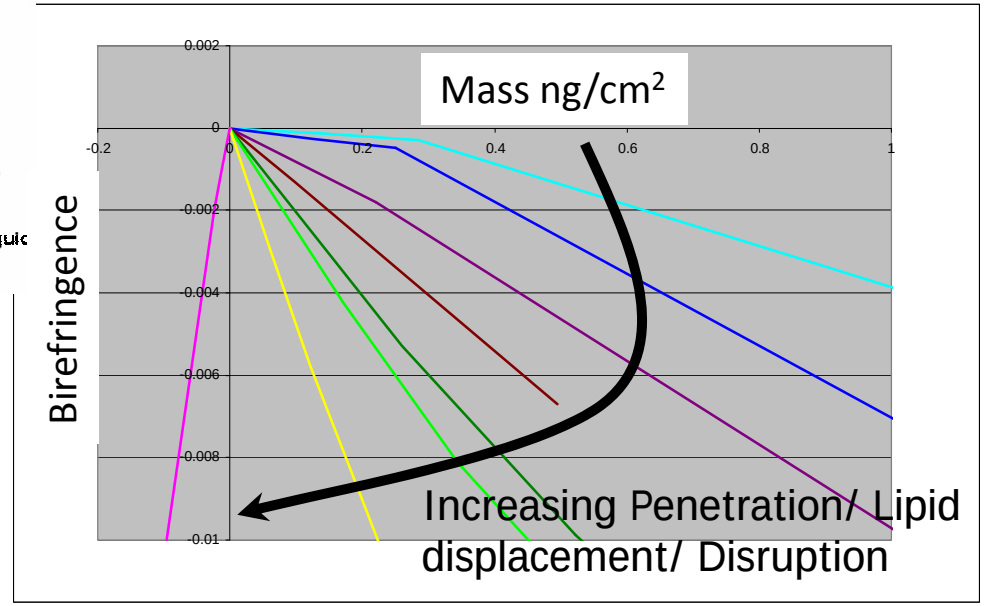


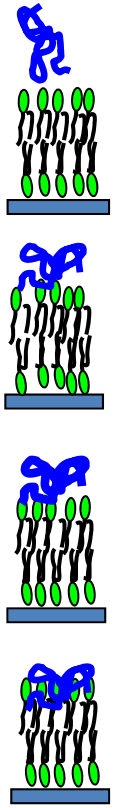
Concept – waveguide spectroscopy



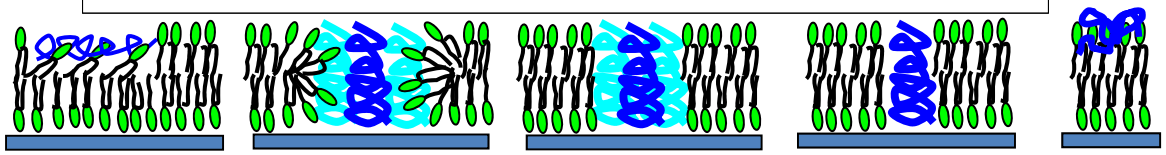
Two waveguide sensor platforms:

- Farfield Analight Dual Polarisation Interferometry
- MicroVacuum Optical Lightmode Waveguide Spectroscopy





- Measure conformational changes in proteins through amplified changes in lipid alignment
- Platform for integrating native and protein containing liposomes for evanescent optical sensing



ASMENA main objectives

Official project start date: 01.09.2008
Official project end date: 30.08.2011

Work package number	Work package title	Person months	Start month	End month
WP1	Fabrication of nanostructured supports	72	1	32
WP2	Chemical surface functionalisation of nanoscale features for guiding assembly and sensor integration of (proteo)lipid membranes by function	77	1	24
WP3	Formation of planar lipid bilayers on nanostructured surfaces	133	1	36
WP4	Integration of transmembrane protein assays with waveguide biosensors	93	1	36
WP5	Functional assays of membrane proteins	89	1	34
WP6	Application for drug screening	85	20	36
WP7	Management activities	21	1	36
	Total:	570		

Project leaders

Project coordinator: Prof. Marcus Textor (ETH Zurich)
Scientific coordinator: Dr. Erik Reimhult (ETH Zurich)

Work package leaders

Work package	Work package leader institution
1	Leister – Marco di Berardino
2	ETHZ – Erik Reimhult
3	ETHZ – Janos Vörös
4	Farfield – Marcus Swann
5	PSI – Louis Tiefenauer
6	Roche – Walter Schilling/Michael Hennig/Thilo Enderle
7	ETHZ – Marcus Textor

Tasks

- manage the scientific and technical aspects of the work package;
- organize work package meetings to discuss progress, problems and newly emerging ideas;
- maintain close contact with all work package participants;
- report to the PC on progress, problems as well as on the milestones, deliverables and financial aspects of the work package.

ASMENA consortium

Group photo ASMENA General Assembly meeting in Budapest, Spring 2009

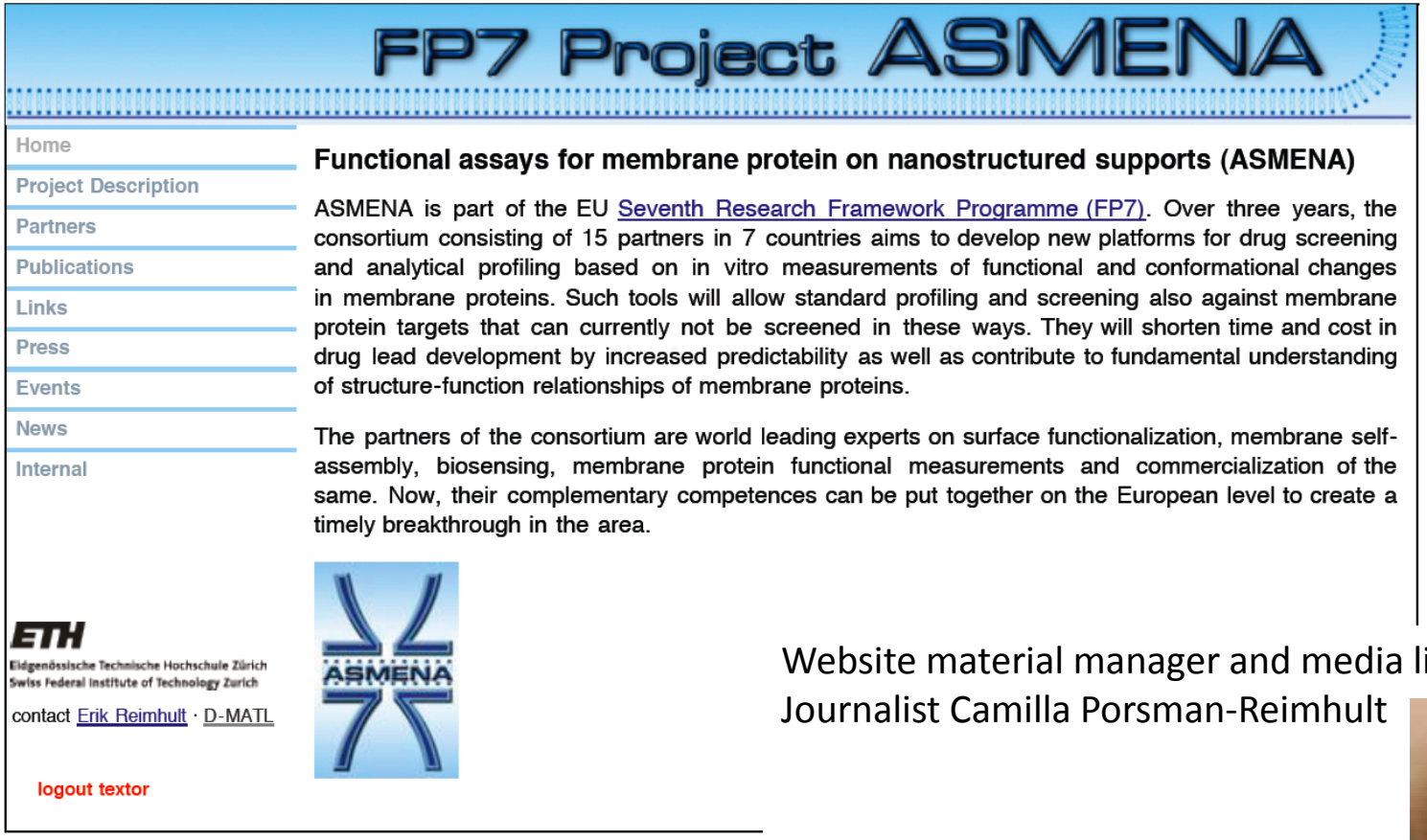
ASMENA partner roles

7 academic partners; 7 industrial partners, 7 European countries
Budget: 4000 kEUR over 3 years

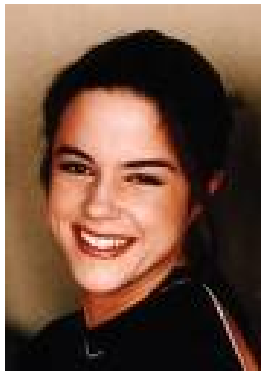
Partner	Main responsibilities and contributions in ASMENA
ETHZ	Substrate fabrication, waveguide sensing, surface functionalization, membrane spanning
PSI	Membrane spanning, functional assays (ion channels and transporters)
Chalmers	LSPR, directed liposome assembly, microfluidics, functional assays
MPI	Membrane spanning, functional assays
UB1	Directed liposome assembly, native liposomes
ELTE	Modeling and simulation
MESA	Functional polymer supports
Leister	Chip fabrication, systems integration, platform testing and commercialization
LayerLab	Directed liposome assembly
SuSoS	Surface functionalization chemistry
Farfield	Waveguide spectroscopy platform, platform testing and commercialization
MicroVacuum	Waveguide spectroscopy platform, platform testing and commercialization
Bioinfiniti	Aquaporin drug lead discovery, aquaporin supplier
Roche	Ion channel drug lead discovery, ion channel supplier, final platform tester

Dissemination and Outreach

Website: http://www.asmena.ethz.ch



Website material manager and media liasion:
Journalist Camilla Porsman-Reimhult



Website includes press release material

Industrial Advisory Board (IAB)

Chair: Prof. Dr. Wolfgang Knoll, Scientific Director of the ARC, Austria
Partner 8 / Leister: Mrs. Christiane Leister, Owner of Leister
Partner 9 / LayerLab: Dr. Torbjörn Pettersson, CEO
Partner 10 / SuSoS: Dr. Samuele Tosatti, Founder and CEO
Partner 11 / Farfield: Dr. Gerry Ronan, CEO
Partner 12 / MicroVacuum: Dr. Istvan Szendrö, Founder and Owner
Partner 13 / Hydrogene AB: Prof. Per Kjellbom, CEO
Partner 14 / Roche: Dr. Christof Fattinger, Leader Microtechnologies and Automation unit

Partner 1 / ETH Zurich: Prof. Marcus Textor, Dr. Erik Reimhult (PC)

ASMENA consortium

Group photo ASMENA Kick-off meeting in Wasserstelz, Spring 2008