Biomedical Sensors Foresight Workshop

with the theme
"How do we get there?"

- Technology premises and boundaries
- Technology driven scenario development:
  non invasive monitoring, home tests, early diagnosis, "semicontinuous" health checks, internet based evaluations and more

Some of the issues: Sensors and instrumentation for primary health care and home based medical tests and diagnosis. De-centralized tests but centralized evaluation.

One interesting question: Dedicated solutions for each parameter of interest or the use of a general platform for all parameters

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Suggestion:

Computer screen photo-assisted techniques controlled and evaluated via internet is a promising alternative to a generally available instrumental platform for color based medical tests to be performed at primary health care units, pharmacies, service houses for elderly and in individual homes

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Computer screen photo-assisted techniques (CSPT):

Measuring platform: the use of RGB colors

Light absorption and emission in CSPT

Review of biosensing possibilities with CSPT:
Light transmission through melanophores
ELISA
Cell viability
Colorimetry

Difference optical fingerprinting (“CSPT difference spectroscopy”)

CSPT and Google Earth

Ingemar Lundström, 3rd Nordic Workshop on Biomedical Sensors
Stockholm , March 3, 2006

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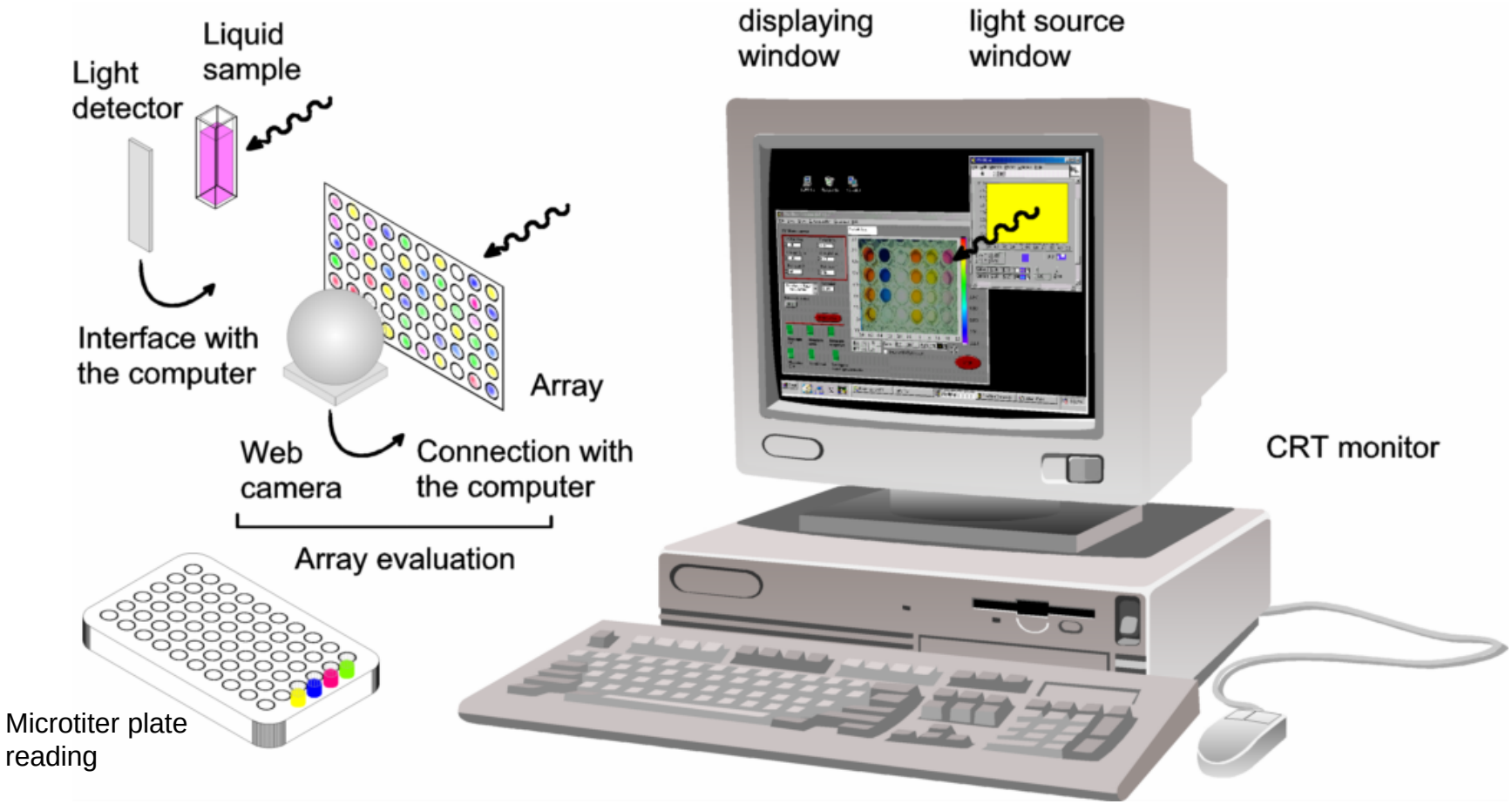
Measuring platform



Computer Screen Photo-assisted Technique - CSPT

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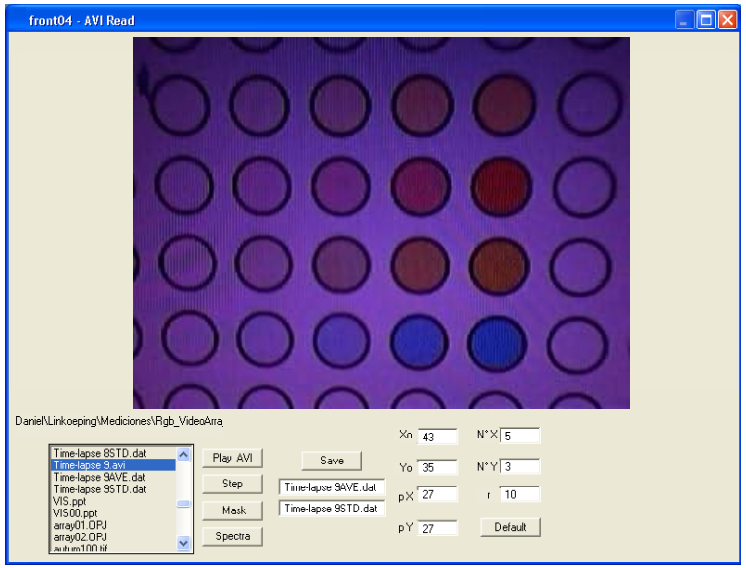
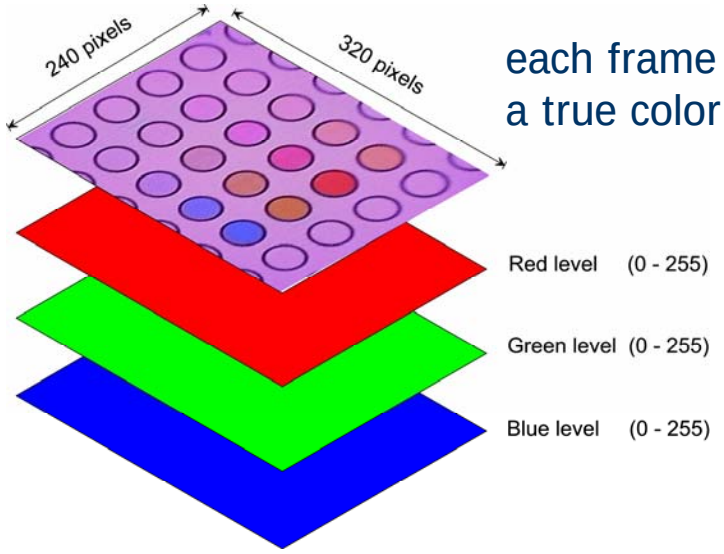
CSPT reading





each frame is
a true color file

r	097	000	000	000	255	255	255	128
g	033	000	255	255	255	128	000	000
b	161	255	255	000	000	000	000	000

Screen colors through magnitude of intensities of three primaries in 256 levels. Electronically determined through the choice of the three levels (color indices, rgb)

D. Filippini, T. Andersson, S. Svensson and I. Lundström,
Biosensors & Bioelectronics 19 (2003), 35-41.

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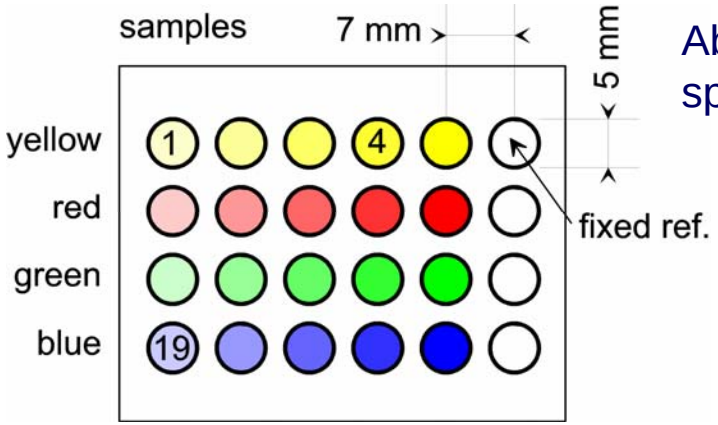
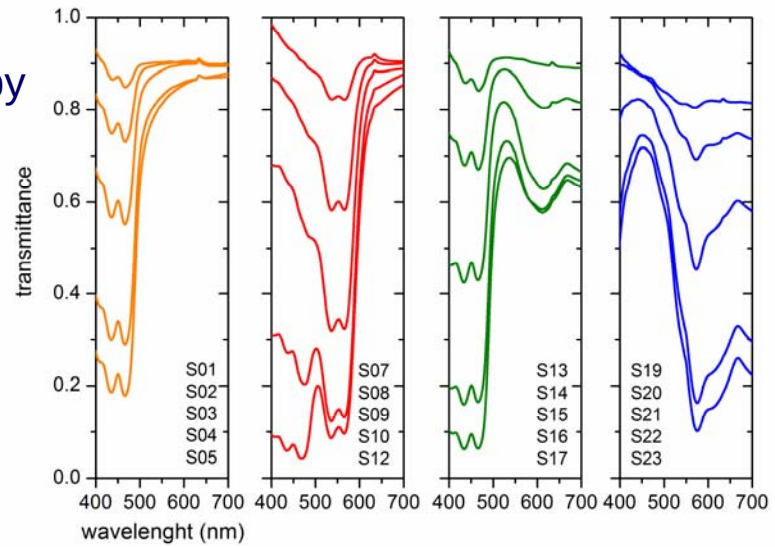
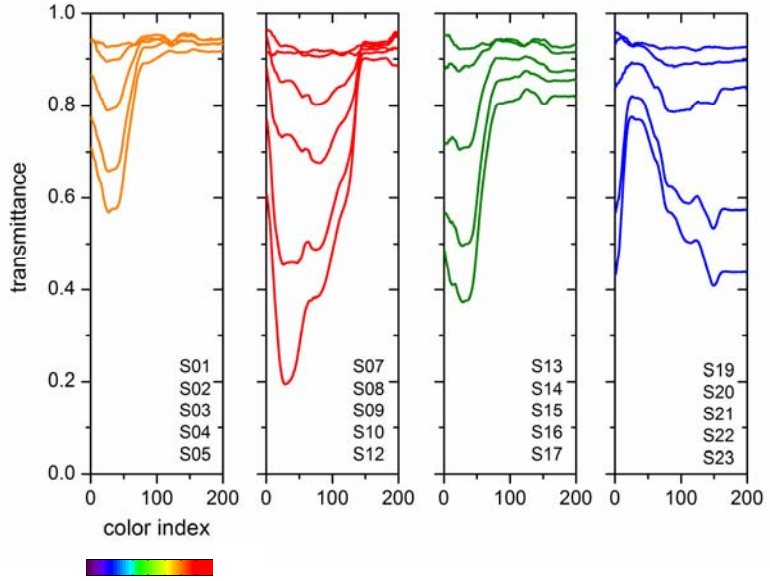
CSPT spectral features



Absorptions spectroscopy



$\tau(i)$



$$\tau(i) = \frac{I_R(i) + I_G(i) + I_B(i)}{I_{R0}(i) + I_{G0}(i) + I_{B0}(i)}$$

Some examples

1. Microtiter plate with rows of dyes at different concentrations:

Aniline

Fluorescein

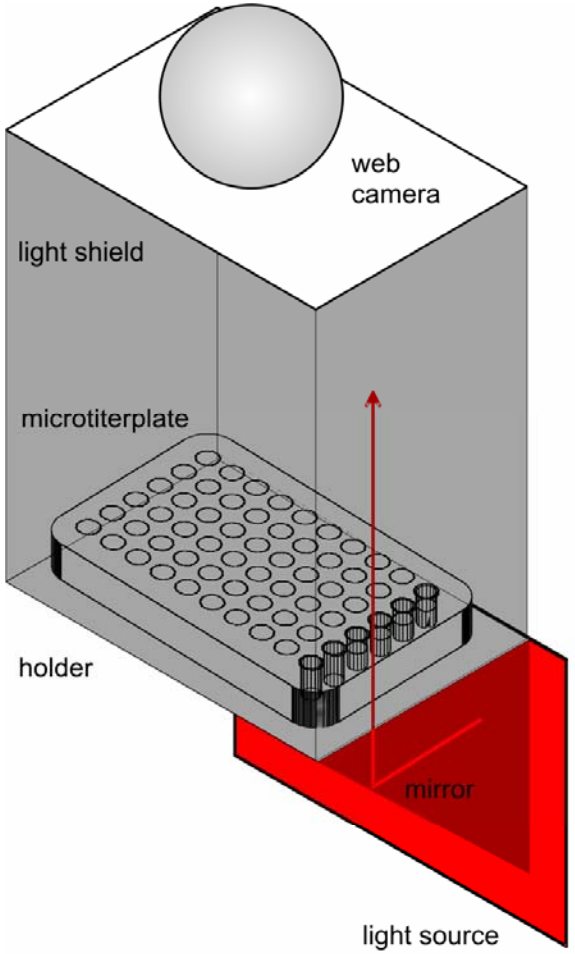
Acridine orange

Cy 3

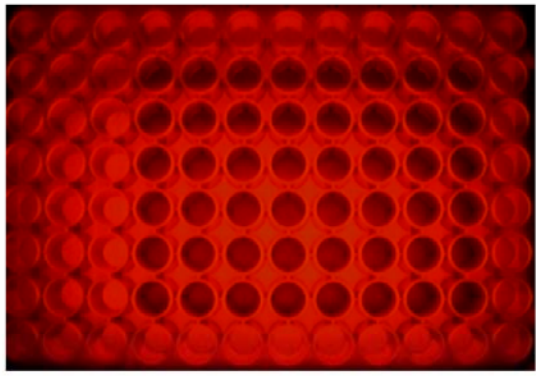
Rhodamine

Cy 5

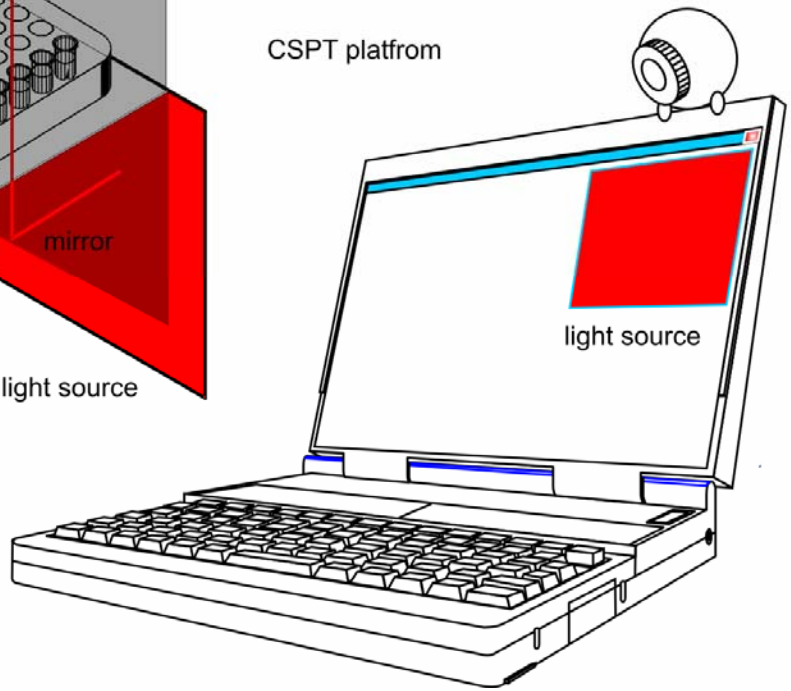
CSPT setup



assay image



CSPT platfrom



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Computer light window

Web camera image

Aniline
Fluorescein
Acridine
Cy 3
Rhodamine
Cy 5

1 mM ⟶ 1µM

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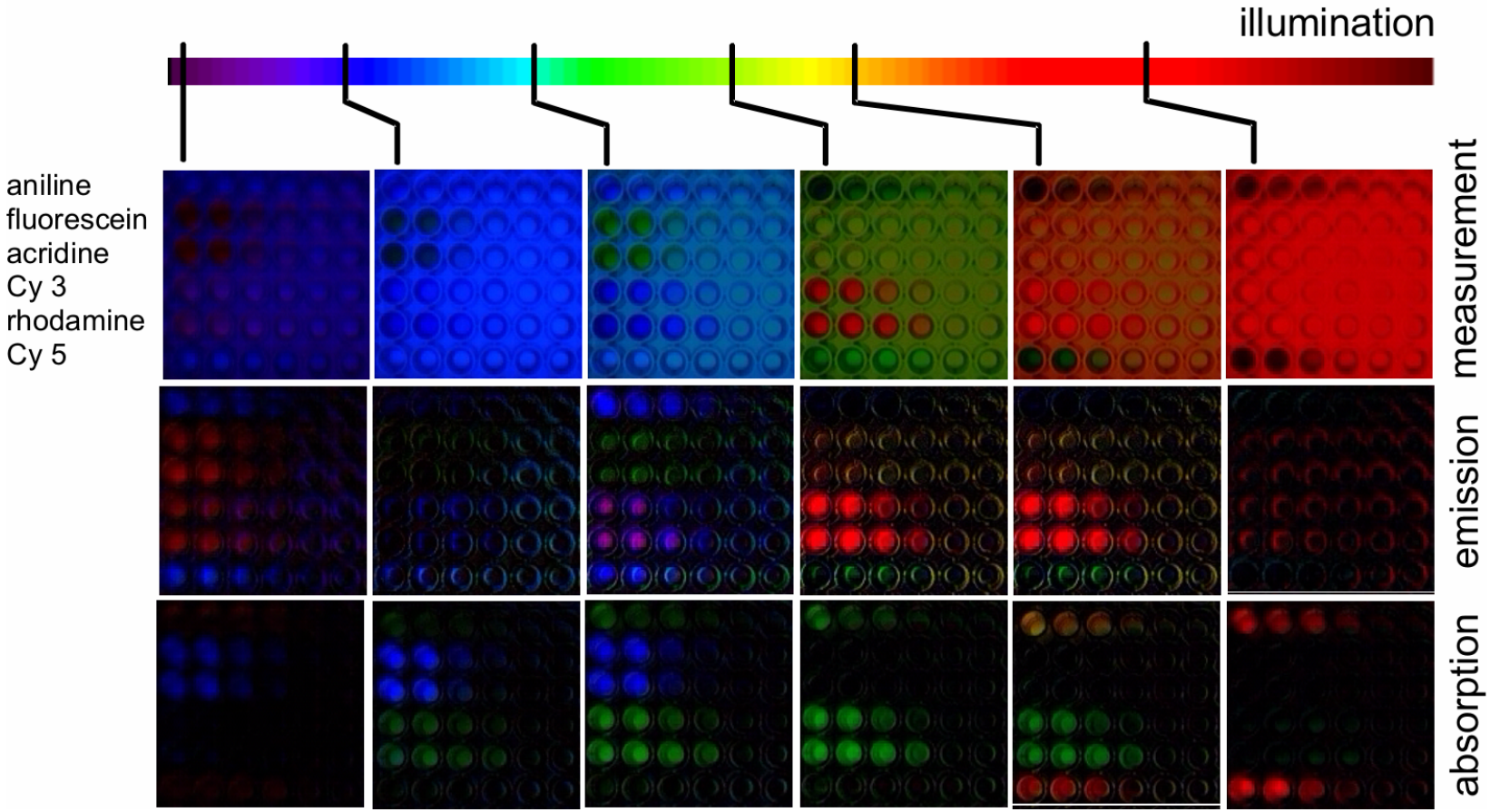
Reconstructed assay image



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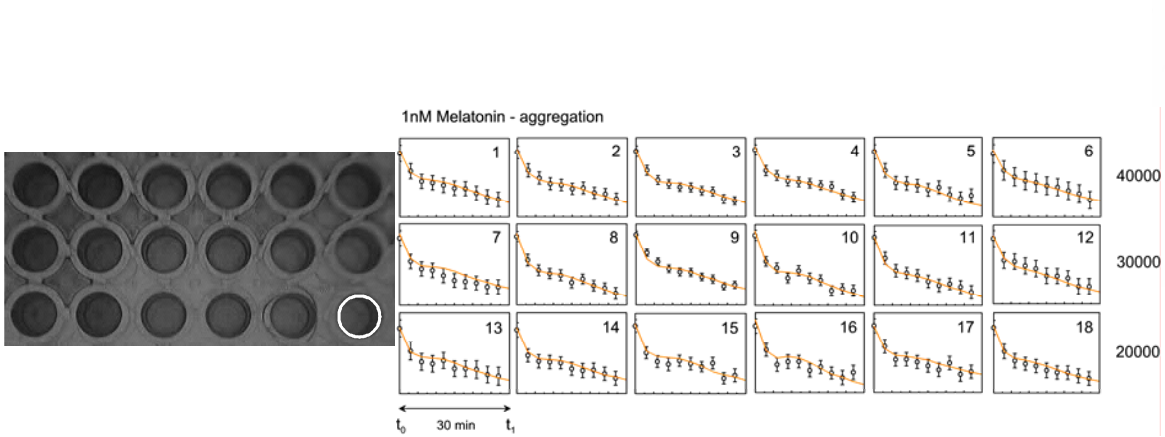
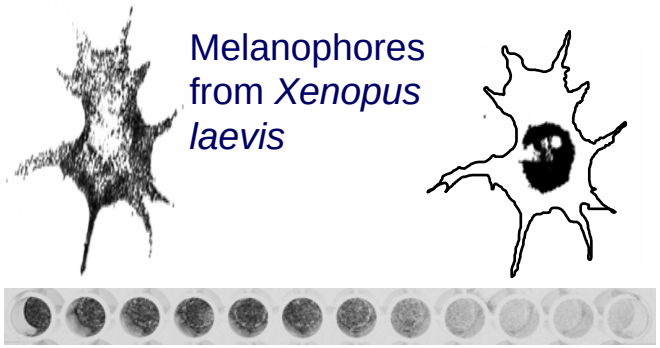
2. COLLAGE OF SINGLE COLOR MICROTITER PLATE RESULTS

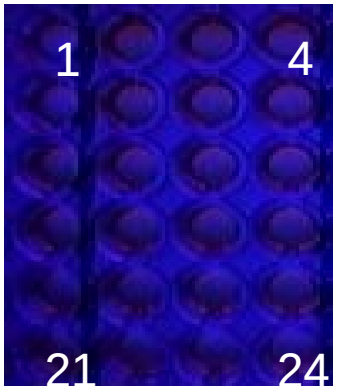


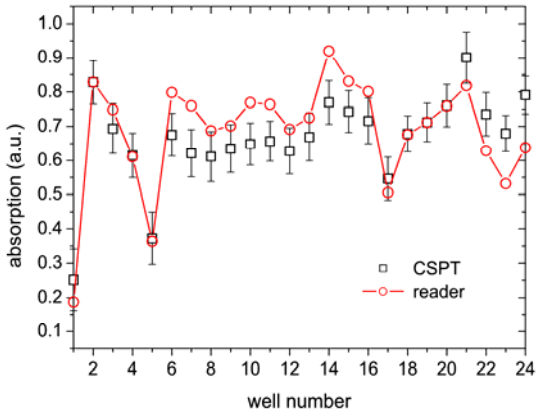


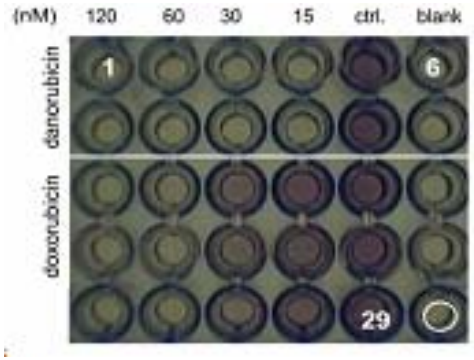
Light transmission through pigment particle containing cells (melanophores)

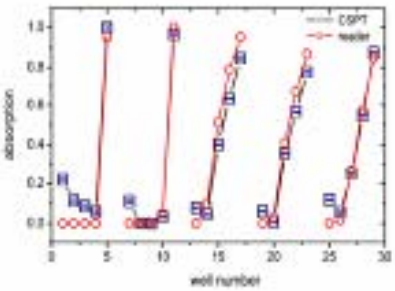
Reader 650 nm

CSPT: (255, 000,000)









Reader: 410 nm CSPT: (000, 000,255)

ANCA-ELISA test for ulcerative colitis diagnosis (ANCA, Anti-neutrophil cytoplasm antibodies; ELISA, enzyme linked immuno sorbent assay)

Cell viability test for antibiotic resistence (yellow salt metabolized into blue product by viable cells)

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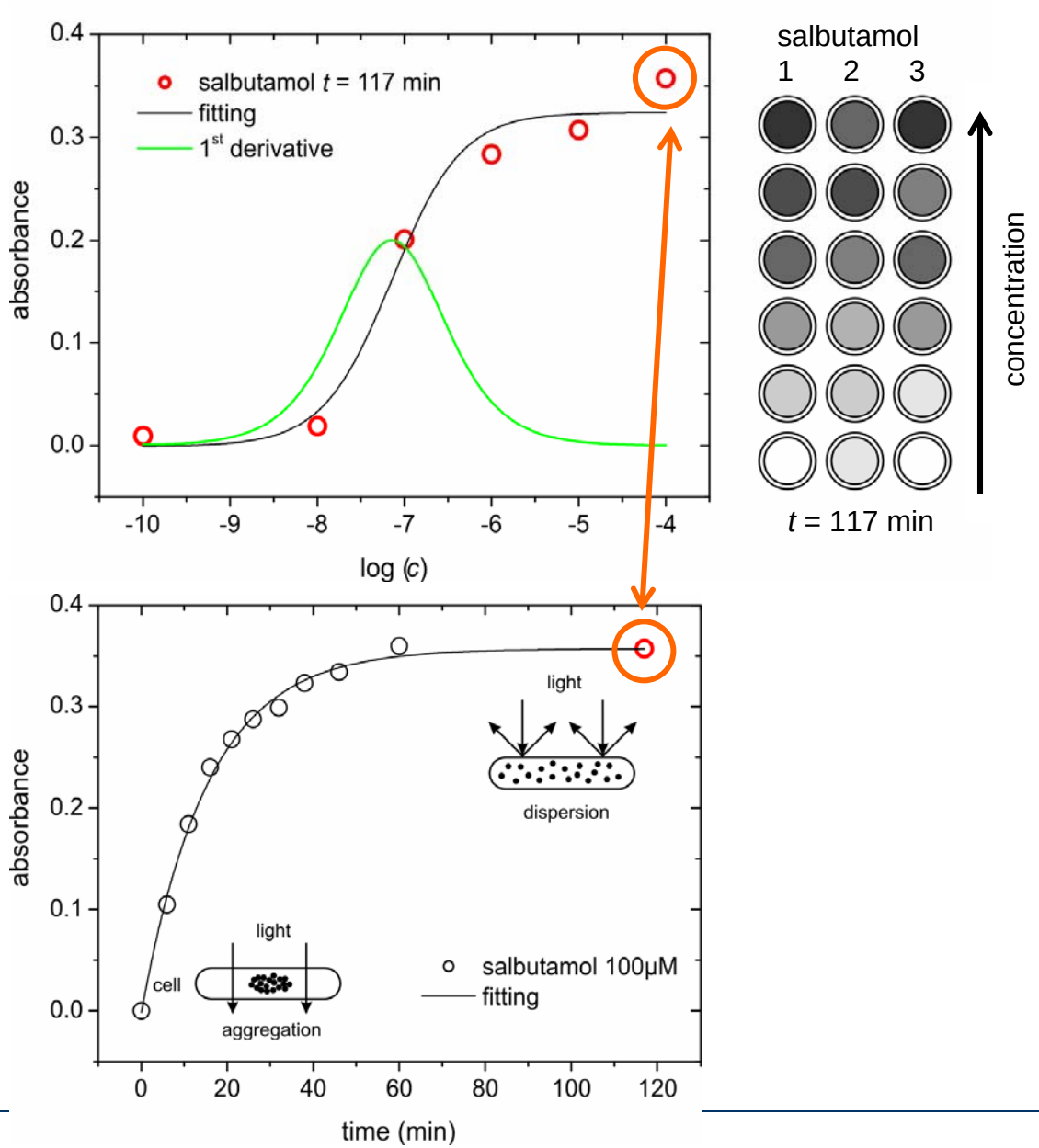
Typical evaluation



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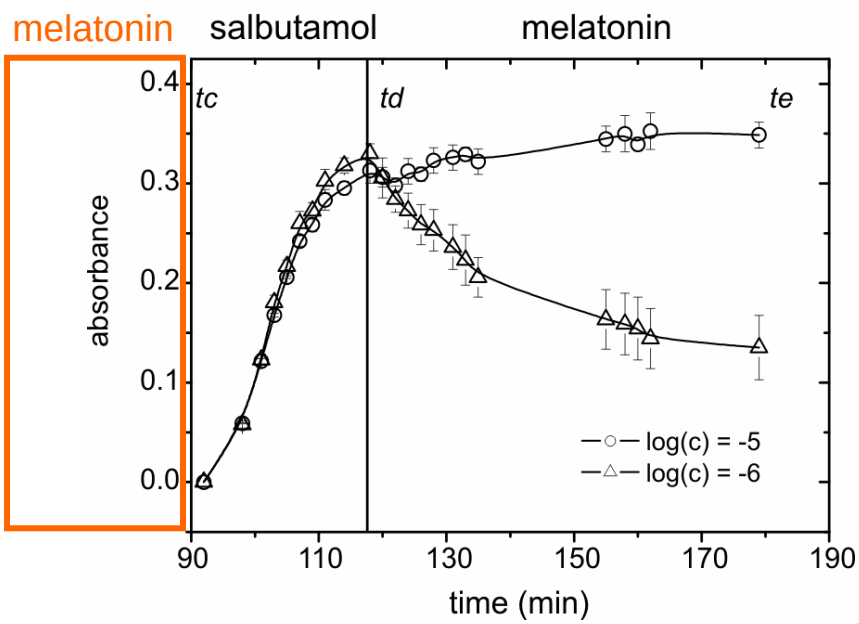
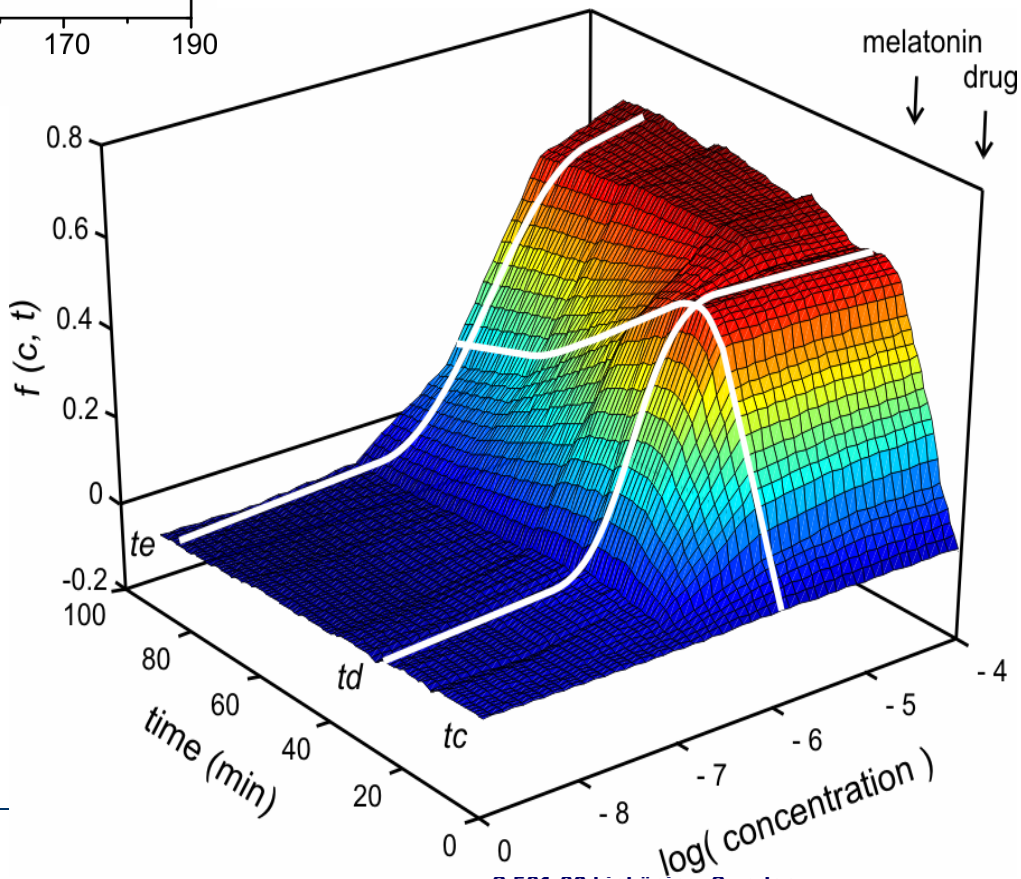
Kinetic assay protocol





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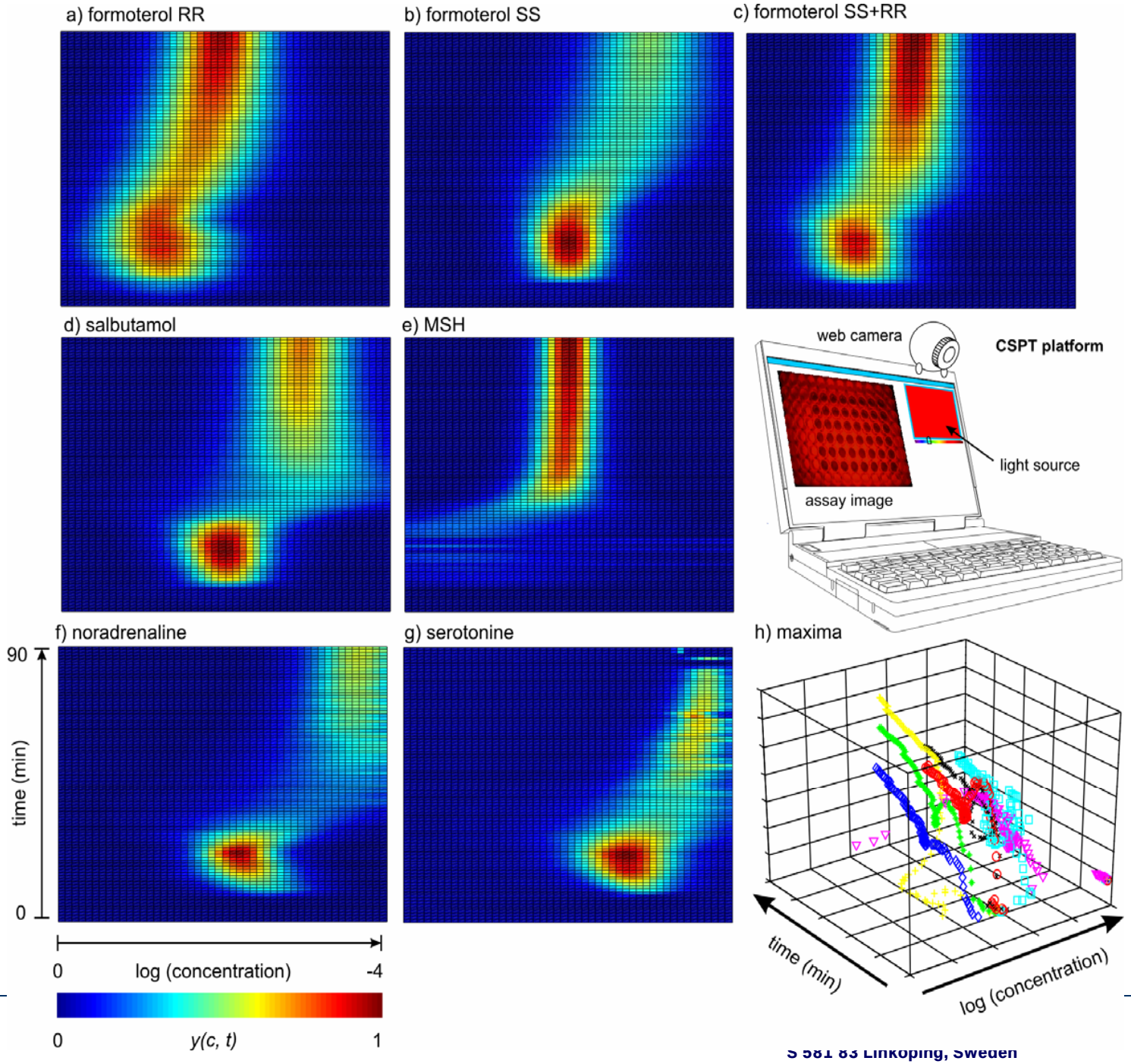
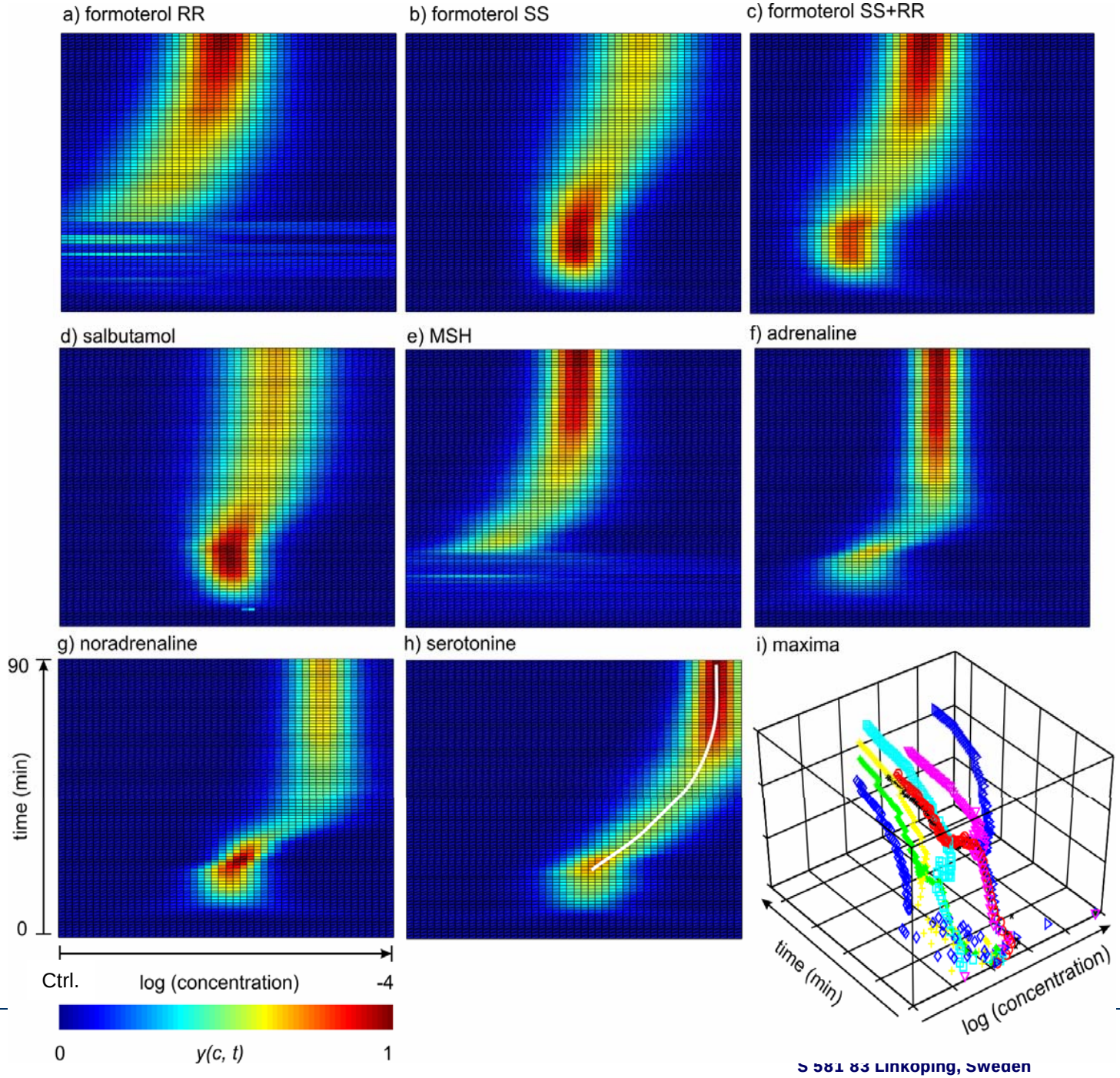
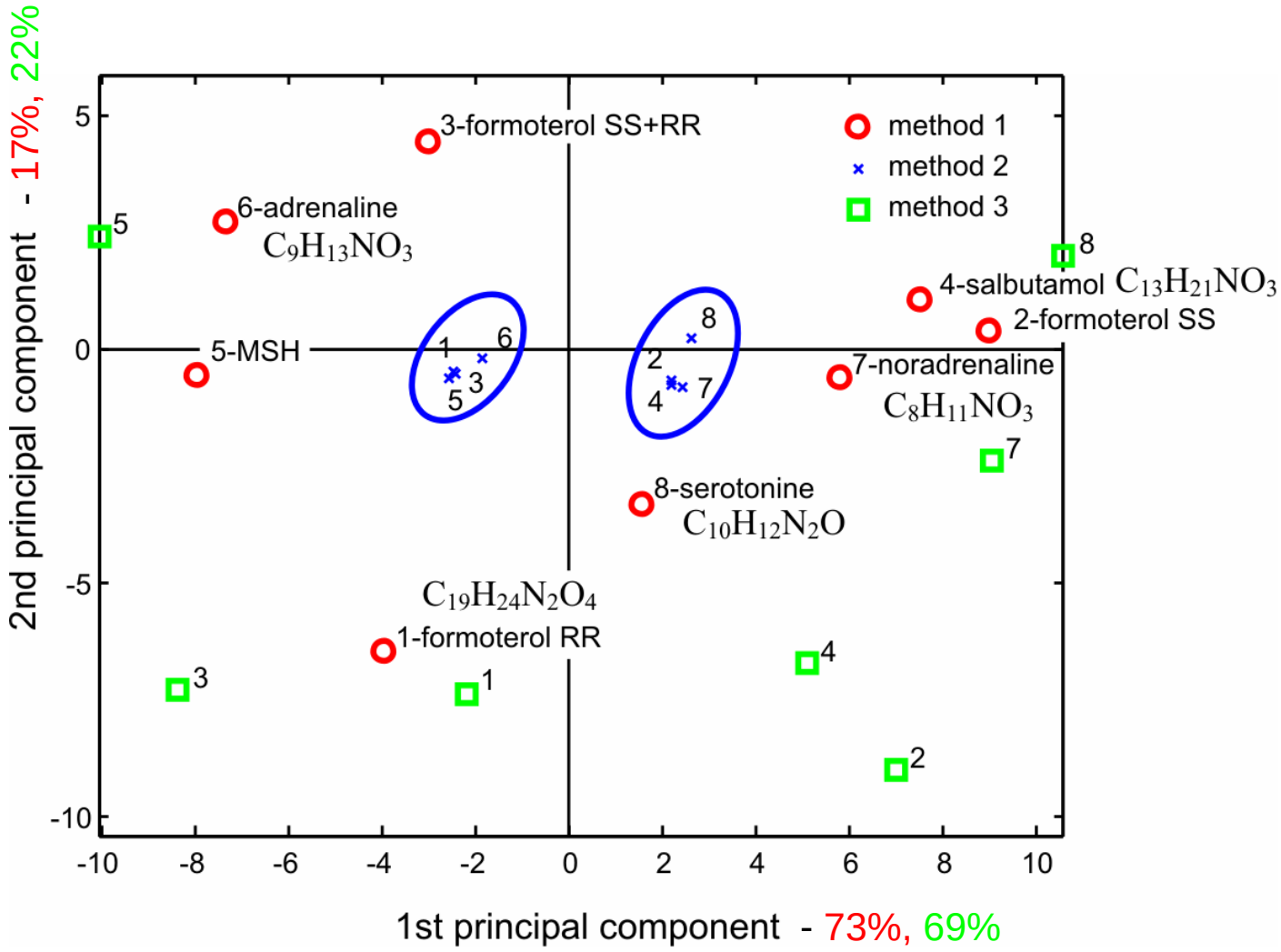
CSPT evaluation



Distinctive biochemical images (using plate reader)



Classification



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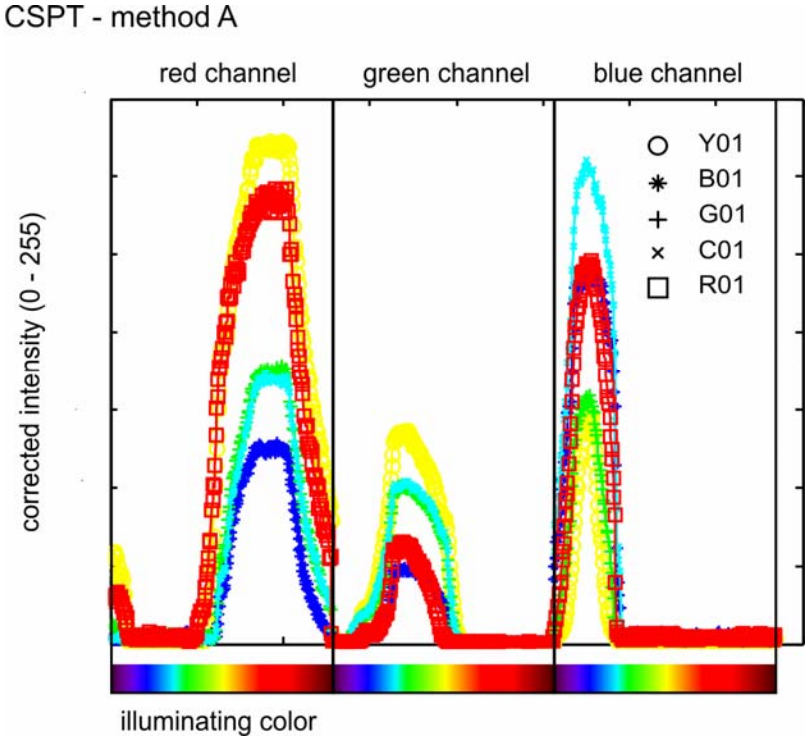
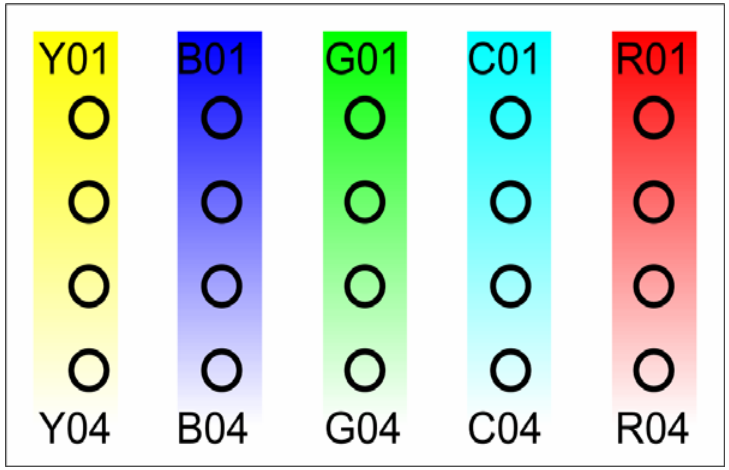
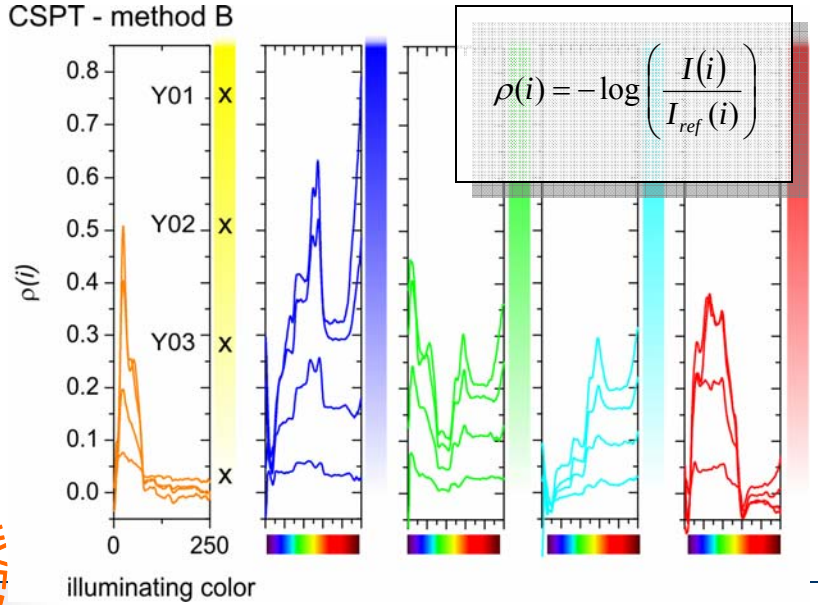
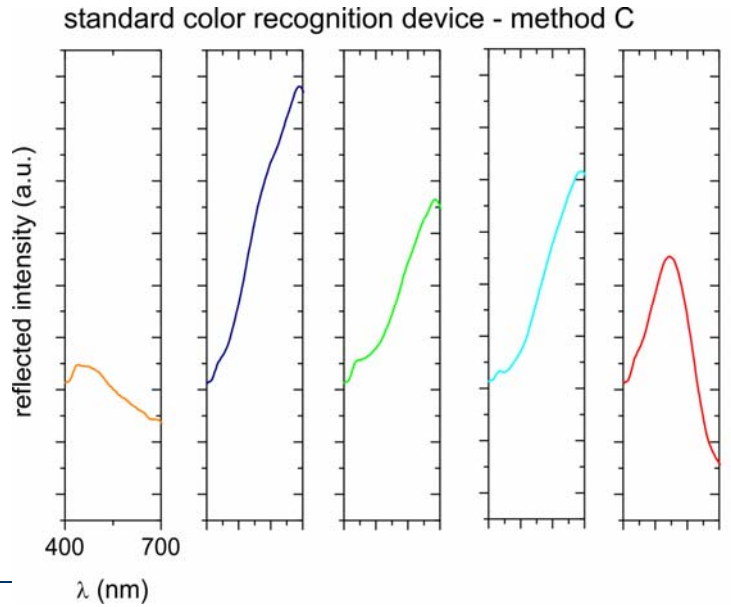
3. Reflectance fingerprints









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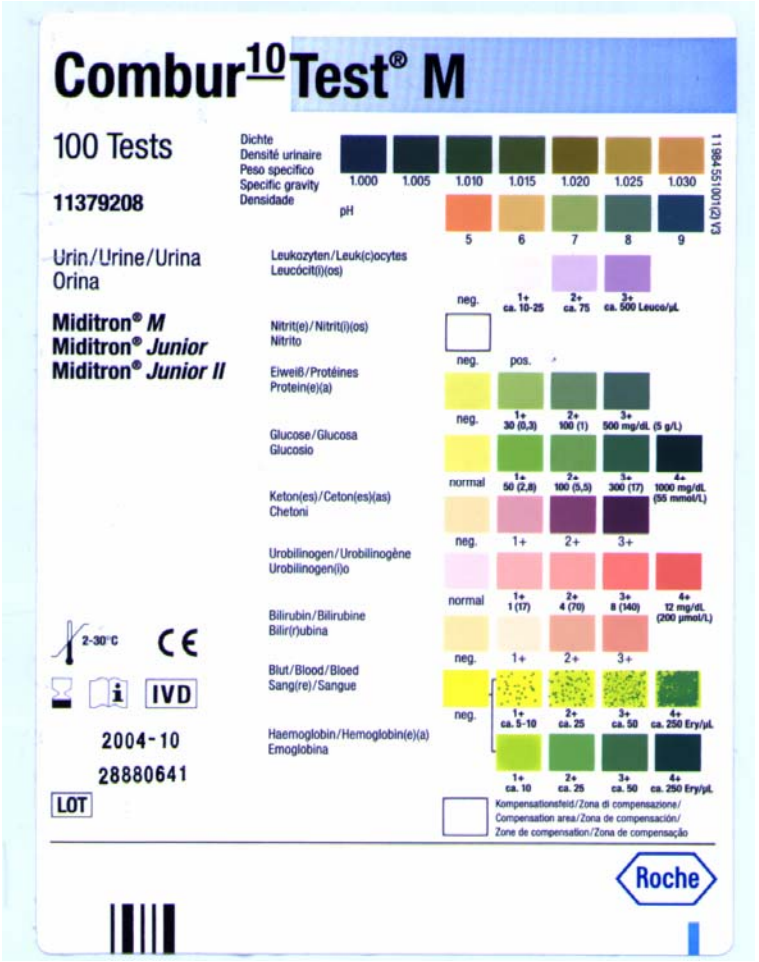
Colorimetric - 10 parameters in urine



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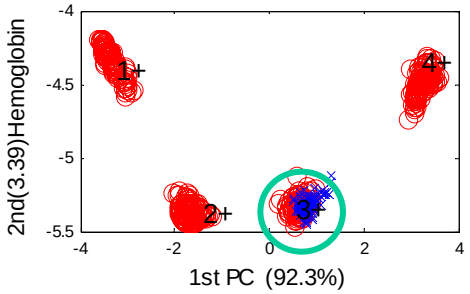
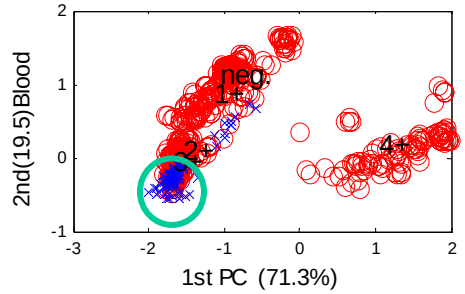
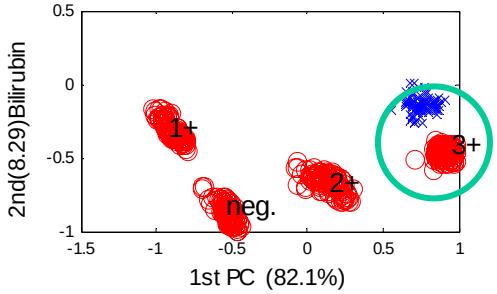
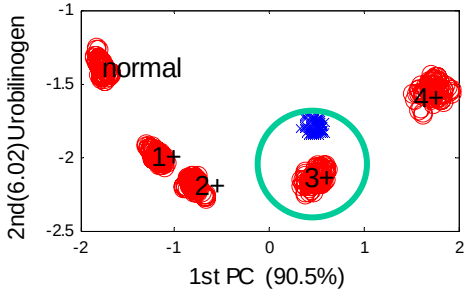
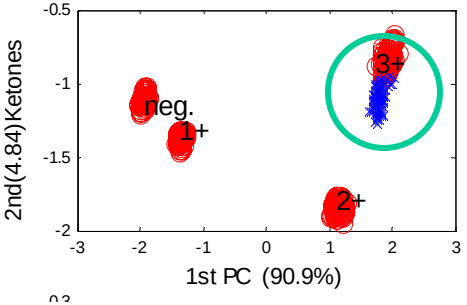
Combur Test classification (under development by RGB Technologies)

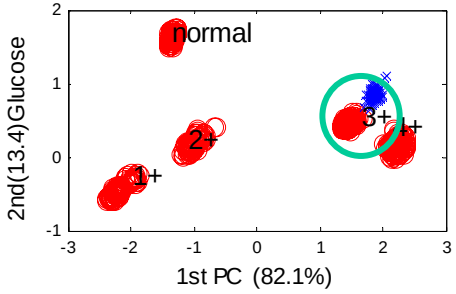


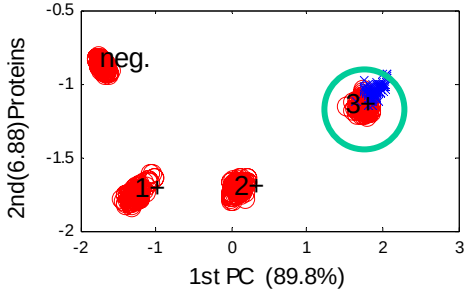


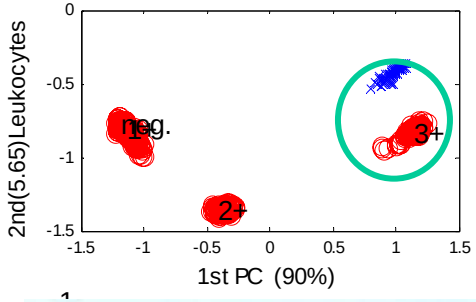


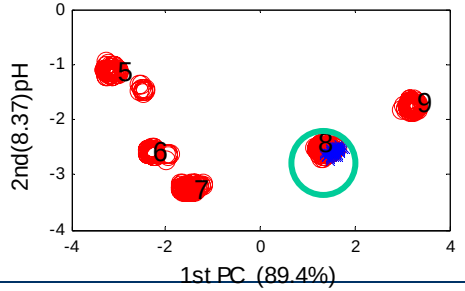


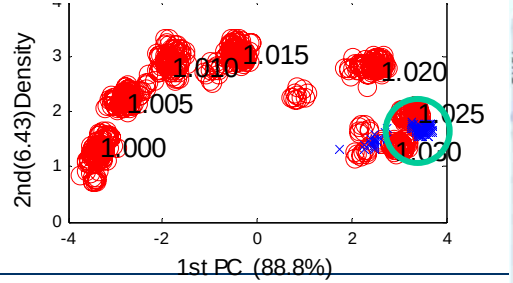












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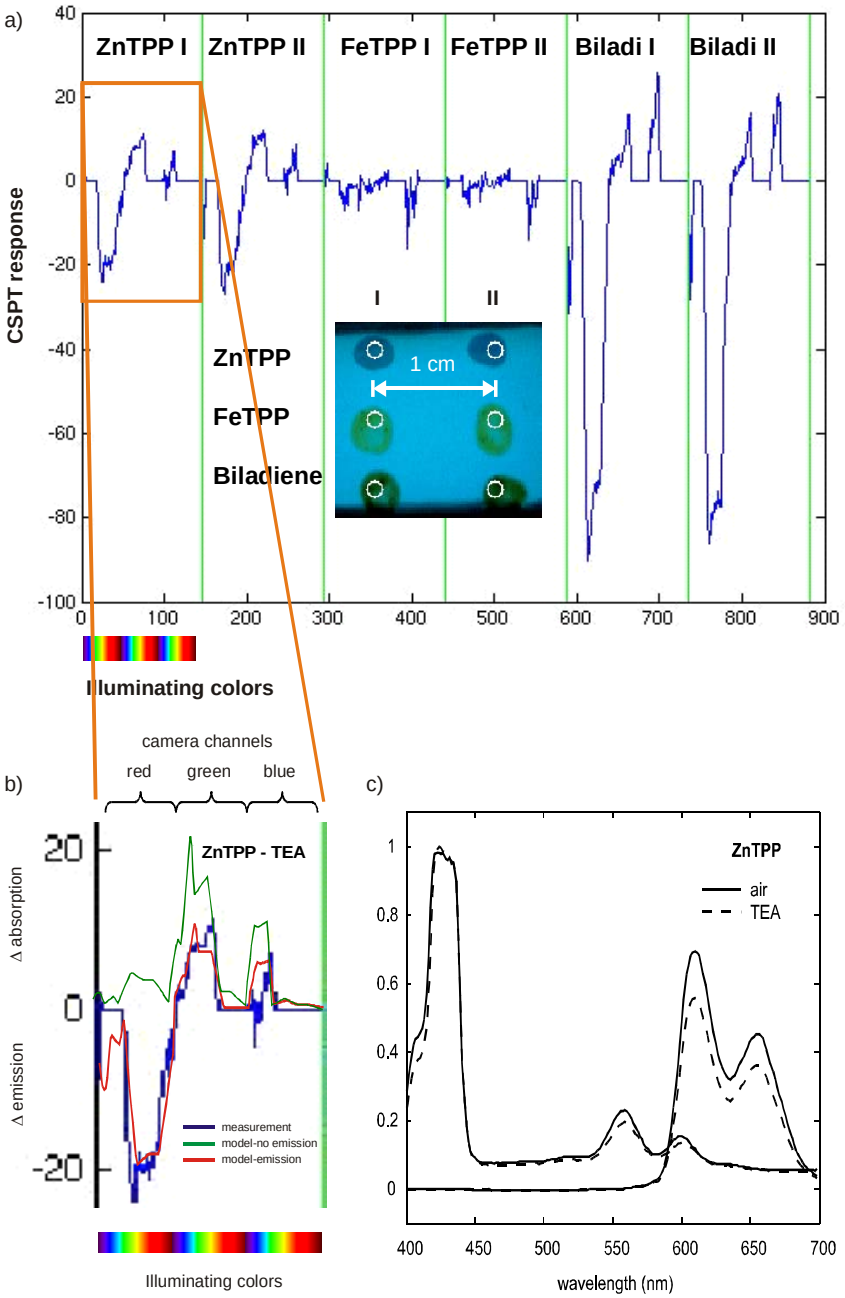
MOST “FUNDAMENTAL” APPLICATION SO FAR:
Classification of molecules in gas phase with color indicators (with potential applications for breath analysis, food freshness, bacterial classification,...)

“*Difference optical fingerprinting*”

- Arrays of thin films of metallophorphyrins in a PVC matrix
- Optical properties determined by a sequence of (50) RGB-colors and images stored as individual intensities in the different camera channels
- Exposure to test molecules (NO, triethylamine, ammonia, CO,...)
- Difference in intensities in the three channels with and without test molecule in the ambient registered for each color index (r,g,b)
- Each sequence generates 50 data points in each channel of the camera (i.e. 150 points)
- Classification made by pattern recognition



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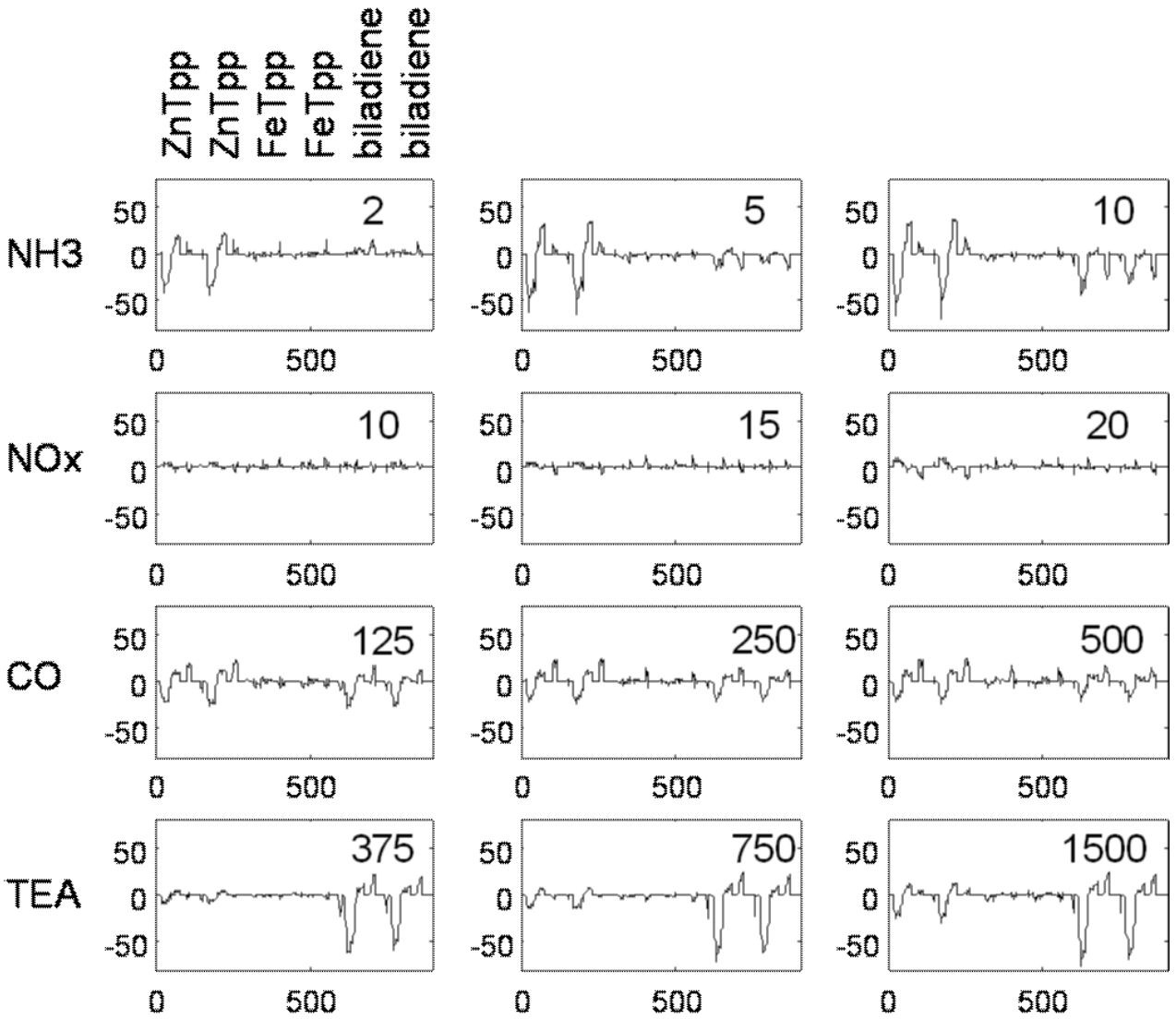

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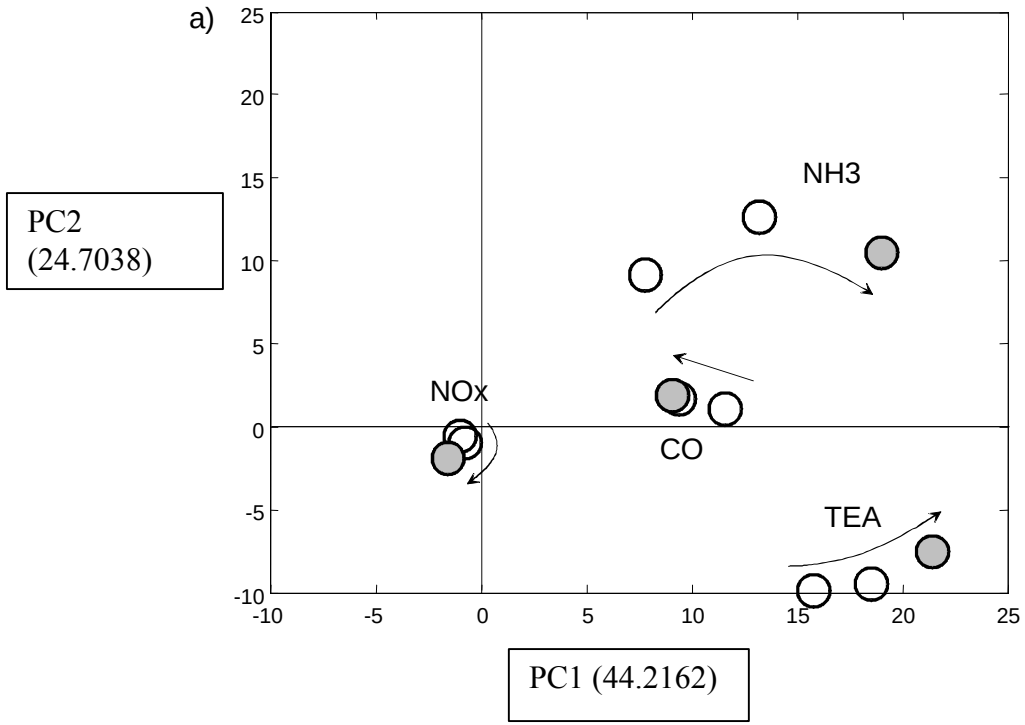

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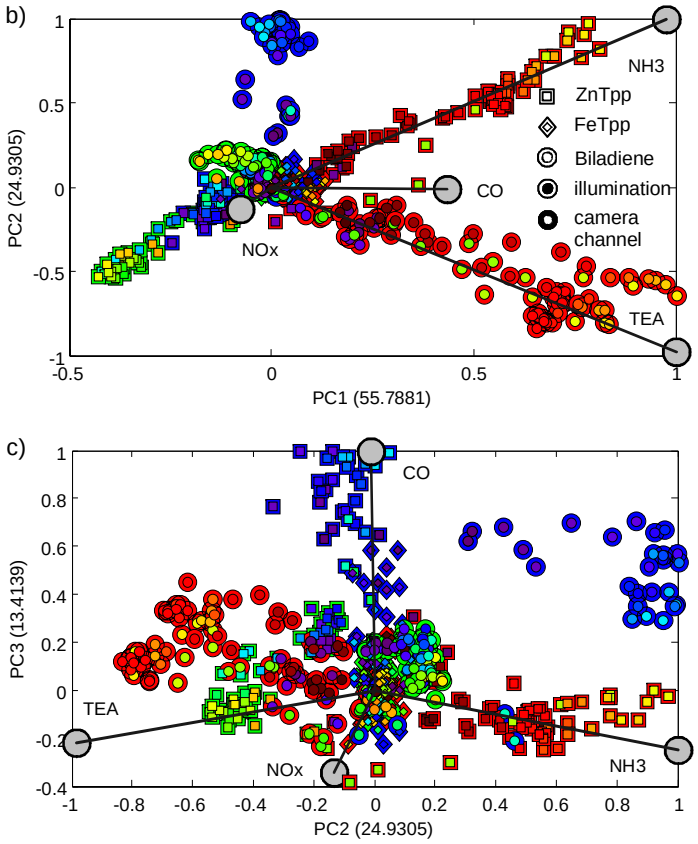

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Computers as analytical instruments

Possibilities:

- Light source of any color, intensity and shape through choice of color index
- Programmed scanning of colors possible without extra devices
- Programmed movement of light spots without extra devices
- Chopped light source created by programming
- Data collection and evaluation integrated with the light source
- Experimental control and data evaluation over internet

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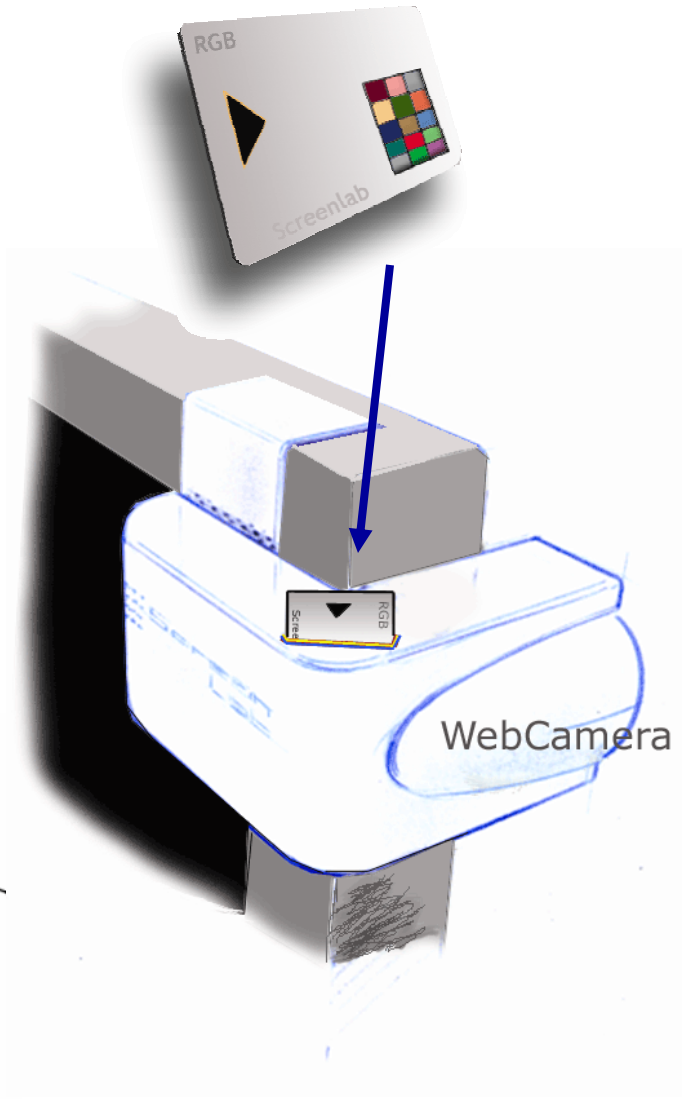
RGB
Technologies AB

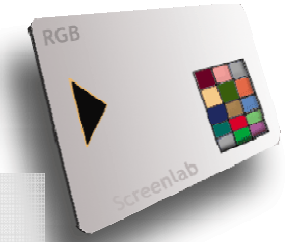
Ongoing commercial development: ”Screenlab”

- Target application
  - Evaluation of colorimetric assays
- Principle
  - Spectral fingerprinting with discrimination between absorption and emission signatures
- Setup
  - Standard computer set plus a web camera (mobile telephones)



RGB
Technologies AB

Multiple tests=>One reader



- One reader for all colorometric tests
- Enabels multipel test matrix
- No expensive equipment (PC and a webcamera)
- Uses today accepted tests chemistry

A POSSIBILITY AND A PROBLEM AT THE SAME TIME:

DEVELOP SOFTWARE TO ALLOW AN ARBITRARY SCREEN – CAMERA PAIR TO BE USED, CONTROLLED AND EVALUATED VIA INTERNET

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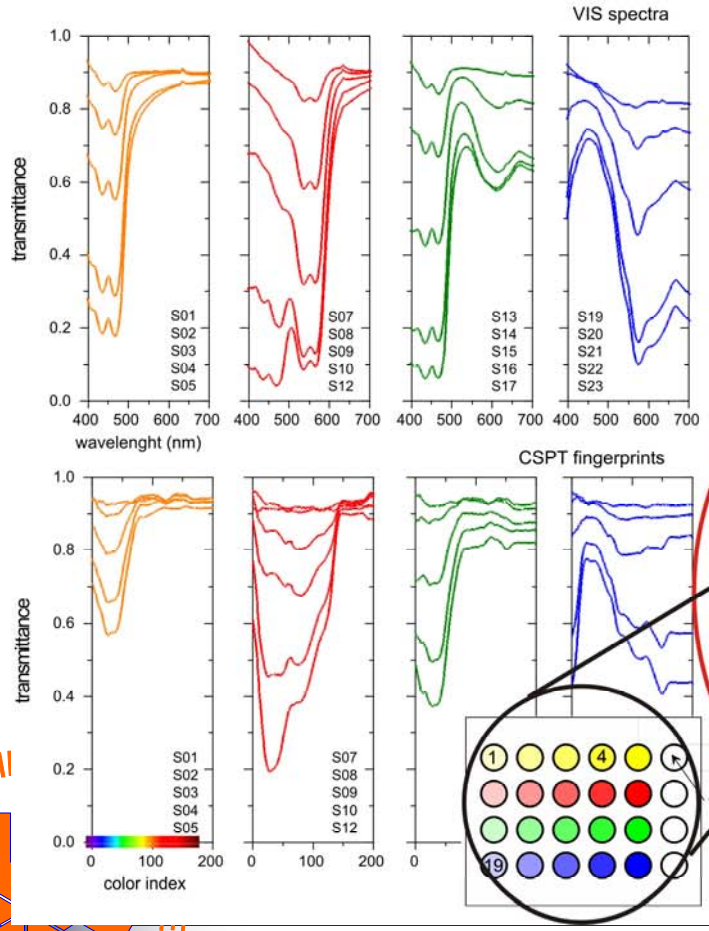
CSPT personal to global monitoring of environmental and sanitary parameters

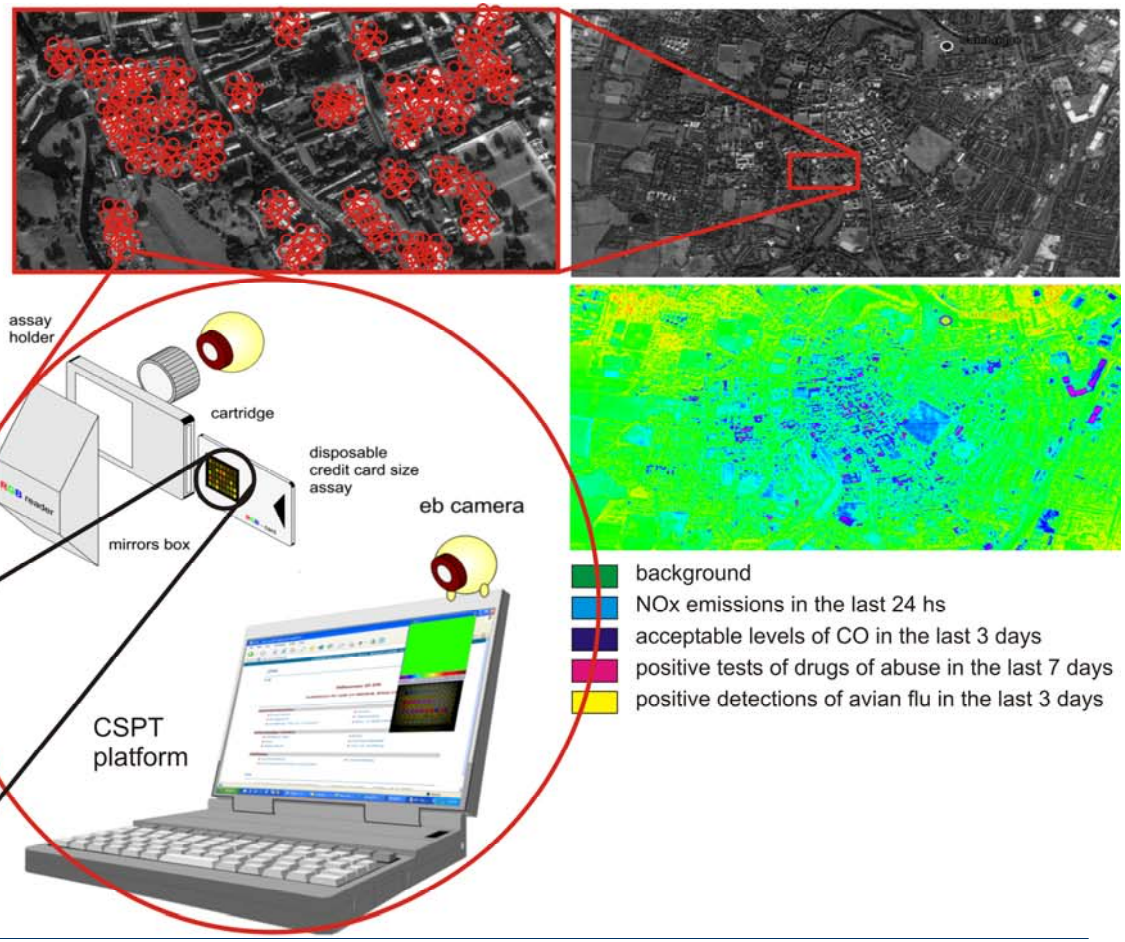
Division of Applied Physics, Department of Physics, Chemistry and Biology, Linköping University

Prof. Ingemar Lundström
Dr. Daniel Filippini

CSPT spectral fingerprinting



Google Earth projected detections



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- RGB Technologies for practical developments of CSPT
- VINNOVA, SSF, VR for research grants

For more details see poster by Daniel Filippini

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A few references

"Measurement strategy and instrumental performance of a computer screen photo-assisted technique for the evaluation of a multi-parameter colorimetric test strip", D. Filippini, I. Lundström, *The Analyst* **131** (2006), 111-117.

"Adaptive illumination in computer screen assisted spectral fingerprinting", D. Filippini, I. Lundström, *Appl. Phys. Lett.* **86** (2005), 084101 1-3. Selected for the *Virtual Journal of Biological Physics Research* **9** (2005).

"Computer screen photo-assisted detection of complementary DNA strands using a luminescent zwitterionic polythiophene derivative", D. Filippini, P. Åsberg, P. Nilsson, O. Inganäs, I. Lundström, *Sensors and Actuators B* (2005), in press

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"Microplate based biosensing with a computer screen aided technique", D. Filippini, T. P. M. Andersson, S. P. S. Svensson, I. Lundström, *Biosensors and Bioelectronics* **19** (2003), 35-41.

"Computer screen as a programmable light source for visible absorption characterization of (bio)chemical assays", D. Filippini, S. P. S. Svensson, I. Lundström, *Chem. Commun.* **2** (2003), 240-241.