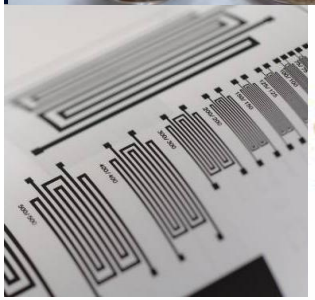
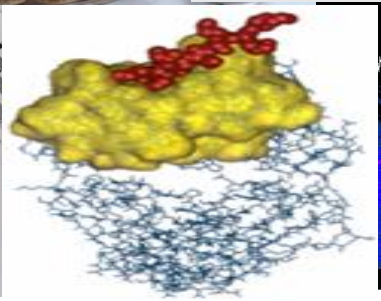
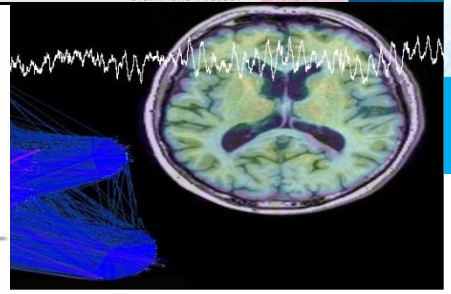


VTT Technologies for health – tools for future personalized, pre-empitive and predictive health care

Harri Siitari, Ph.D

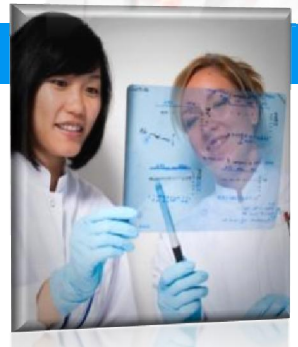
Senior Chief Scientist, Programme director

December, 13. 2011

Japanese-Finnish joint symposium
ICT and Technology in Medical and Health Research

VTT Technical Research Centre of Finland

- Turnover 292 M€
- Personnel 3,167



Customer sectors

- Biotechnology, pharmaceutical and food industries
- Electronics
- Energy
- ICT
- Real estate and construction
- Machines and vehicles
- Services and logistics
- Forest industry
- Process industry and environment

Focus areas of research

- Applied materials
- Bio- and chemical processes
- Energy
- Information and communication technologies
- Industrial systems management
- Microtechnologies and electronics
- Services and the built environment
- Business research

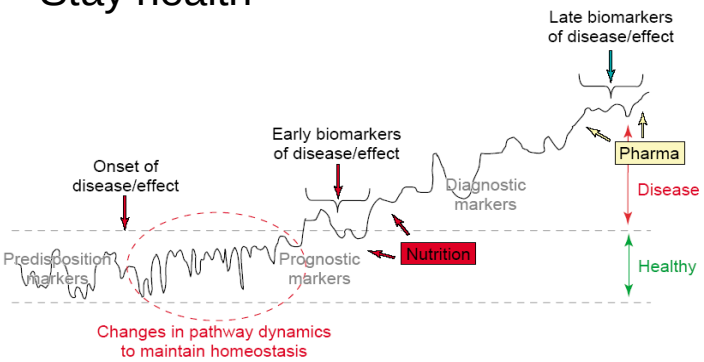
A globally networked multi-technological applied research organisation with extensive cross-disciplinary technological and business expertise

VTT on map


Saint Petersburg. Russia
Brussels. Belgium
Silicon Valley. USA
Seoul. South Korea
Tokyo. Japan
Shanghai. China
Finland
Oulu
Raahe
Kajaani
Kuopio
Jyväskylä
Tampere
Lappeenranta
Turku
Rajamäki
Espoo

Future health care?
Goals for predictive, preventive and participatory HC

Stay health

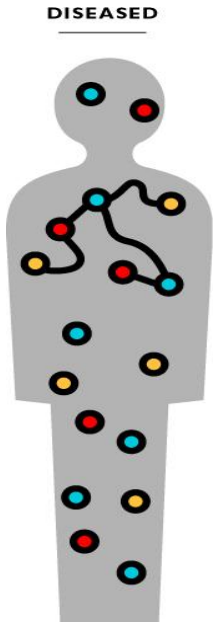


Follow-up health

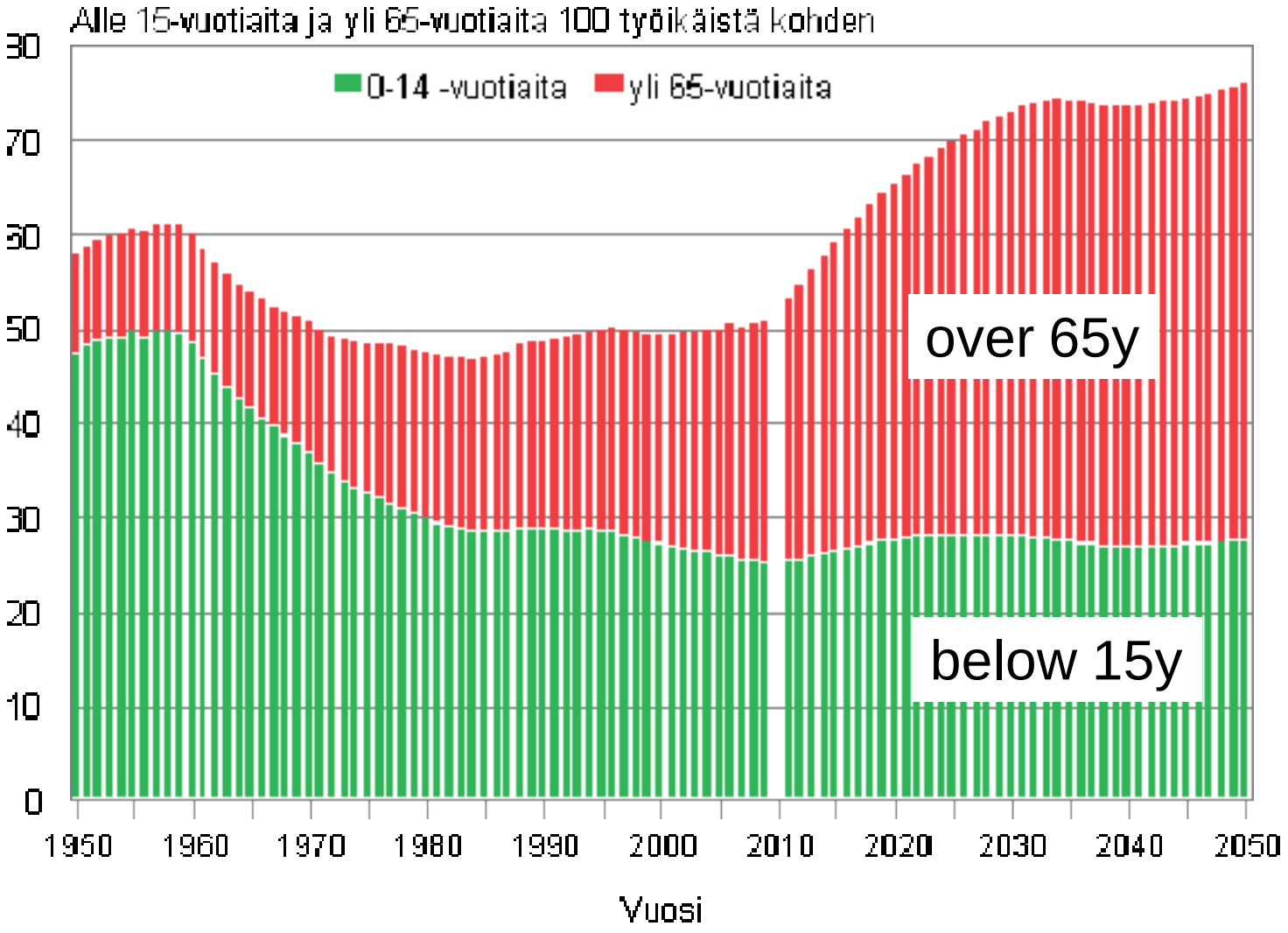
Disease management
Living at home

Cost efficient
Processes in
Health care

Right drug
Right disease
Right time



Future age distribution in Finland



Finland - Resource usage I; primary health care

Measured as inpatient hospital days

Age group	35 - 39 y-o	20 000	inpatient days
	55 - 59 y-o	200 000	
	over 85 yo	2 Million	
	over 65 y-o	approx. 6 Million	All age

groups together 7.3 Million inpatient days

-> Resource usage strongly increasing with age

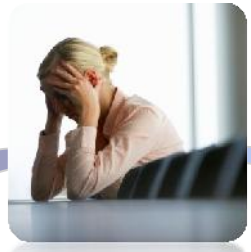
Diagnosis groups requiring most inpatient hospital days (as inpatient days):

- Cardiovascular diseases 1 800 000
- Psychiatric disorders (dementia) 2 000 000 (1.6 M)
- Malignancies 306 000
- Musculoskeletal diseases 278 000
- Gastrointestinal system diseases 139 000
- Neurological disorders (Alzheimer) 856 000 (453 000)
- Injuries 596 000

total inpatient hospital days: 7.3 milj

Key research area 1: Life span strategy in Brain and cognition

Working age
Stress, depression,
Other diseases



Retired
Early biomarkers for AD,
Ambient assisted living

Young
Finnbird-brain injury
Centre in Turku
- Treatment proc.
- diagnostics

SEVENTH FRAMEWORK PROGRAMME

Childhood
- predictive biomarkers

TBIcare

PREDICT

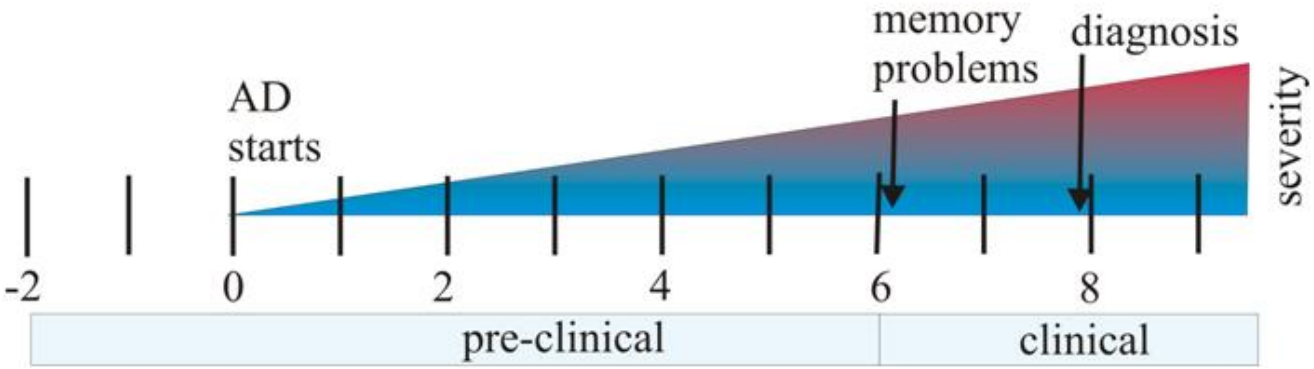
Disease management
Living longer at home

VARSINAIS-SUOMEN SAIRAANHOITOPIIRI
EGENTLIGA FINLANDS SJUKVÅRDSDISTRIKT

http://www.vsshp.fi/fi/finnbird
Prof. Olli Tenovuo, VSSHP

Motivation - Alzheimer's Disease

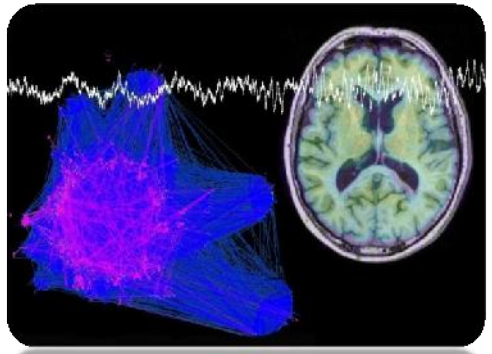
- Alzheimer's disease is a progressive neurodegenerative disease.
- Alzheimer's disease will be one of the main health issues of the next decades:
  - costs are 1 % of the gross-domestic product (GDP) of the whole world, and
  - 27 million people (2006) -> 114 million (2050).
- Delaying both the onset and progression only by modest one year would reduce the number of Alzheimer's cases by 10 %.
- Current medical problems:
  - no effective medication but new drugs under development, and
  - **no objective and efficient early diagnostics**.



PREDICT

ICT-based solutions for diagnostics?

- In healthcare domain, **huge amounts of data** are acquired from patients: various databases contain **hidden information** about variability of humans that could be utilized in diagnostics.

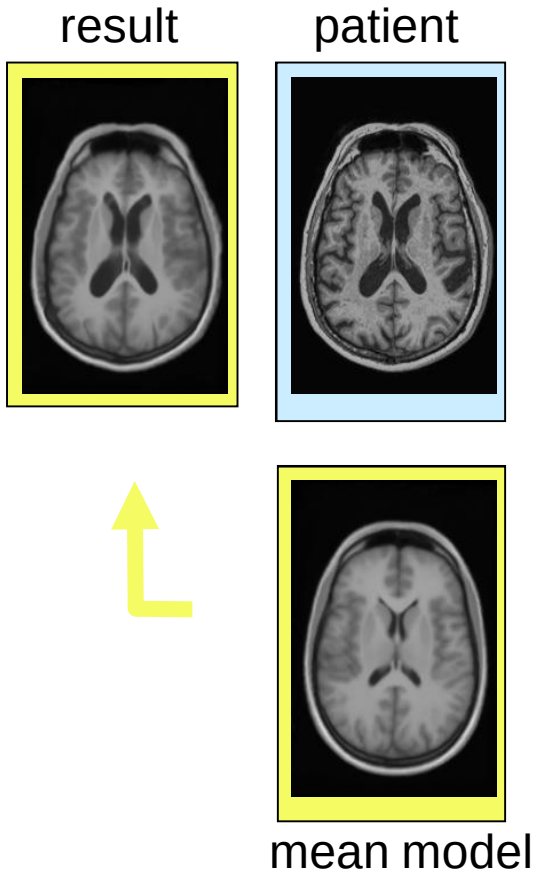


- **data quantification** is difficult, e.g., automated image segmentation tools are rare in clinical practice,
- there are no solutions for **integrating heterogeneous data** (holistic view) although 85 % of clinicians would like to have, and
- diagnostics should be performed at very early stage for successful treatments – a need for **pre-clinical screening**.

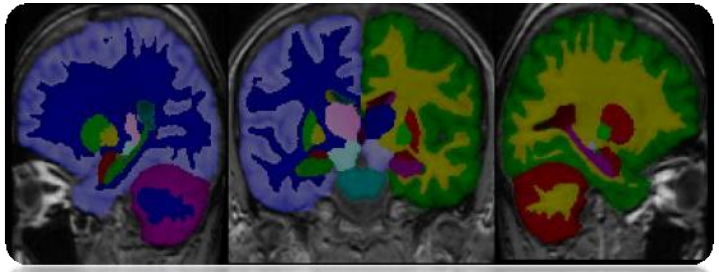
PREDICT

Image quantification - Brain

- VTT has developed a new VolumeWarp solution to image segmentation:
  - only 2 minutes in a standard laptop,
  - accuracy comparable to manual segmentation (gold standard)
  - licensed already to one global player, discussions going on with three other companies.
- Other solutions for tensor-based morphometry, manifold learning, and atrophy measurements.



HIPPOCAMPUS FROM MRI	Similarity index	Correlation of volumes
VolumeWarp (N=340)	0.87	0.94
Manual segmentation (inter-rater):		
Morra, NeuroImage, 2009 (N=21)	0.85	0.71
van der Lijn, NeuroImage, 2008 (N=20)	0.86	0.83
Niemann, Psych. Res, 2000 (N=20)	-	0.93



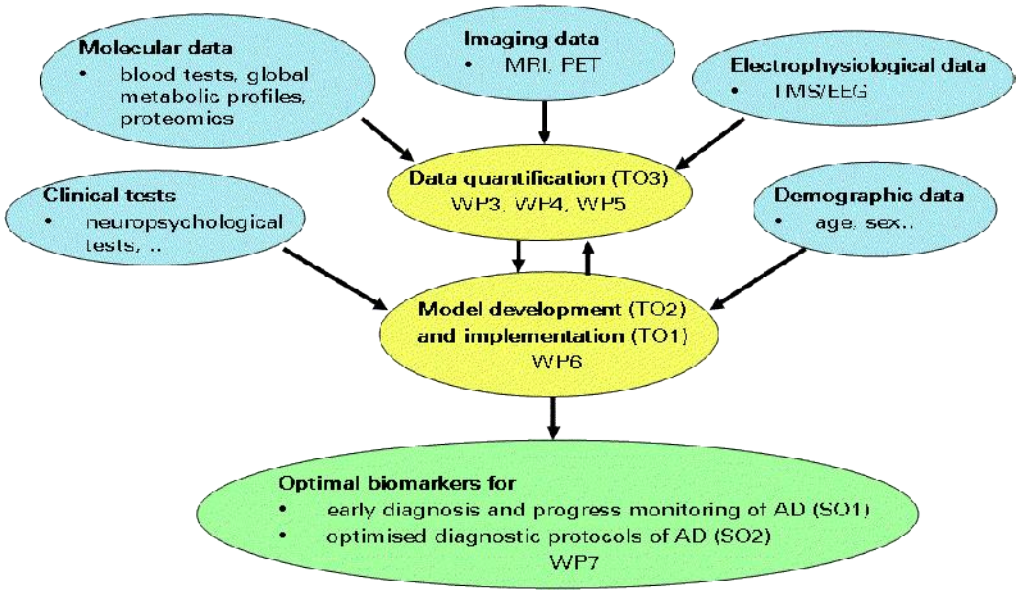
Lötjönen: NeuroImage, 2010 & 2011
Koikkalainen: NeuroImage, 2011

VTT & Alzheimer's Disease

- VTT has diverse **offering** in the scope of Alzheimer's disease:
  - **image quantification tools** (segmentation, multi-template tensor-based morphometry),
  - **metabolomic biomarkers from blood**, and
  - **decision support solution** for integrating heterogeneous patient data and for providing evidence based objective index of the state of the patient.
- Solutions developed in an EU funded research project of eight partners: **PredictAD (www.predictad.eu).**

PREDICT

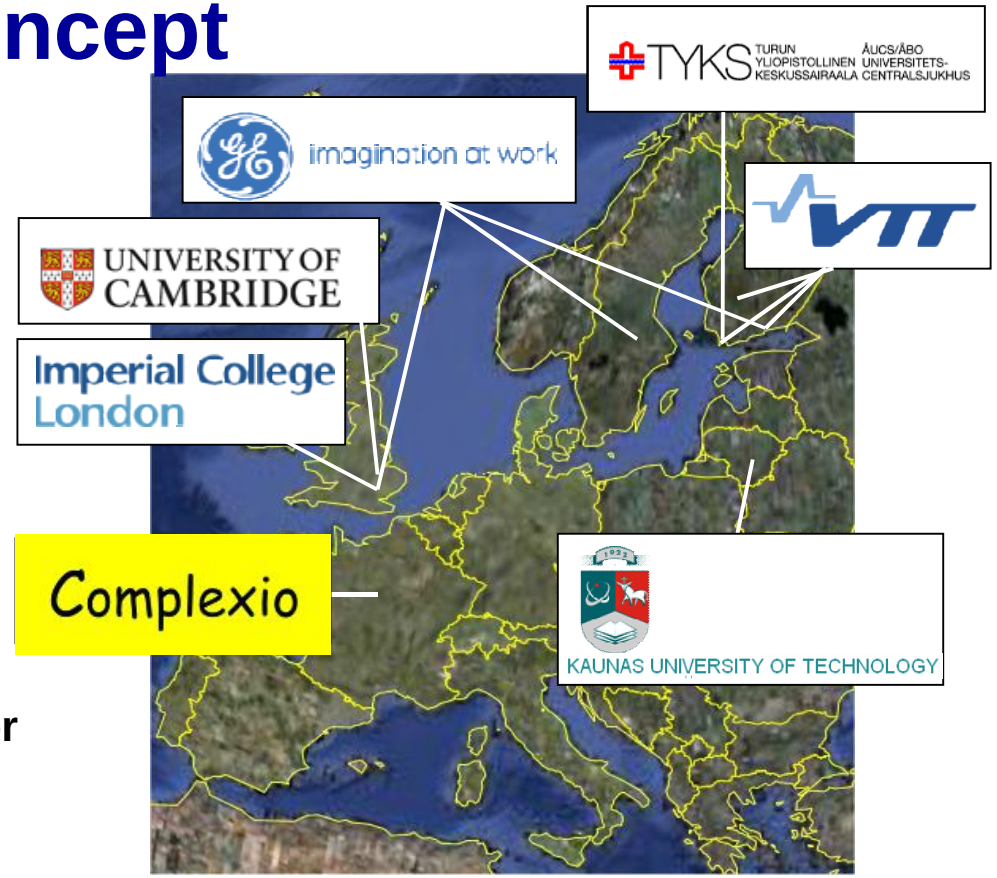
European Commission
Information Society and Media



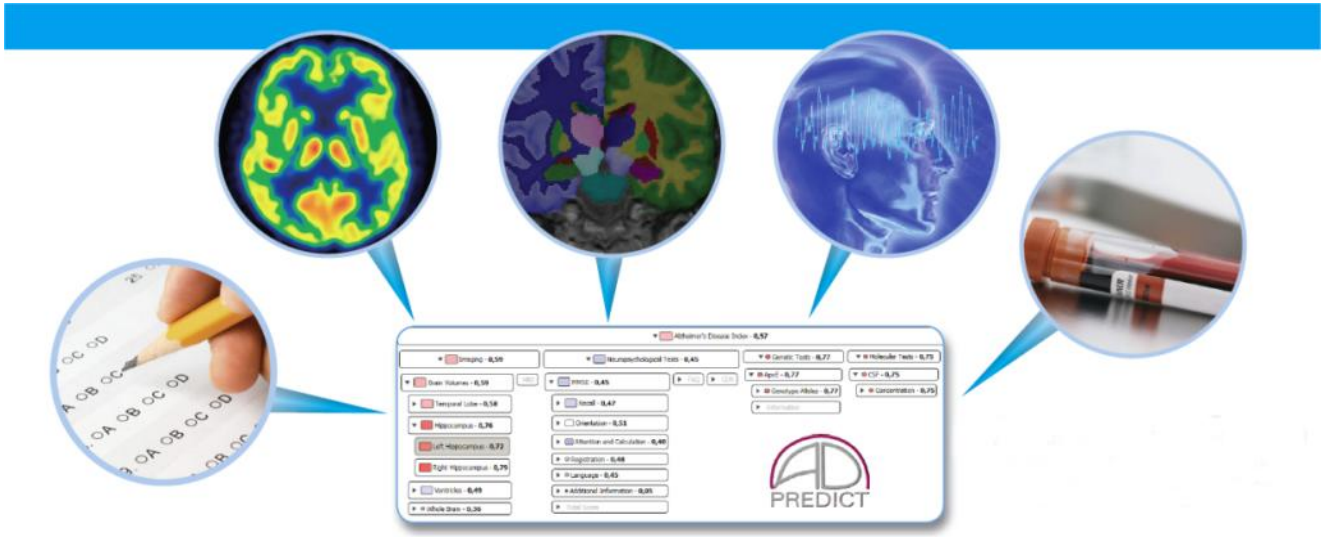
TBIcare - Concept

Expected results:

- a strictly evidence based software solution for diagnostics and treatment planning,
- new biomarkers and their combinations for TBI,
- datamining-based statistical framework for fusing highly heterogenous data, and
- new efficient data quantification tools.
- software tools for clinicians use



Biomarkers
from imaging and blood samples



PREDICT

Key research area 2 : biomarkers/metabolomics platform

Experiment design + Analytical chemistry + Chemometrics + Bioinformatics

EU FP6

- HEPADIP (metabolic syndrome // partner)

EU FP7

- ATHEROREMO (vulnerable plaques // WP leader)
- DIAPREPP (type 1 diabetes // WP leader)
- METACANCER (breast cancer // WP leader)
- MITIN (insulin resistance // WP leader)
- PredictAD (Alzheimer's disease // partner)
- ETHERPATHS (systems biology & nutrition // coordinator)
- TORNADO (gut microbiota // WP leader)

Juvenile Diabetes Research Foundation

- T1D prevention project (coordinator)

Human Frontier Science Program

- Gut microbiota project (co-applicant)

↓

Biomarkers, biological insight

Dysregulation of lipid and amino acid metabolism precedes islet autoimmunity in children who later progress to type 1 diabetes

Matej Orešič,[1] Satu Simell,[2] Marko Sysi-Aho,[1] Kirsti Näntö-Salonen,[2] Tuulikki Seppänen-Laakso,[1] Vilhelmiina Parikka,[2] Mikko Katajamaa,[1] Anne Hekkala,[4] Ismo Mattila,[1] Päivi Keskinen,[5] Laxman Yetukuri,[1] Arja Reinikainen,[6] Jyrki Lähde,[5] Tapani Suortti,[1] Jari Hakalax,[2] Tuula Simell,[2] Heikki Hyöty,[7,8] Riitta Veijola,[4] Jorma Ilonen,[3,9] Riitta Lahesmaa,[6] Mikael Knip,[5,10] and Olli Simell[2]

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[8]Centre for Laboratory Medicine, University Hospital of Tampere, Tampere FI-33520, Finland
[9]Department of Clinical Microbiology, University of Kuopio, FI-70211 Kuopio, Finland
[10]Hospital for Children and Adolescents, University of Helsinki, Helsinki FI-00014, Finland

J. Exp. Med. (2008)

This sort of metabolomic approach to T1D natural history may be a pioneering example of environmental data-driven approaches.

From commentary about our T1D study
by P. Bougnères & A.-J. Valleron
J. Exp. Med. (2008)

Key research area 2: Diagnostics

Understanding diagnostics needs

- **Biomarker search**
- **Marker genes**
- **Microbes**
- **Lipids**
- **Antigens**

Reagent development

- **Antibody development**
- **Probes and primers**
- **Large-scale production of reagents**

Assay development

- **HTtranscription profiling**
- **Immunoassays**
- **Microbial population profil.**
- **Metabolomics**
- **Multiplexed detection**

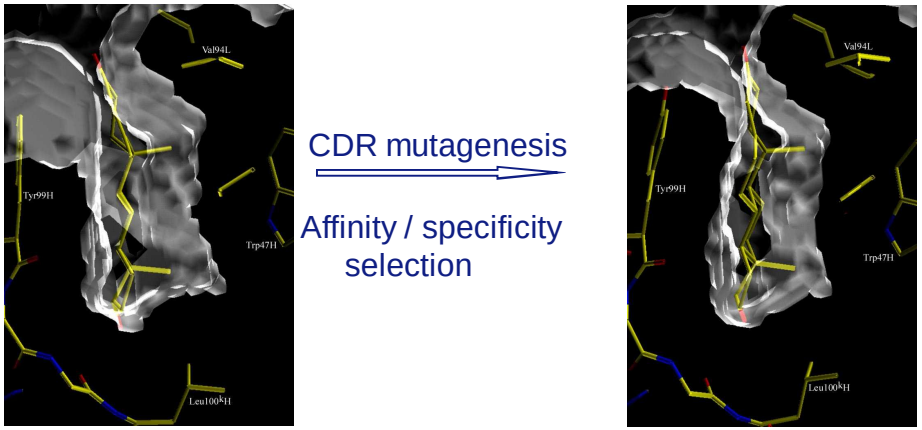
Device development for point-of-care applications

- **Portable detectors**
- **Microfluidics**
- **Roll-to-roll printing**
- **Label free detection**
- **Capillary electrophoresis**
- **Wireless data processing and transfer**

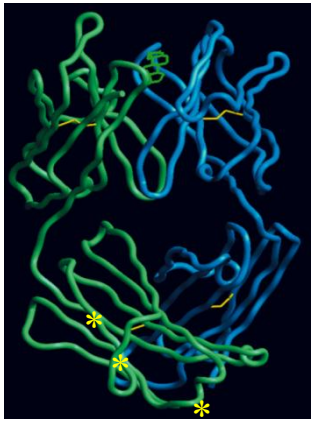
By integrating VTT's know-how on biotechnology, electronics, material sciences and ICT new innovative bioanalytical and diagnostic platforms are developed

Antibody engineering possibilities

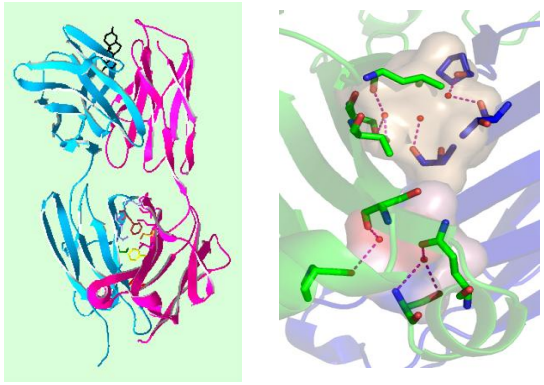
Tailoring the affinity and specificity



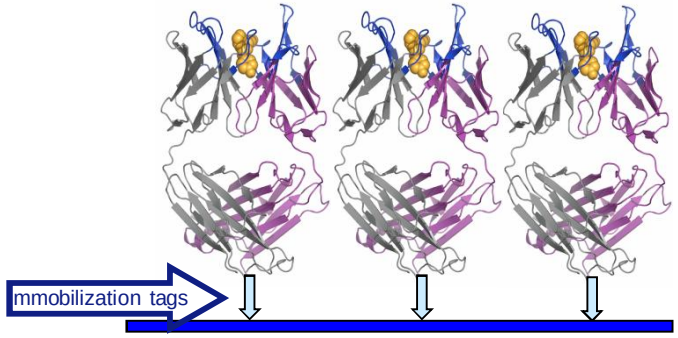
Improved labelling



Stability improvement



Oriented immobilization

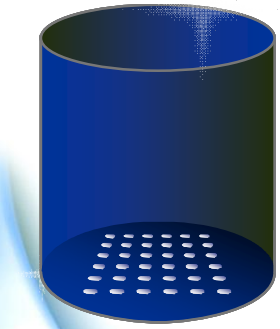


His tag, protein- and peptide tags, Cys-tag, tag for biotinylation

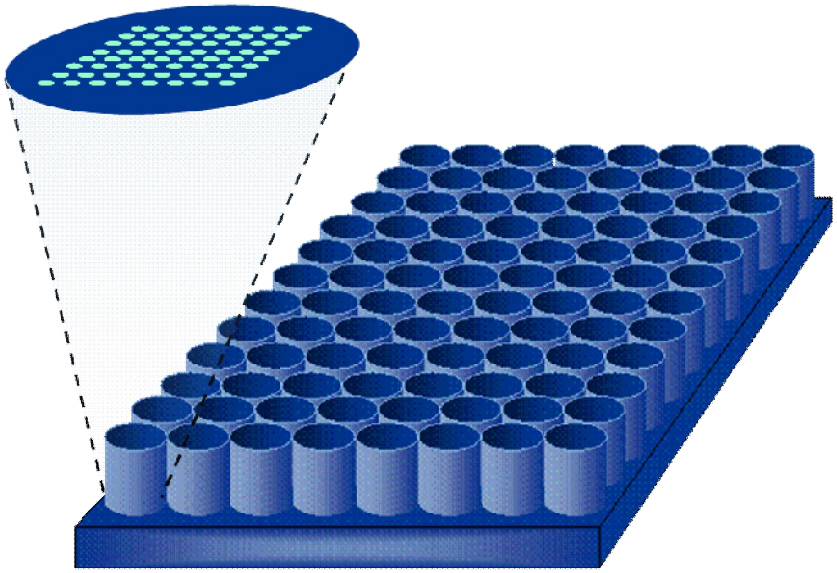
Arrays-in-Wells for Multiplexed Bioassays

Array types

- Oligonucle otide
- Antibody
- Antigens
- Allergens



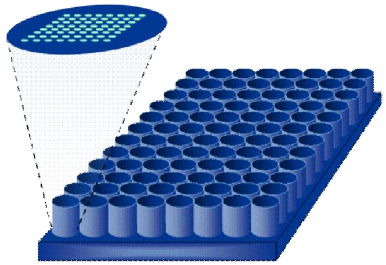
- *Microarrays in 96-well plates*
- *Compatible with standard lab equipment*
- *Simple Assays – Multiple Results*



Applications

- Rapid viral diagnostics
- Analyte panels e.g. CVD
- Pathogen diagnostics
- Autoimmune disease
- Allergy
- Genotyping

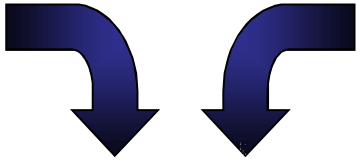
Dr. Petri Saviranta, VTT
Liisa Hattara, VTT

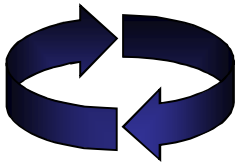


Assay Logistics

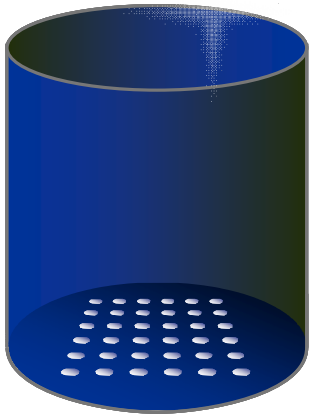
Sample
25 µl

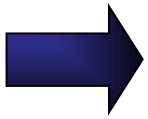
Buffer
25 µl





- **Shake 15 min**
- **Wash**
- **Dry**





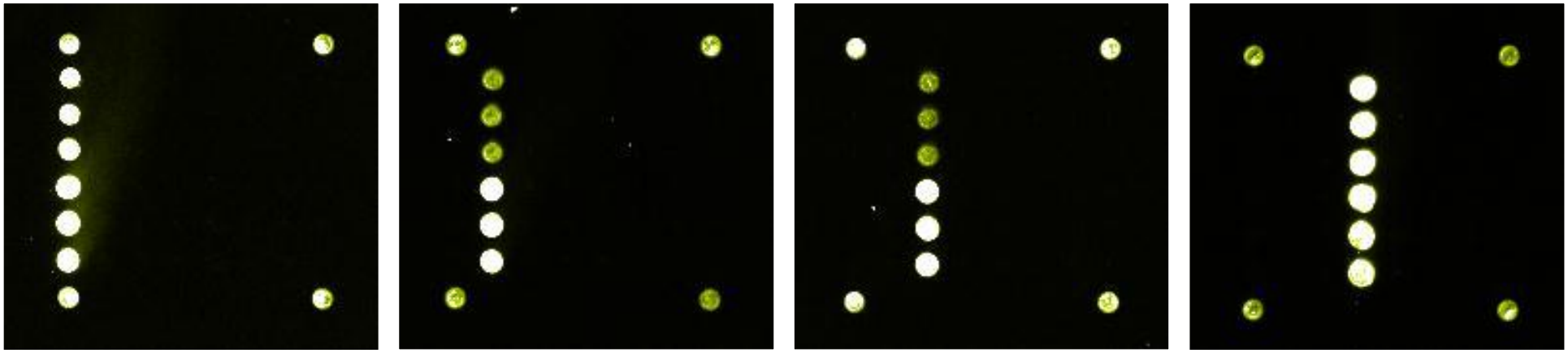
<u>Readout:</u>

- **Optical scan (fluorescence)**
- **Automated image analysis**
- **Quantification spot signals**
- **Data analysis**

=> *<u>Result</u>*

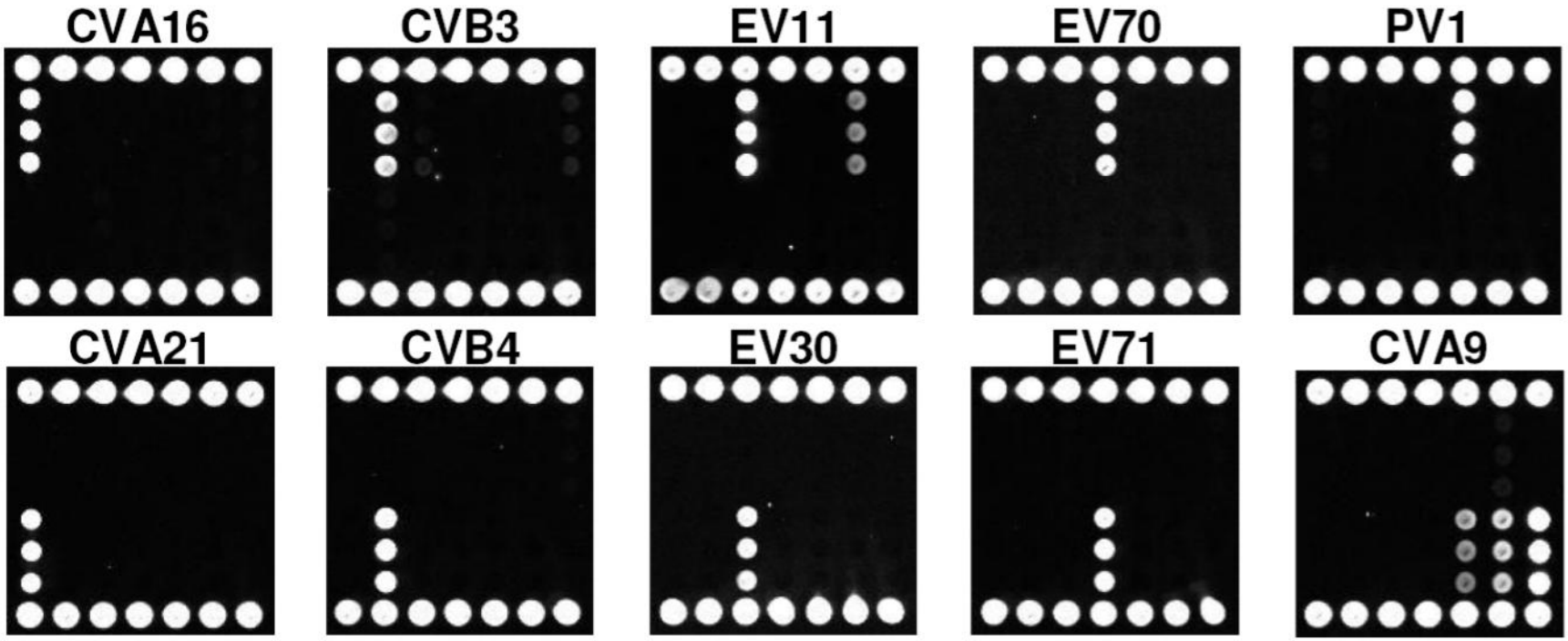
Control samples

Adeno | **RSV** | Influenza A | **Influenza B**



	Adeno	RSV	Inf A	Inf B	PIV1	PIV2	PIV3	neg	Total
Routine assay	16	33	0	4	2	0	2	521	578
Arrays-in-wells	16	33	0	4	3	1	1	520	578

Clear discrimination between serotypes



JOURNAL OF CLINICAL MICROBIOLOGY, June 2009, p. 1863–1870 Vol. 47, No. 6
0095-1137/09/$08.00+0 doi:10.1128/JCM.02226-08

Typing of Enteroviruses by Use of Microwell Oligonucleotide Arrays[▽]†

P. Susi,[1] L. Hattara,[2] M. Waris,[1] T. Luoma-aho,[2] H. Siitari,[2] T. Hyypiä,[1] and P. Saviranta[2]*

Department of Virology, University of Turku, Kiinamyllynkatu 13,[1] and Medical Biotechnology Centre, VTT Technical Research Centre of Finland, Itäinen Pitkäkatu 4C,[2] 20520 Turku, Finland

Business from technology

Arrays-in-Wells for **Multiplexed Bioassays**

Microarrays in 8-well strips
Compatible with standard lab equipment
Simple Assays – Multiple Results

Array types
- Oligonucleotide
- Antibody
- Antigens
- Allergens

Applications
- Rapid viral diagnostics
- Analyte panels for e.g. cardivascular Diseases
- Pathogen diagnostics
- Autoimmune disease
- Allergy
- Genotyping
- Diagnostics for animal diseases, food borne pathogens and environment

Arrays-In-Wells Reader Features
- Easy to use
- Portable, compact size (90 x 170 x 250 mm)
- Quantitative analysis
- Compatible with standard 8-well microtiter strips
- Fast, measurement and analysis of 8-well strip in 60 seconds
- Powerful laser excitation
- High efficiency imaging of the emission

Additional information

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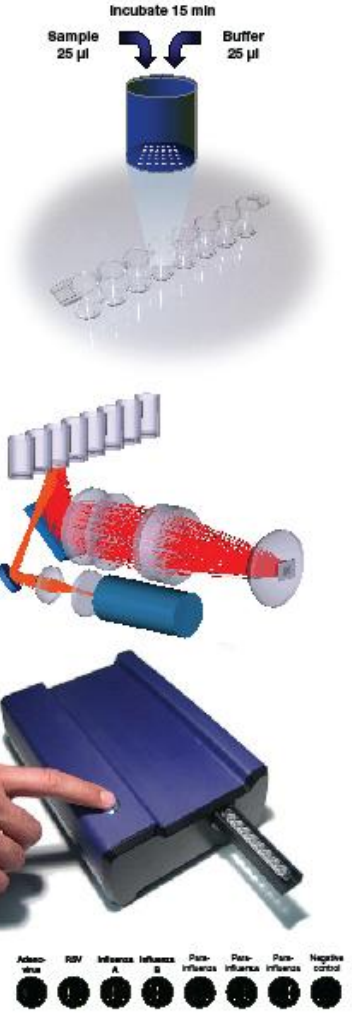
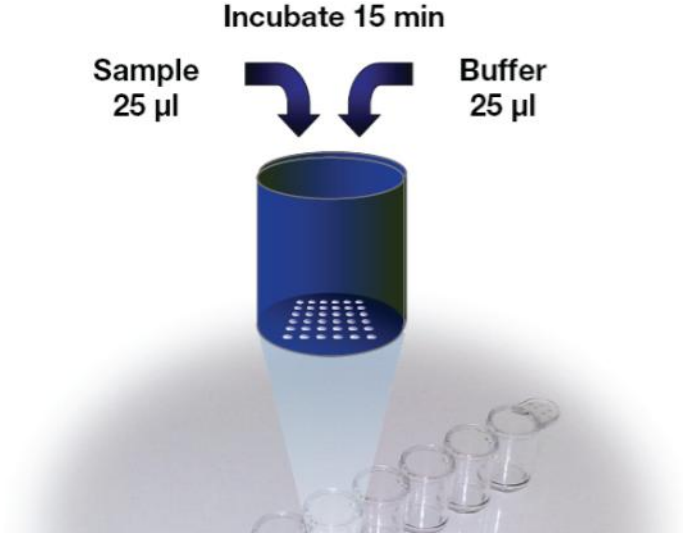
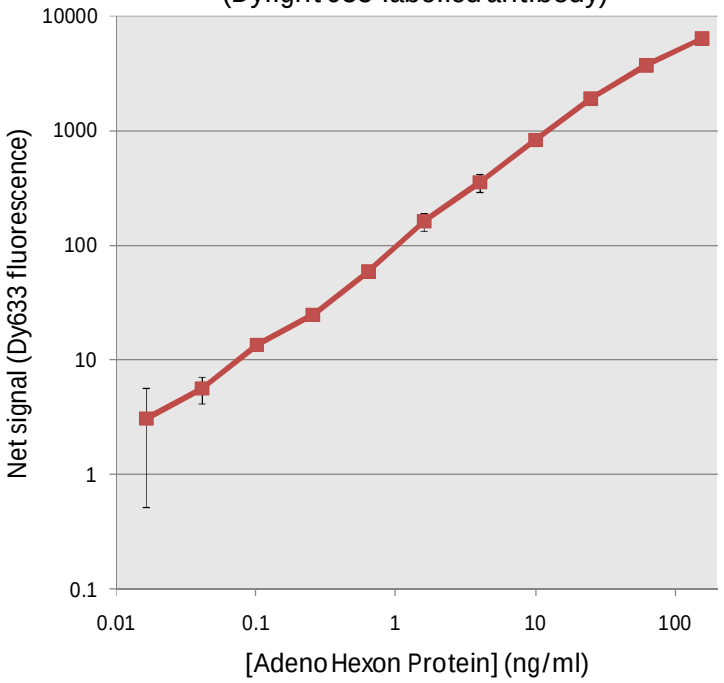
Rapid diagnostics of respiratory viruses





Adenovirus antigen assay on AIW
(Dylight 633-labelled antibody)



Pioneering R2R pilot manufacturing machinery for printed electronics and intelligence

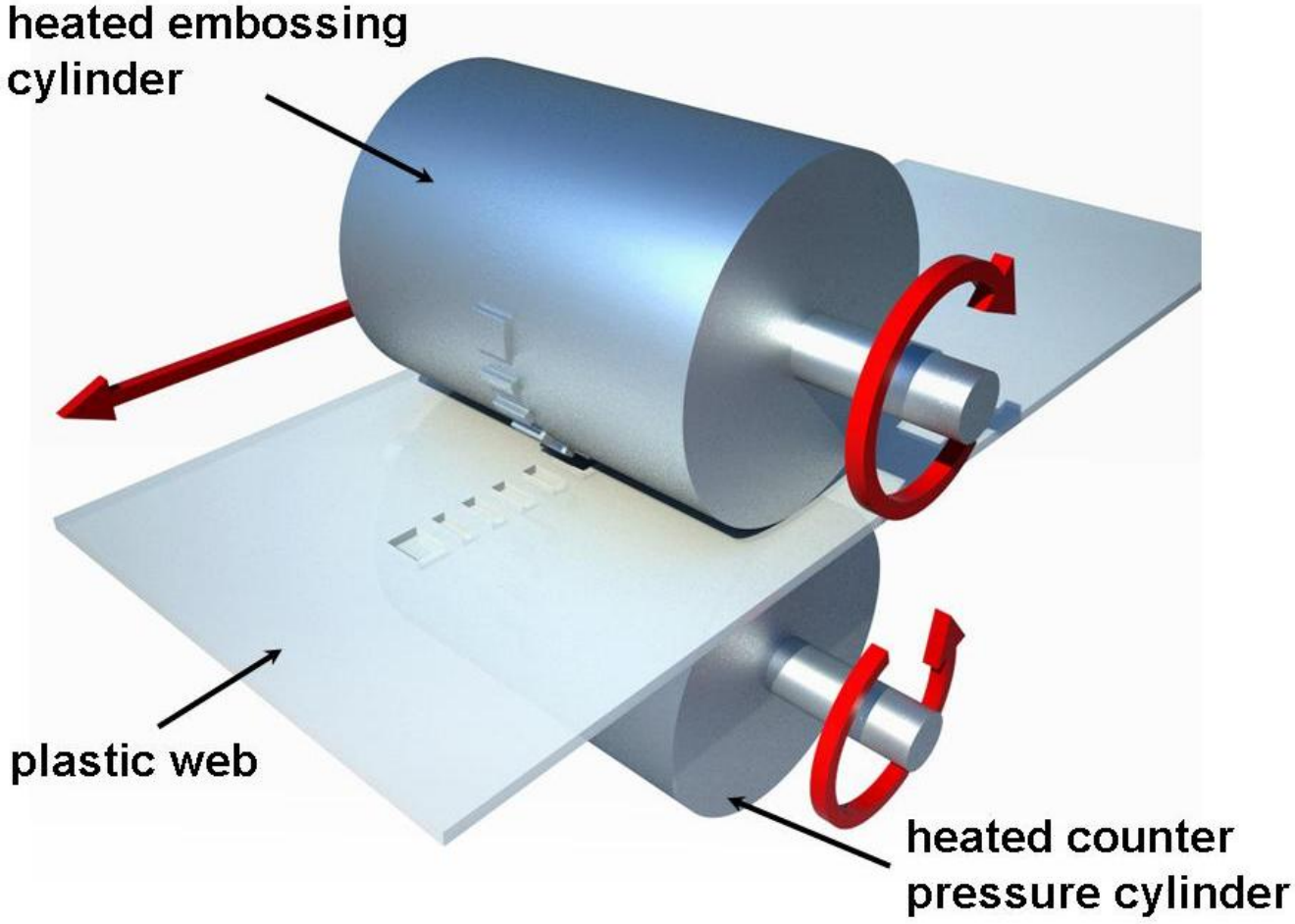
Fig 7: PICO 3 printing unit pilot line, 2003

- ***units: gravure, hot-embossing, lamination***
- ***web width: 20 cm***
- ***web speeds: 0.5-100 m/min***

Fig 8: ROKO 4 printing unit pilot line, 2007

- ***units: gravure, reverse gravure, flexo, rotary screen, lamination (printing units in register)***
- ***web width: 30 cm***
- ***web speed: 10 m/min max***

Roll-to-Roll (R2R) hot-embossing principle



Schematic model of roll-to-roll (R2R) hot-embossing process.

Advantages over static hot embossing:

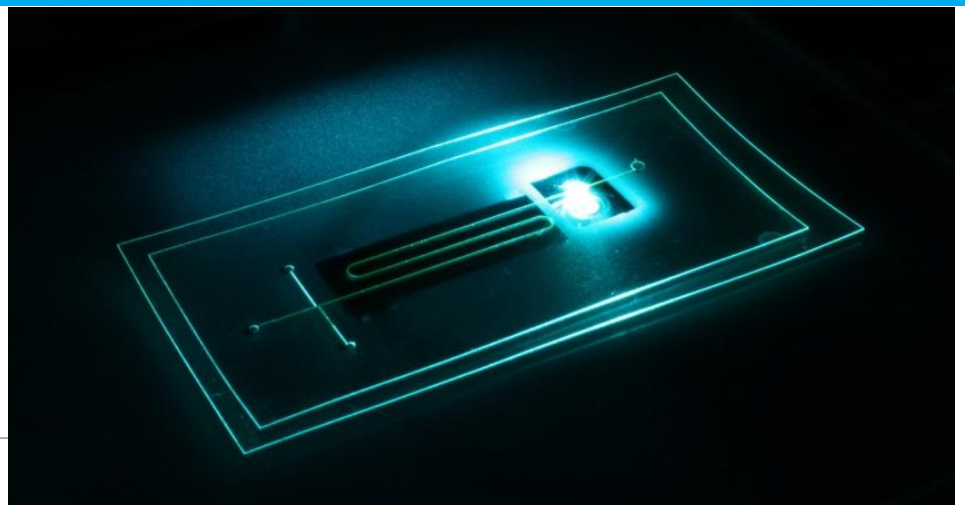
- rotating stamp cylinder enables continuous chip manufacturing (parallel and continuous)
- uniform chip quality
- large area embossings possible
- integration of other roll-to-roll processes in production line (e.g. printing of biomarkers, lamination, online quality control)

Examples of our current activities

Lab on a Chip

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/loc



Disposable roll-to-roll hot embossed electrophoresis chip for detection of antibiotic resistance gene *mecA* in bacteria

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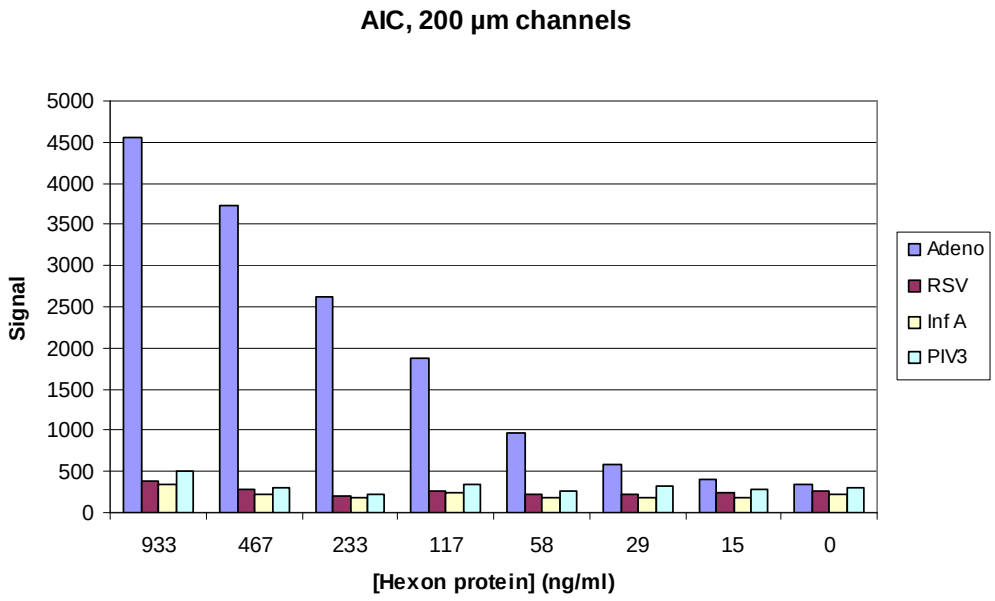
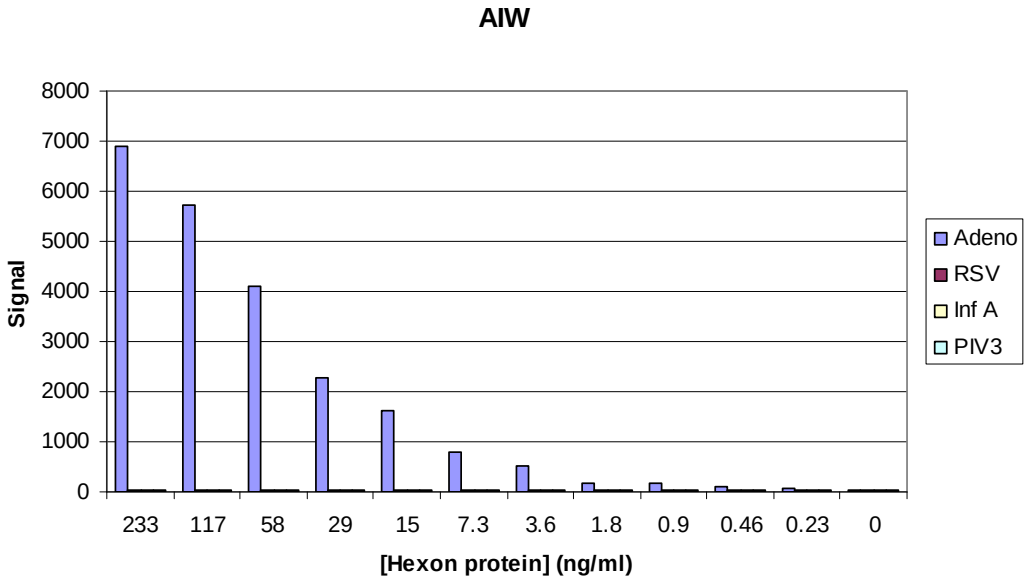
We present a high-throughput roll-to-roll (R2R) manufacturing process for foil-based polymethyl methacrylate (PMMA) chips of excellent optical quality. These disposable, R2R hot embossed microfluidic chips are used for the identification of the antibiotic resistance gene *mecA* in *Staphylococcus epidermidis*. R2R hot embossing is an emerging manufacturing technology for polymer microfluidic devices. It is based on continuous feeding of a thermoplastic foil through a pressurized area between a heated embossing cylinder and a blank counter cylinder. Although mass fabrication of foil-based microfluidic chips and their use for biological applications was foreseen already some years ago, no such studies have been published previously.

Analysis of Adeno Hexon Protein with Arrays-in-channels vs Arrays-in-wells

- Common dilution series was made for AIC and AIW:
- Two-fold dilution series starting from 933 ng/ml
- Dilutions from 933 down to 15 ng/ml were analyzed with AIC
- Dilutions from 233 down to 0.23 ng/ml were analyzed with AIW

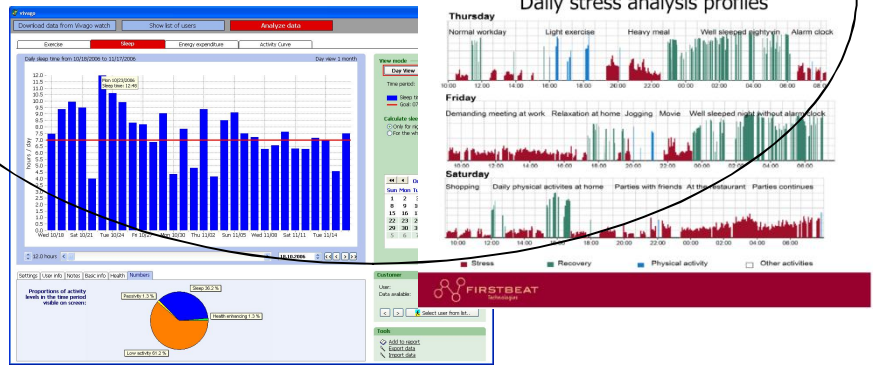




Key research area 3: Personal Health Systems

New wearable devices
- easy, affordable, accurate

Advanced analysis tools
and psychophysiological models
- from data to information and feedback



+ New service models
+ New delivery and business models
+ New peer and social networks

Easy, available, affordable, efficient, personalised, trusted, standard-based, interoperable, citizen-driven

Vivago IST:
ACTIVITY RECOGNITION WITH MOVEMENT SENSORS

- An intelligent wearable social alarm system for elderly
- Enables cost efficient continuous 24/7 monitoring of wellness of the subject
- Reliable user-triggered and automatic alarms for emergency

Conclusions

- VTT has developed and validated state-of-the-art scientific methods for the diagnostics of AD but tools are **applicable also in other domains**.

VTT diagnostics for multiple biomarkers :

- the disease state fingerprint provides a **holistic view of the status** of the patient and allows both **diagnostics** and the **follow-up of treatment efficacy** quantitatively based on the principles of evidence-based medicine,

- the disease state fingerprint profiling technology has potential in **personalized medicine:** to match patients for clinical studies and for treatments.

- Recombinant antibody development with **low-cost multiplexed technologies** provides platforms for future diagnostics

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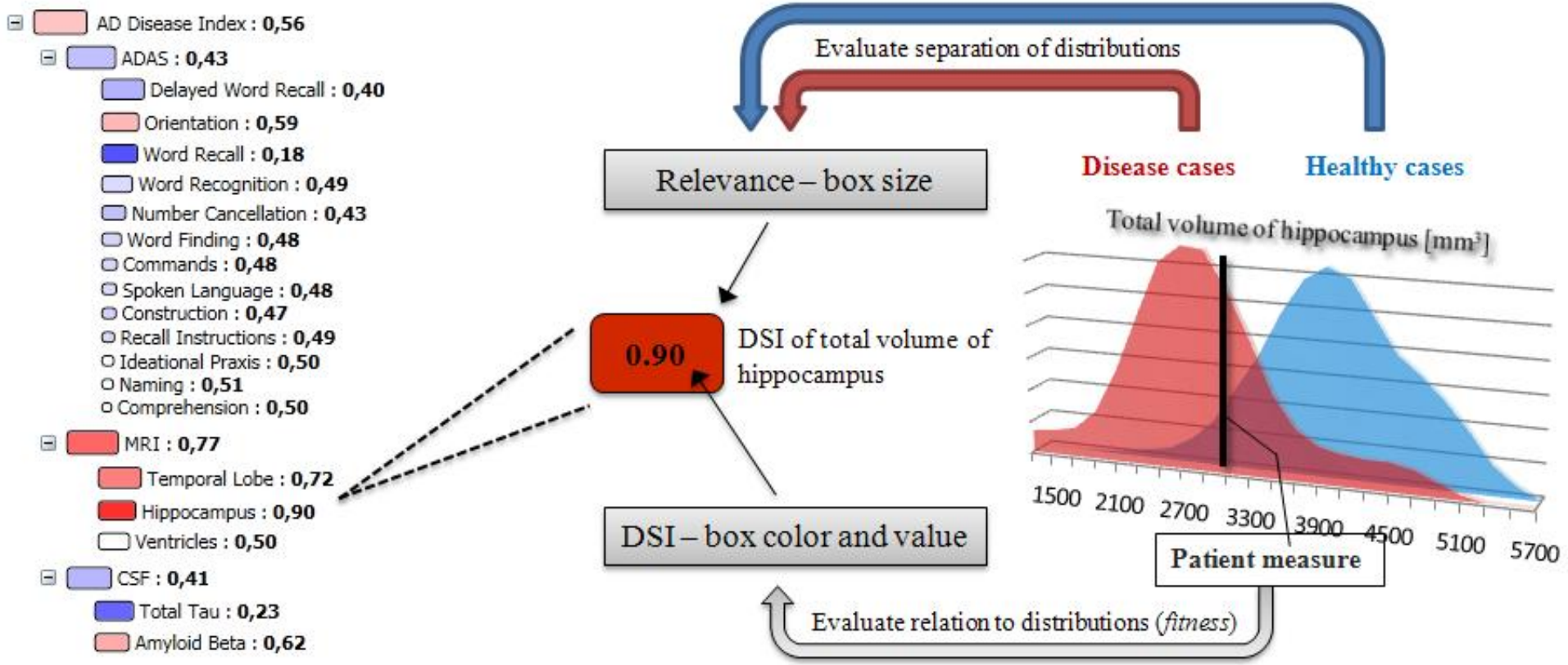
Kirsi Tappura, Team Leader

VTT creates business from technology

Disease state index and disease state fingerprint techniques

- Decision support system developed allows easy visualization of the status of a person relative to different populations available in large databases.



Koikkalainen: Radiology, 2008 & Mattila: JAD, 2011 & One US patent & One patent pending