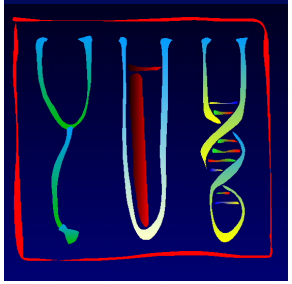


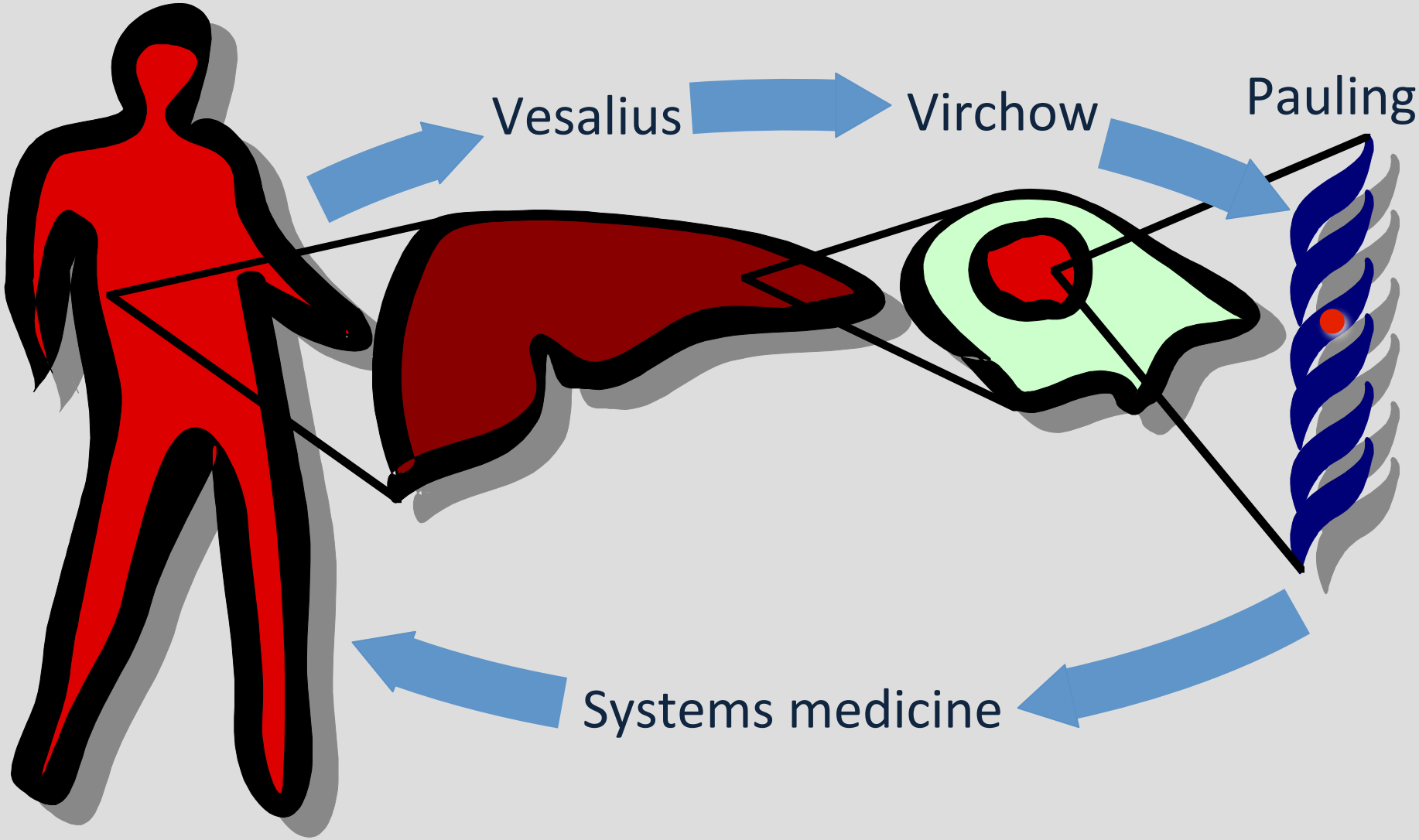
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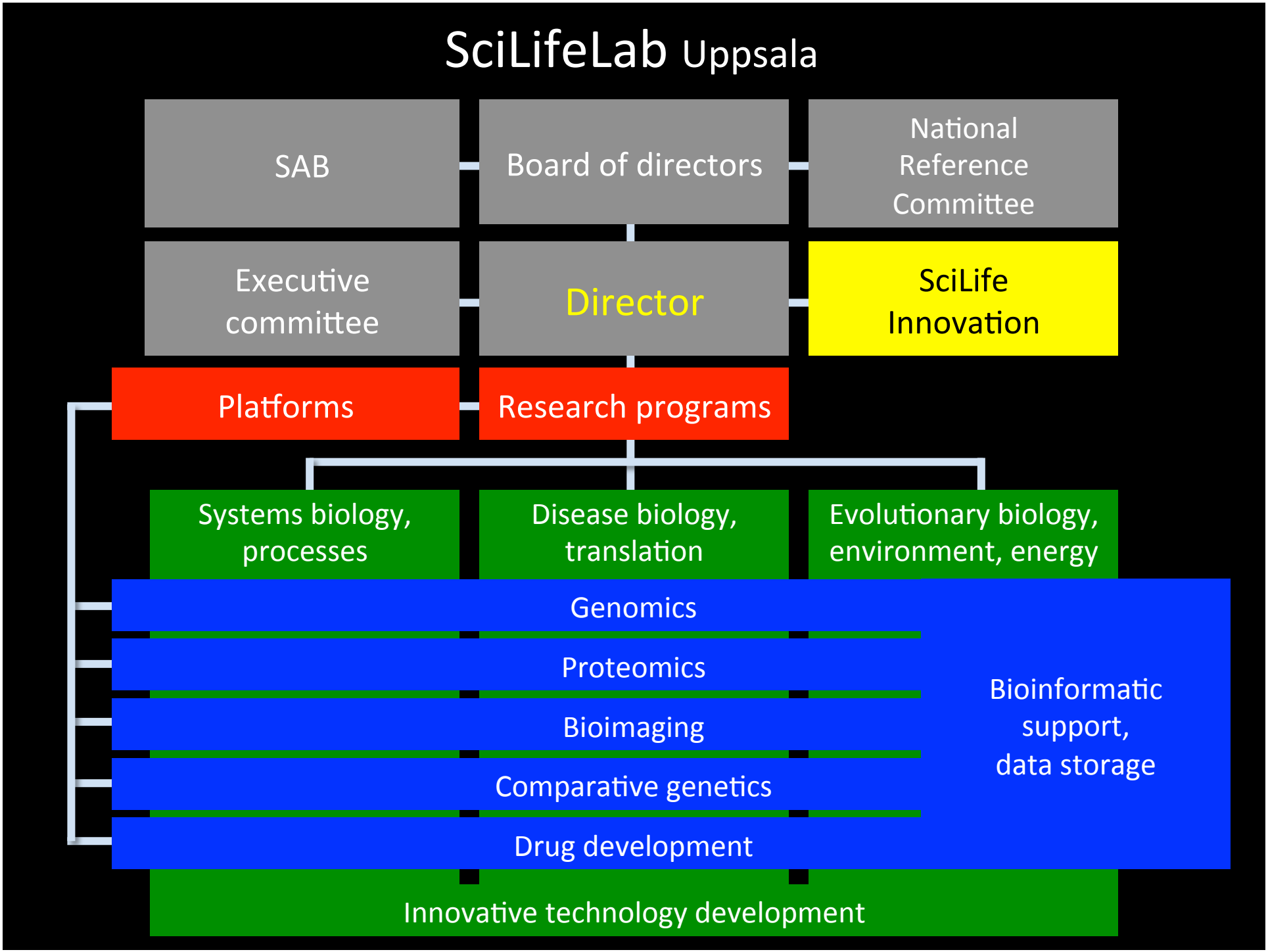
High-performance tools for research and diagnostics

Ulf Landegren
Uppsala University
ScLifeLab

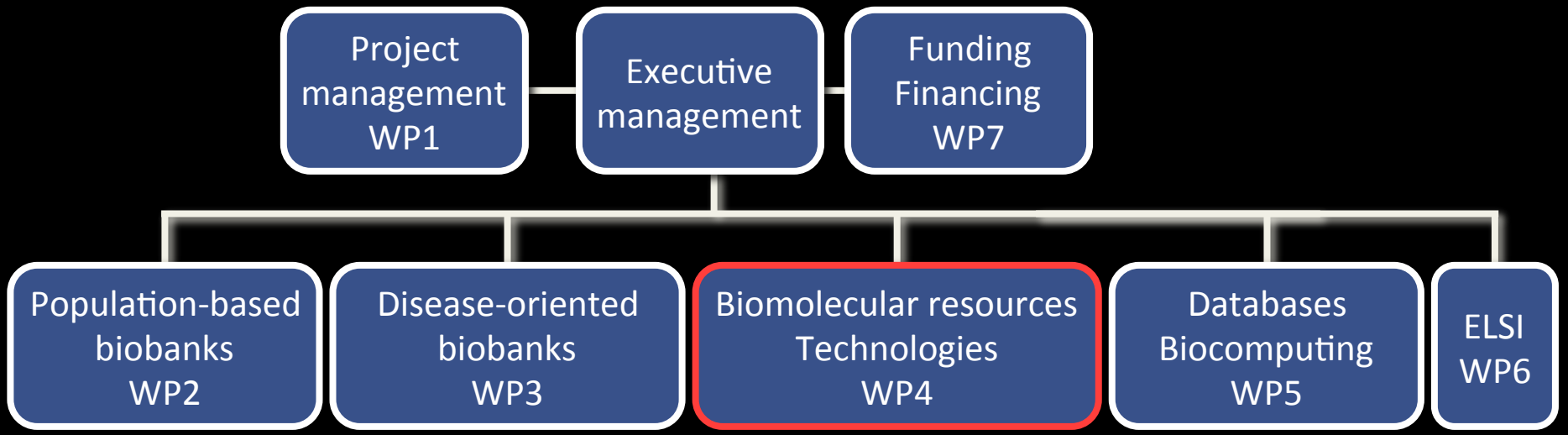


Levels of understanding of disease

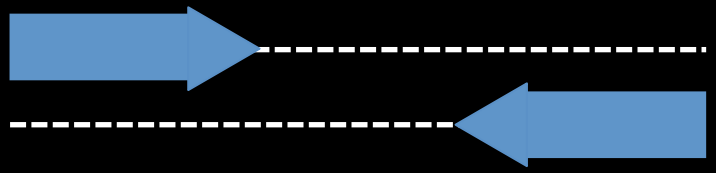



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Innovative technology development

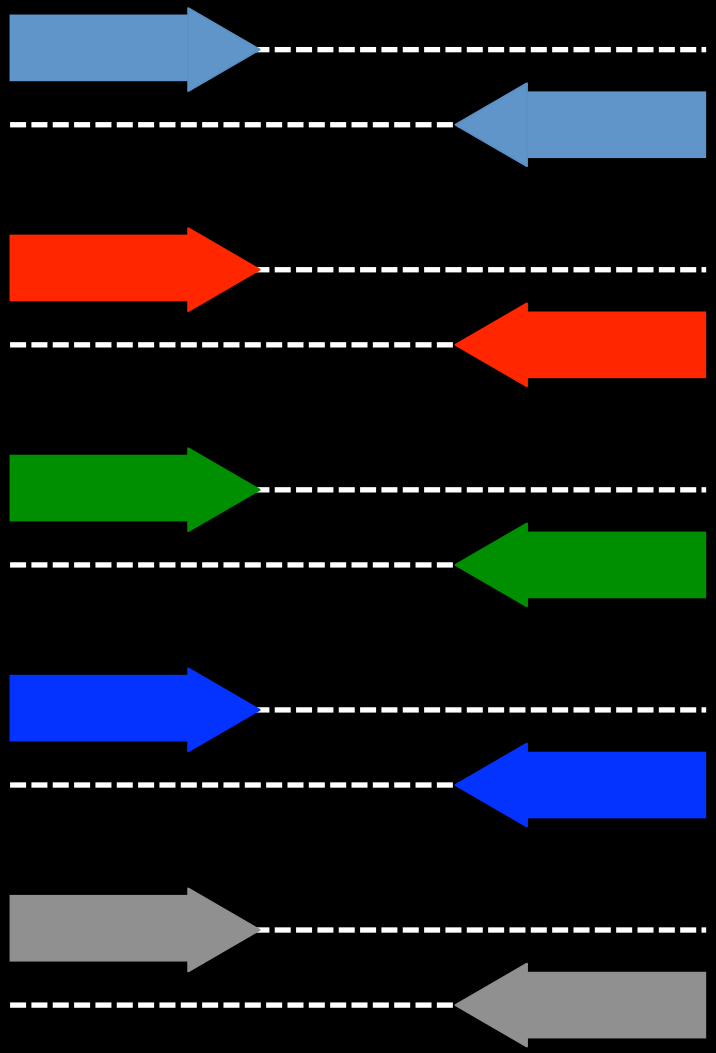
Organized biobanking within BBMRI.eu/.se

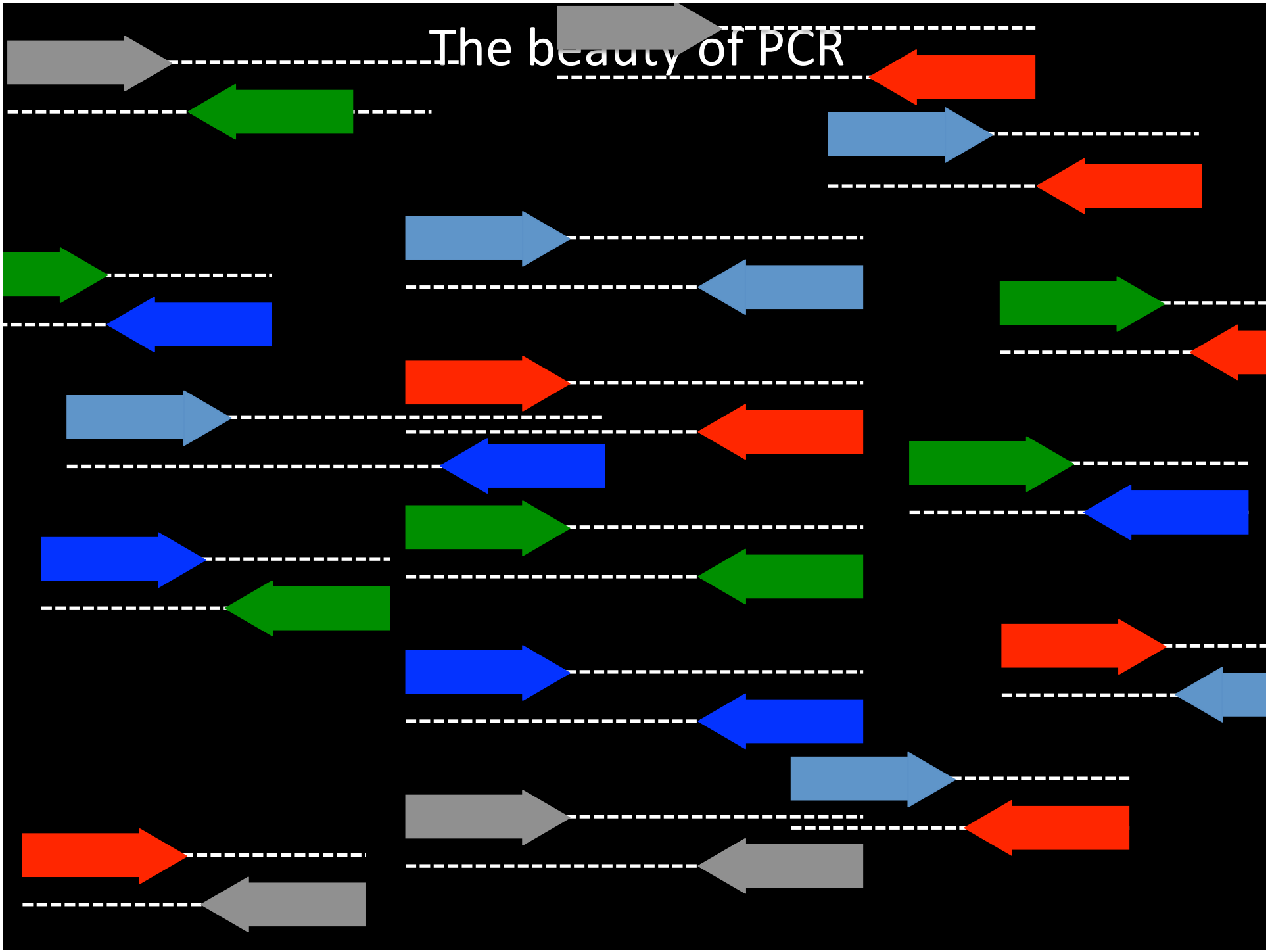


The beauty of PCR



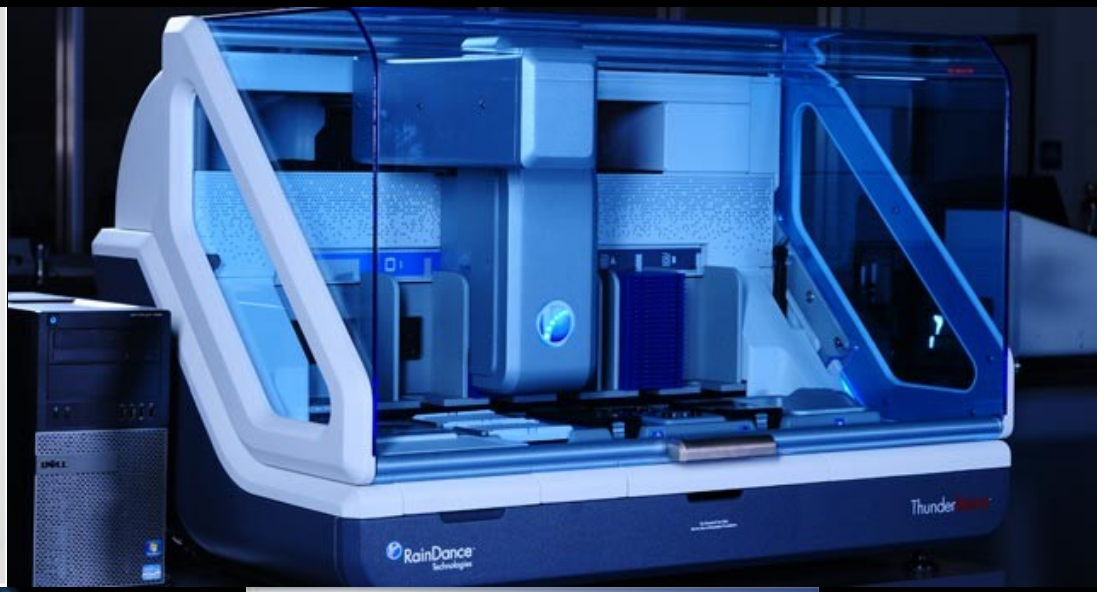
The beauty of PCR

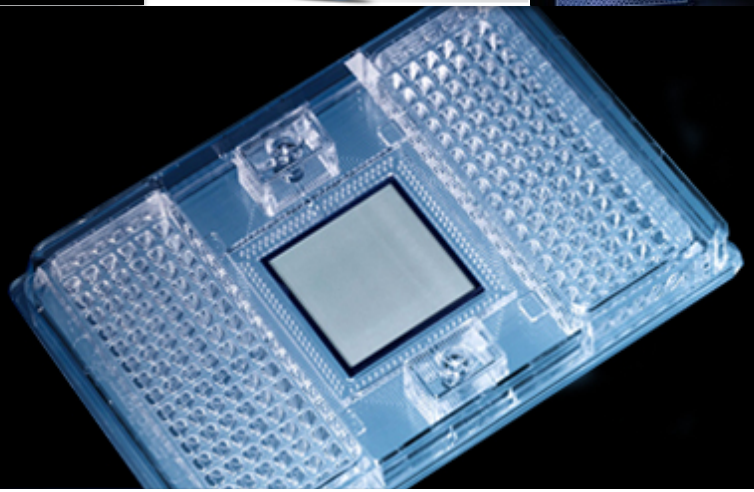


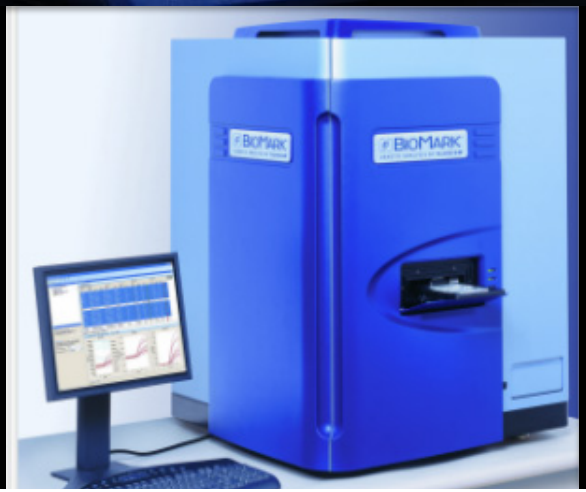

The beauty of PCR

Microfluidic PCR – Disposables and instruments

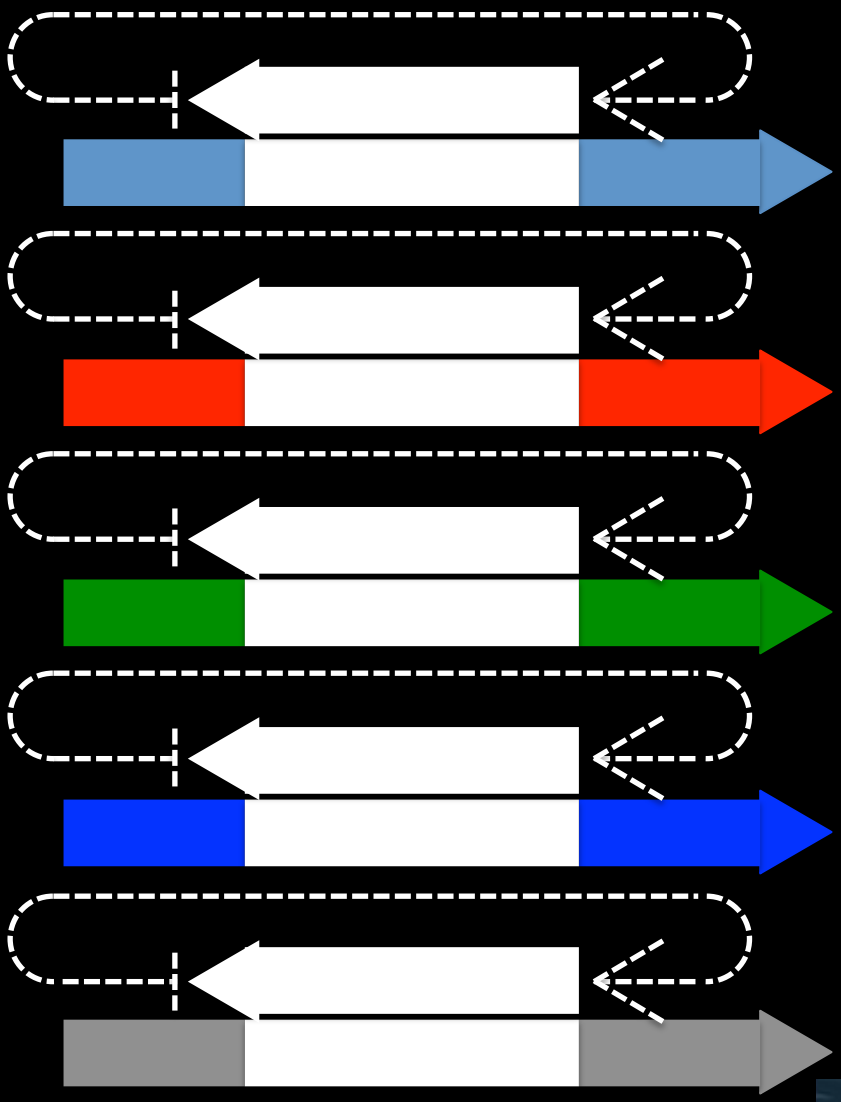








Selector probes



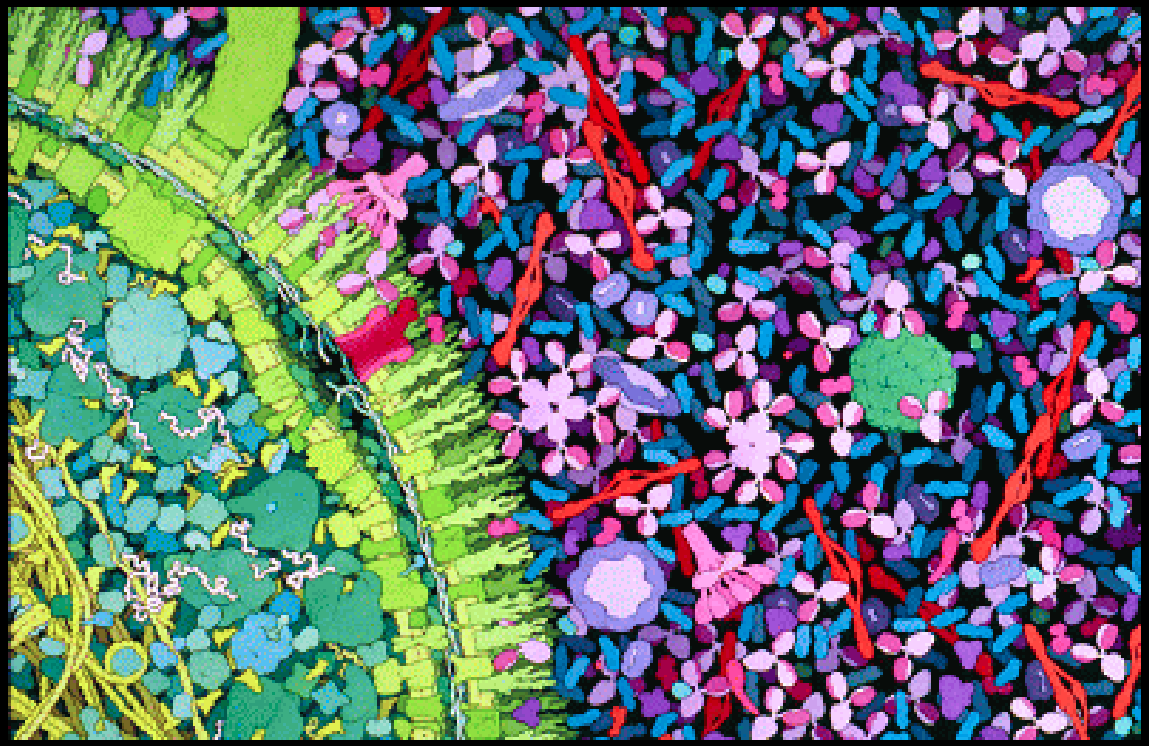


HaloPlex



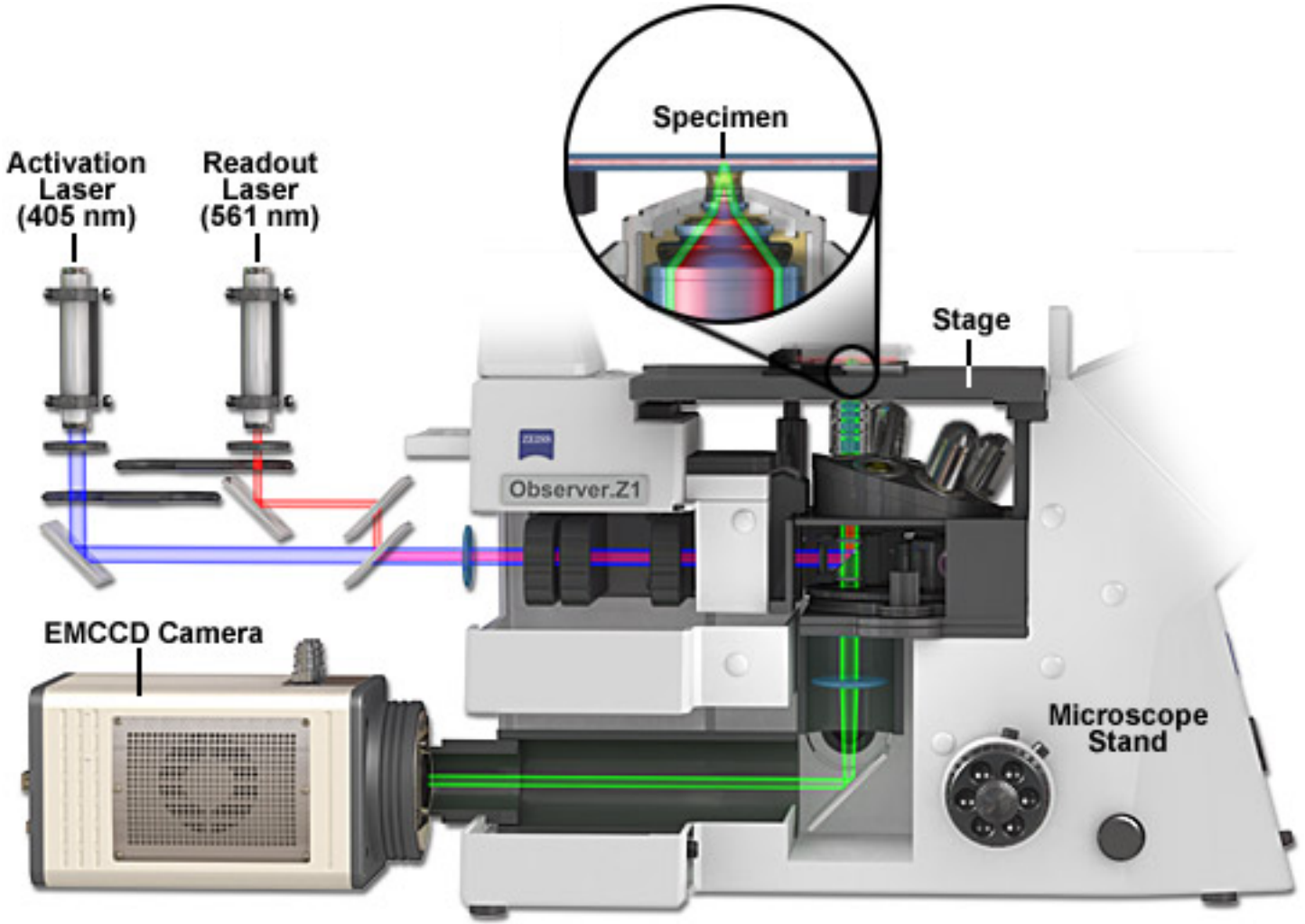
Fredrik Dahl…Mats Nilsson. *Nucleic Acids Res* **33**: e71 (2005)

Visualizing cellular processes at nanometer resolution

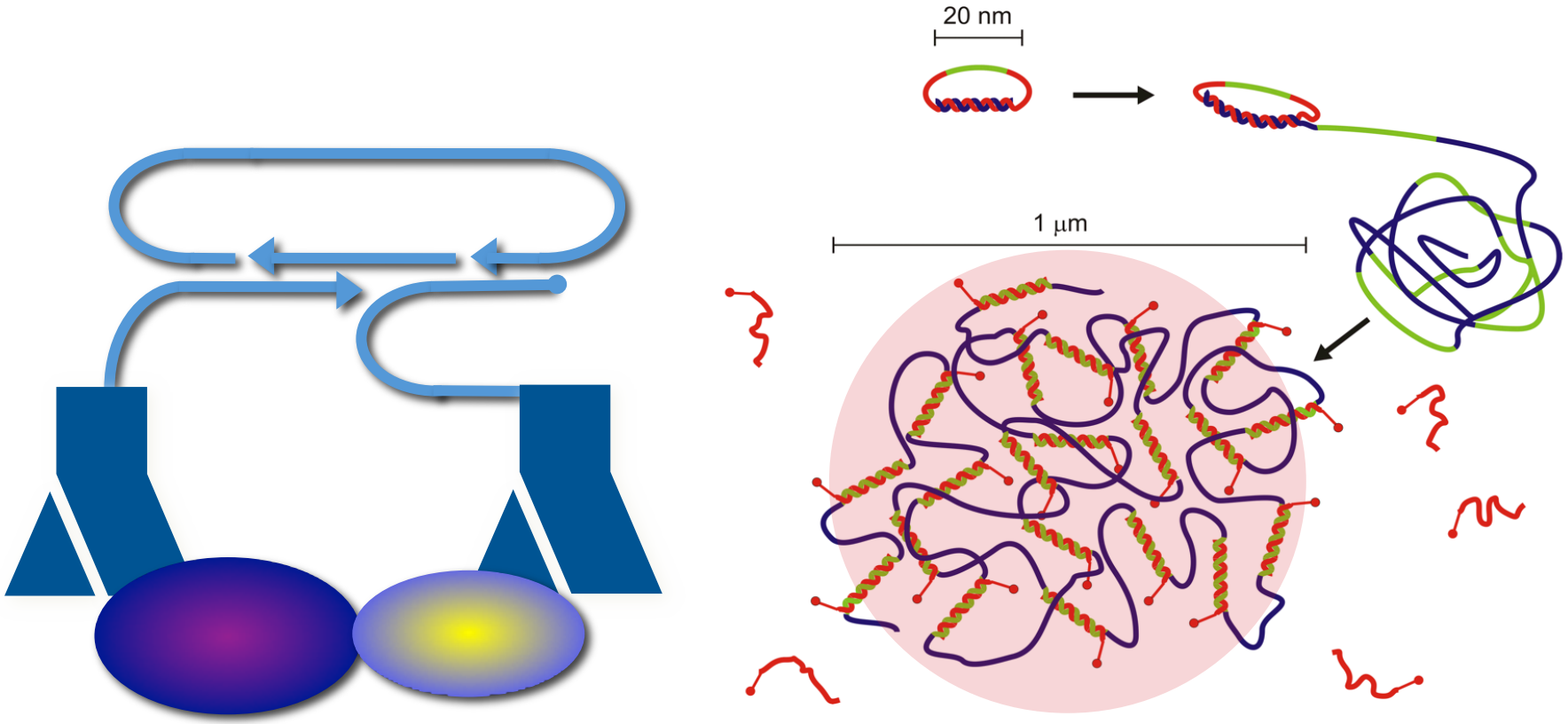


The Machinery of Life; Goodsell

The advent of superresolution microscopy - STED, PALM, STORM, etc

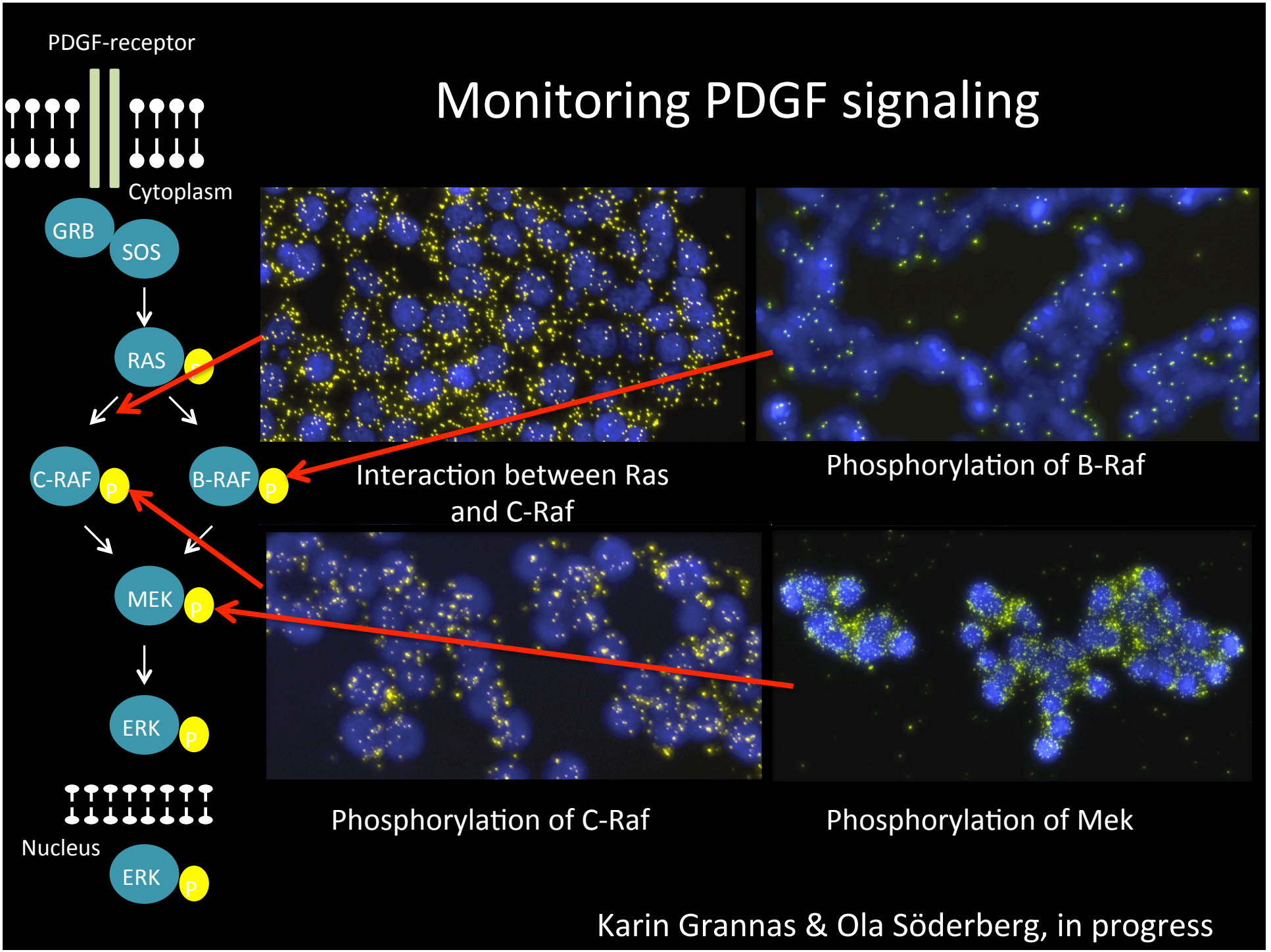


In situ proximity ligation assay: Visualizing proteins, modifications and interactions

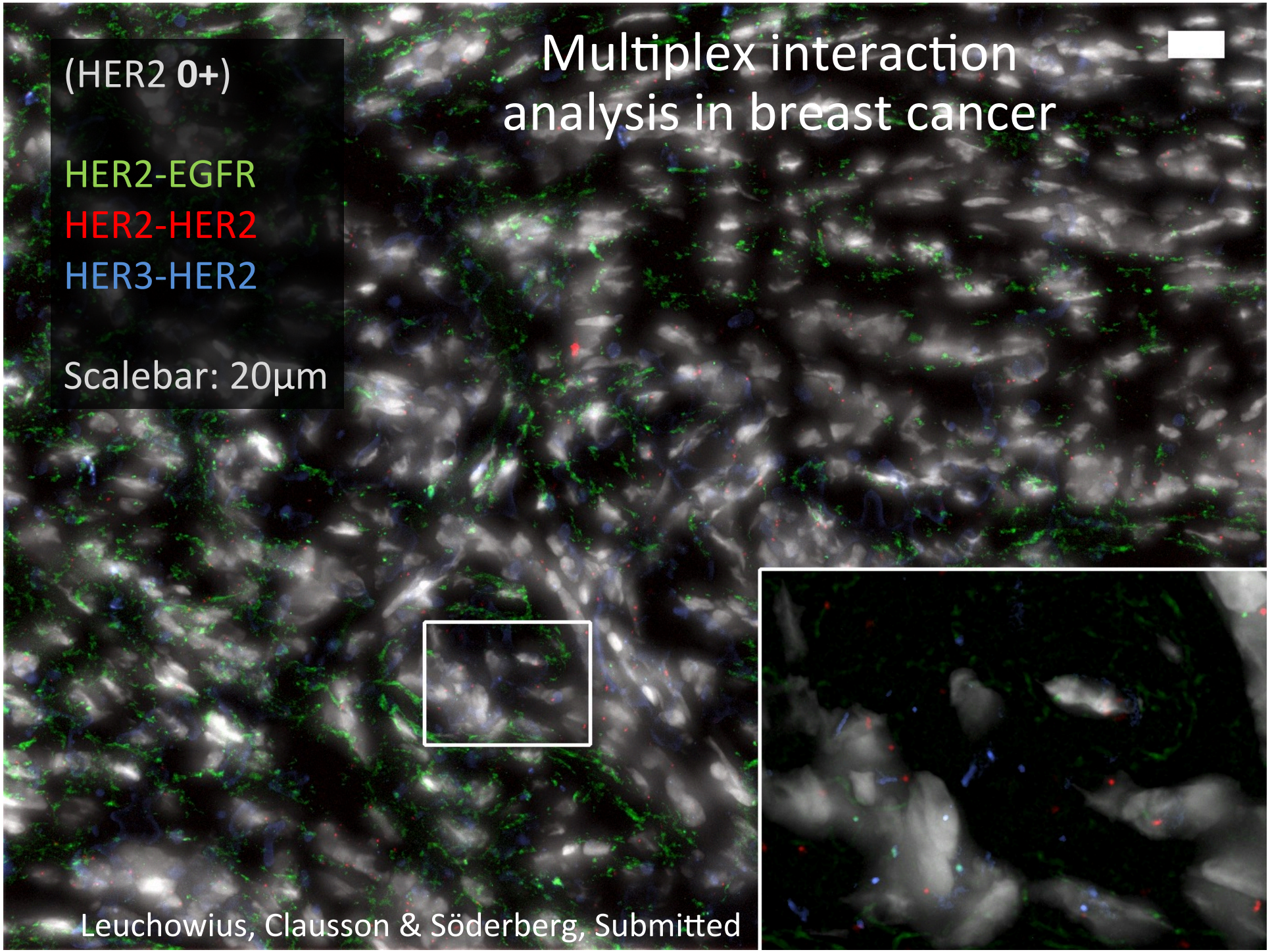


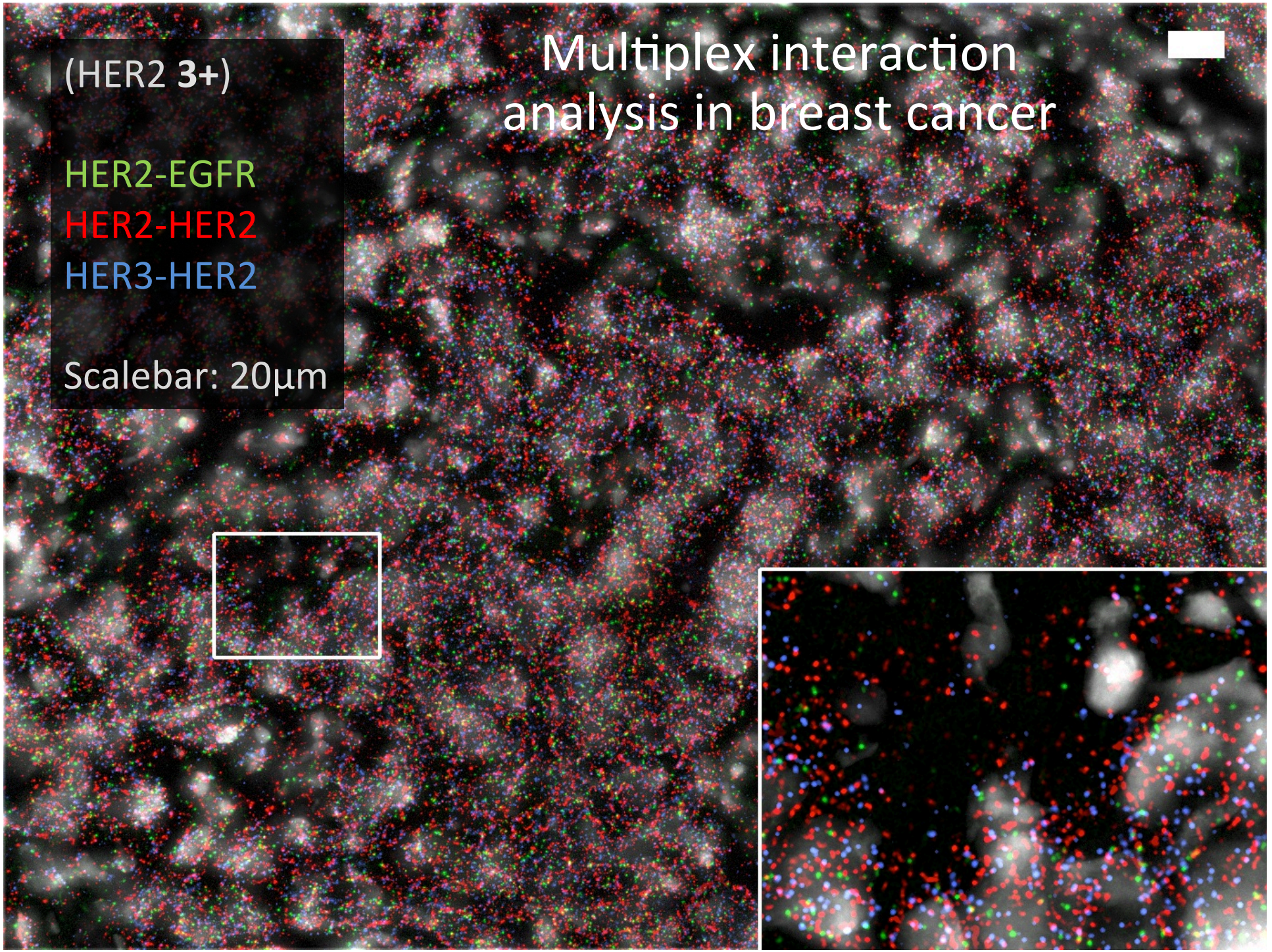
Ola Söderberg, Mats Gullberg & al *Nature Meth* 3:995, 2006

Monitoring PDGF signaling



Karin Grannas & Ola Söderberg, in progress

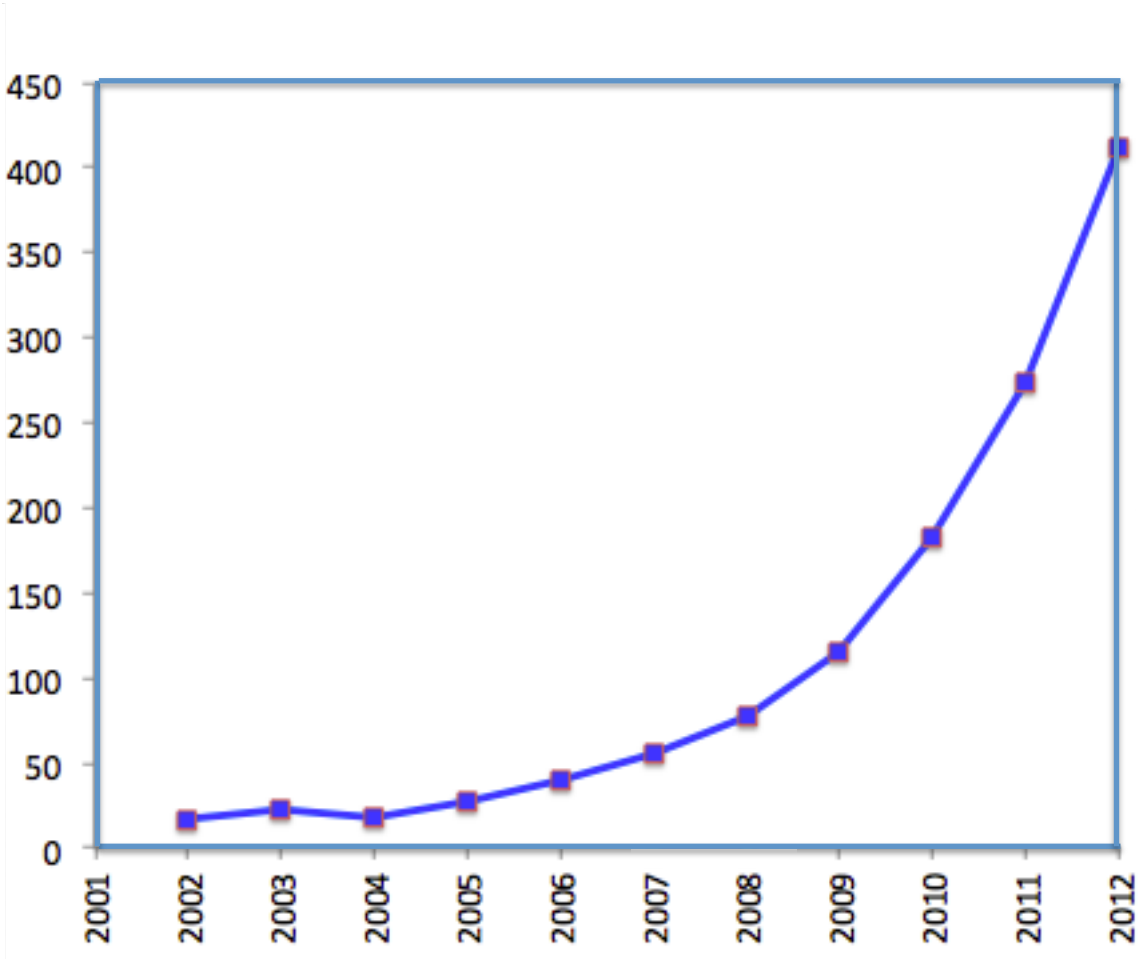

(HER2 0+)
HER2-EGFR
HER2-HER2
HER3-HER2
Scalebar: 20µm
Multiplex interaction analysis in breast cancer
Leuchowius, Clausson & Söderberg, Submitted


(HER2 3+)
HER2-EGFR
HER2-HER2
HER3-HER2
Scalebar: 20µm
Multiplex interaction analysis in breast cancer

Numbers of NEW papers mentioning

Proximity ligation & antibody

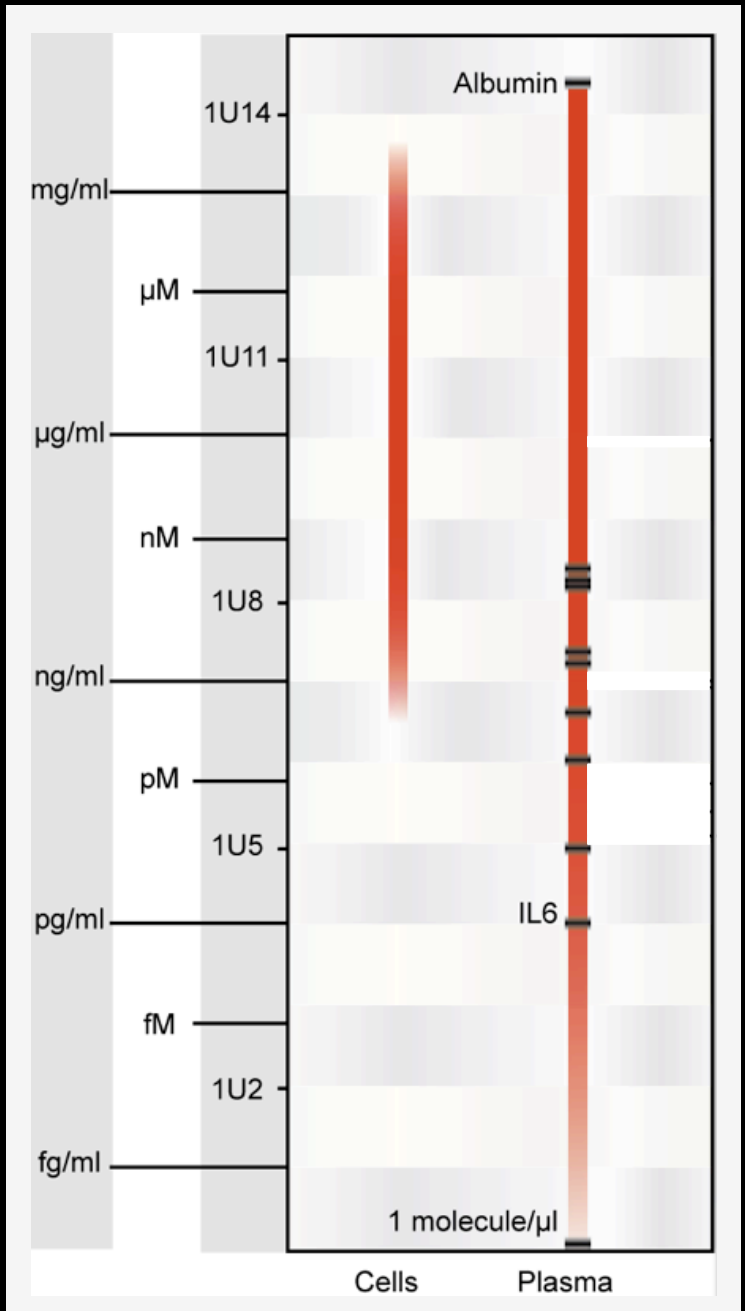
each year according to Google Scholar



Parallel protein measurements via Selected/multiple reaction monitoring - Triple quadrupole mass spectrometer

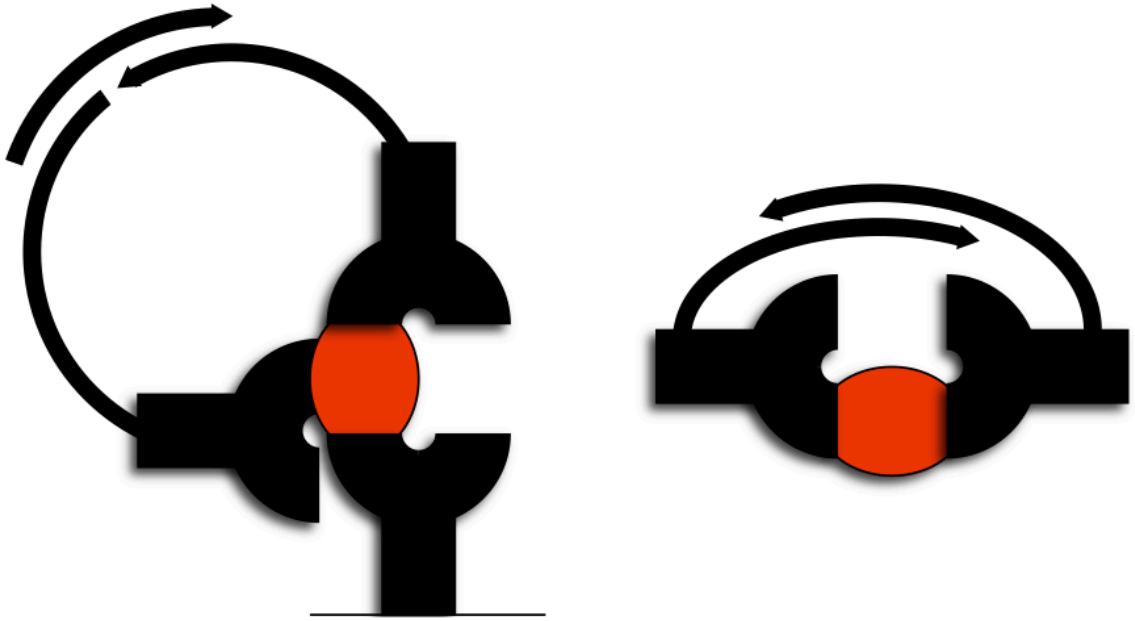


Concentration ranges of proteins



Landegren *Anal Chem* 84:1824, 2012

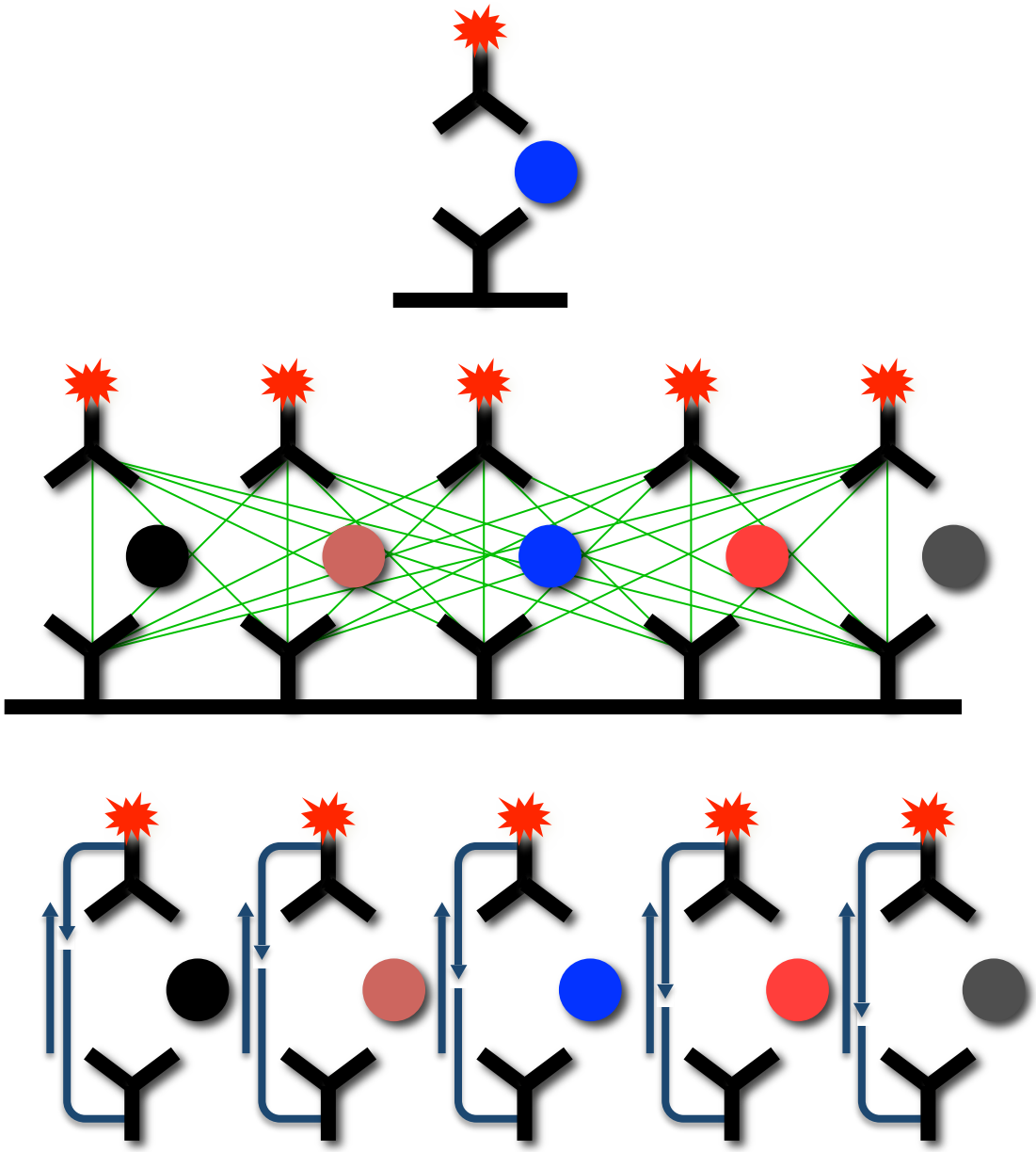
Proximity assays for detecting proteins in solution-phase



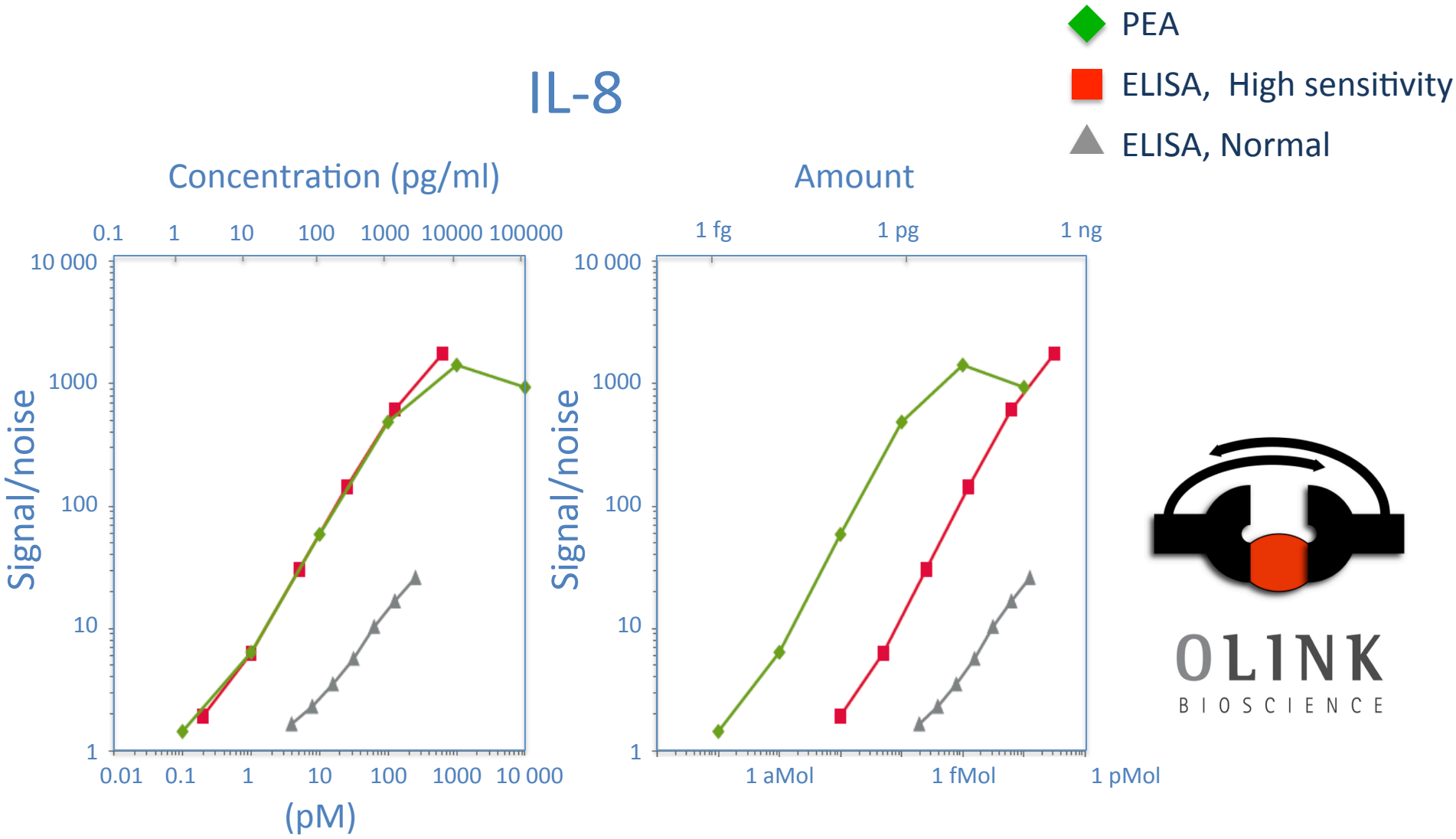
Solid-phase proximity ligation assay (PLA)

Proximity extension assay (PEA)

Avoiding crossreactivity in multiplex sandwich assays



Simplex and multiplex proximity extension assays (PEA)
1 µL vs. ELISA, 50 µL



Simon Fredriksson et al. Olink

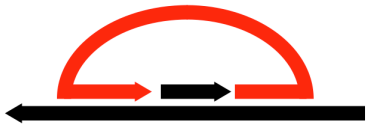
Molecular tools, dissemination



Oligonucleotide ligation assay



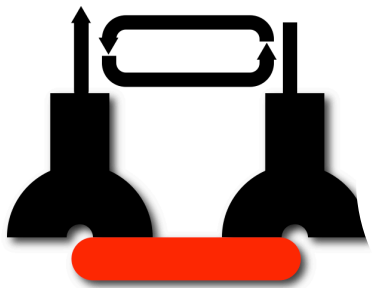
Padlock probes



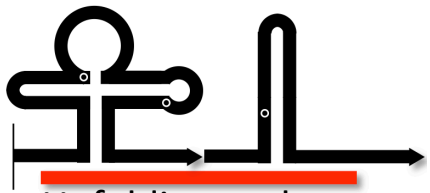
Selector probes



Proximity ligation assay



In situ proximity ligation



Unfolding probes

applied biosystems

GE Healthcare

DUPONT

Pharmacia Biotech

life technologies

Luminex

SIGMA-ALDRICH

"Major diagnostics company"

OLINK BIOSCIENCE

ParAllele BioScience

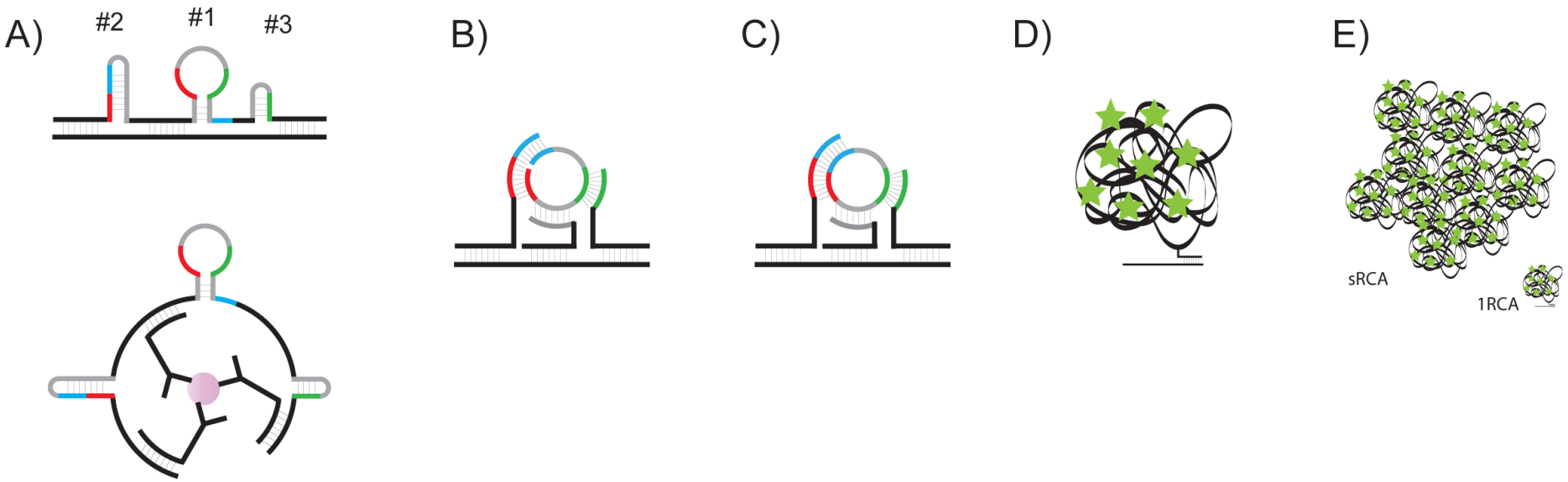
AFFYMETRIX

Halo GENOMICS™

Agilent Technologies

q-linea

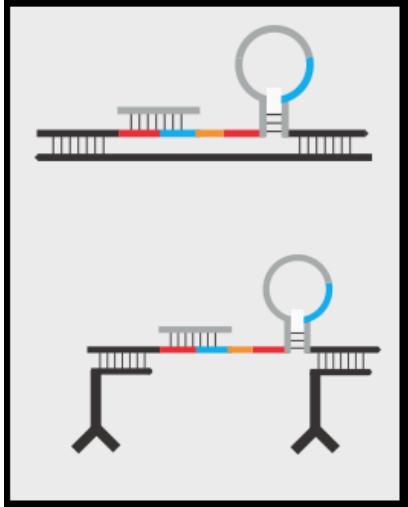
nFold probes for high-performance nucleic acid and protein detection

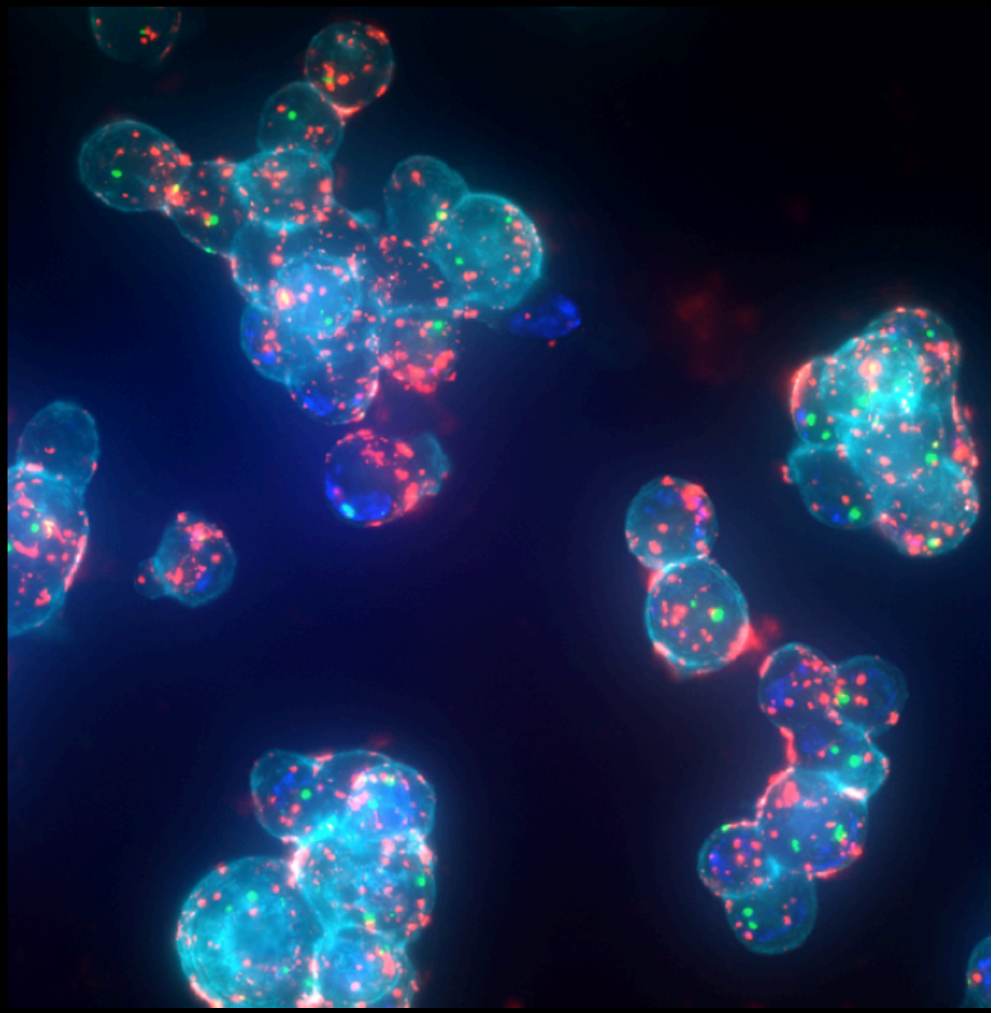


Rachel Yuan Nong, in progress

HCT116 stored in 70% EtOH, -20oC for 3 months

Direct targeting beta actin
Protein
mRNA
Nuclei
Cytoplasm





Rachel Yuan Nong, in progress

Unique features of nFold probes

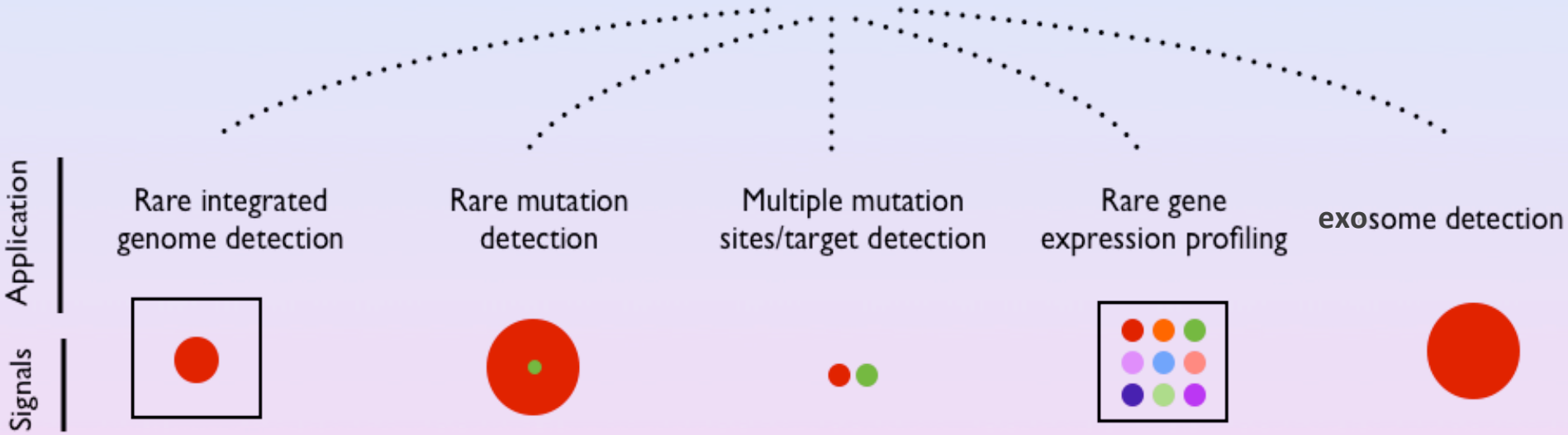
Enhanced kinetics, avidity effects, and multiplexing: All functional elements are embedded in one single probe, hence molecular events are constrained in nanoscale objects

n degrees of specificity: The probes can offer tunable (n>1) specificity by requiring adjustable numbers of target recognition events to generate one correct signals

Topological advantage: nFold probes create locally anchored amplifiable circles, yet unlinked to target molecules

Reconfigurable: The assays can be adapted for combinations of DNA, RNA and protein targets, and other classes of molecules

nFold probes and sRCA for diagnostics



Thanks group members!

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Caroline Gallant
Joakim Galli
Karin Grannas
Ida Grundberg
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Maria Hammond

Ellen Hertz
Masood Kamali-Moghaddam
Johan Oelrich
Karl-Johan Leuchowius
Anne-Li Lind
Liza Löf
Rachel Yuan Nong
Katerina Pardali
Ola Söderberg
Erik Ullerås
Johan Vänelid
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