Myself

- University Research Chair in *Interdisciplinary Life Sciences*
- Expertise:
  - Biophysics and mathematical modelling
  - Biochemistry of metabolism, signal transduction, gene expression
  - Single-cell experiments and theory

Our new building

Pharmacochemistry,
Microbiology,
Microbial pathogens,
Bioinformatics,
Immunology,
Systems Biology,
Microscopy facilities,
GPCR biochemistry and drug development,
Wnt signalling

Our lab and research

- I lead the *Systems Bioinformatics* section with Prof Dr Bas Teusink
- Projects
  - Bacterial growth and protein expression
  - Antibiotic tolerance of bacteria, persister cells, evolution
  - Microbial communities
  - Heterogeneity of bacterial cultures, subpopulations
  - Metabolism of liver cancer cells
  - Signal integration by single cells
  - Regulation of glycolysis
  - Microbial evolution
  - Organisms: *S. cerevisiae, S. pombe, E. coli, B. subtilis, L. lactis*, human cells
- Facilities: general cell biology labs, DNA/RNA, fermentors, fluorescence microscopy, metabolomics, computational biology, flow cytometry,

Molecular Cytology lab

Joachim

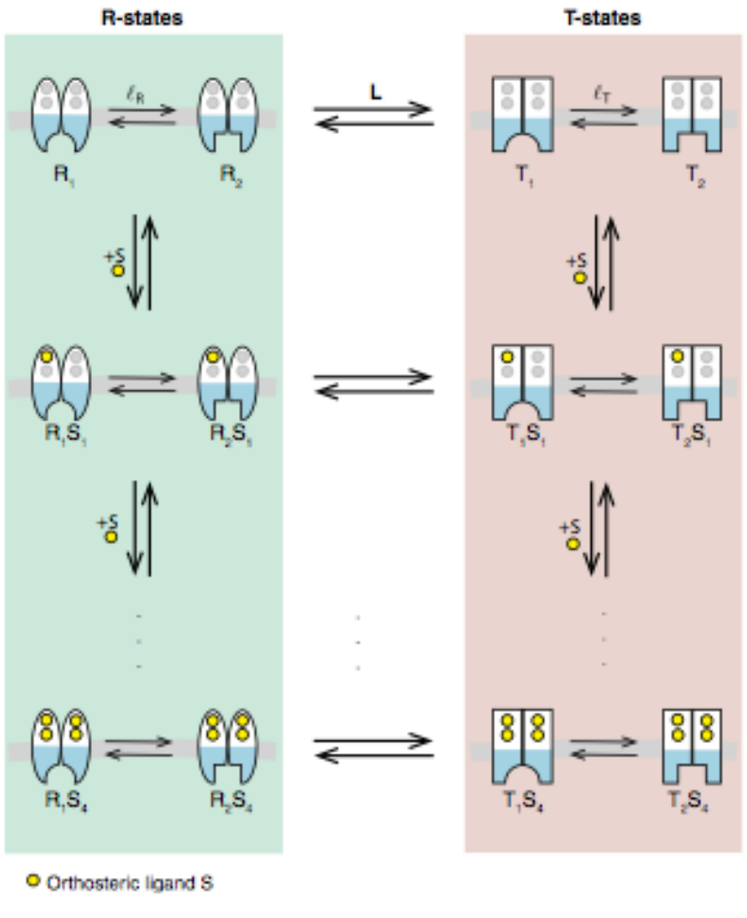
Dorus

- lead by Prof Dr Dorus Gadella
- Microscopy facilities, nearly all methods from whole cell to single molecule
- Nikon Excellence Centre, EU microscopy node
- Joachim Goedhart:
  - development of G-protein FRET sensors
  - many running fluorescence reporters in the lab
- Organoids, WNT signalling, developmental biology

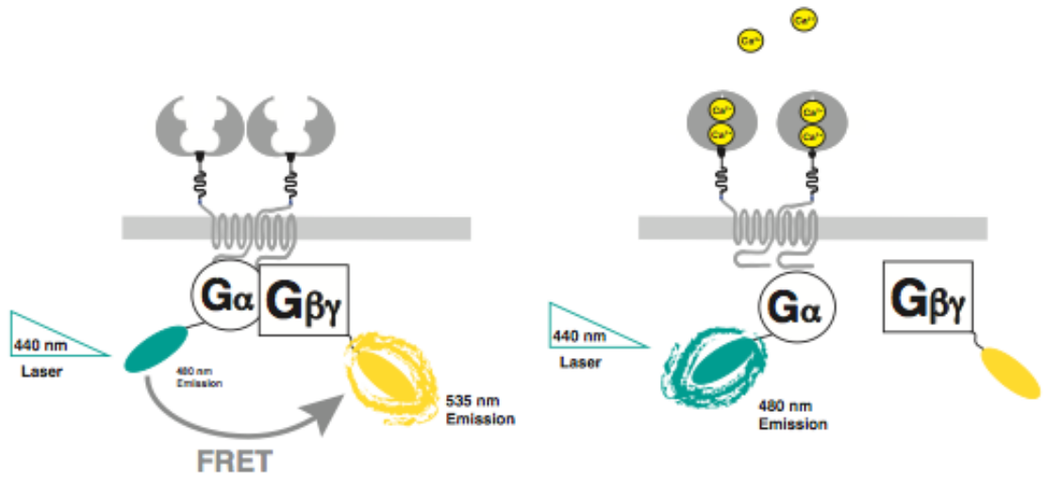
Our previous CASR research

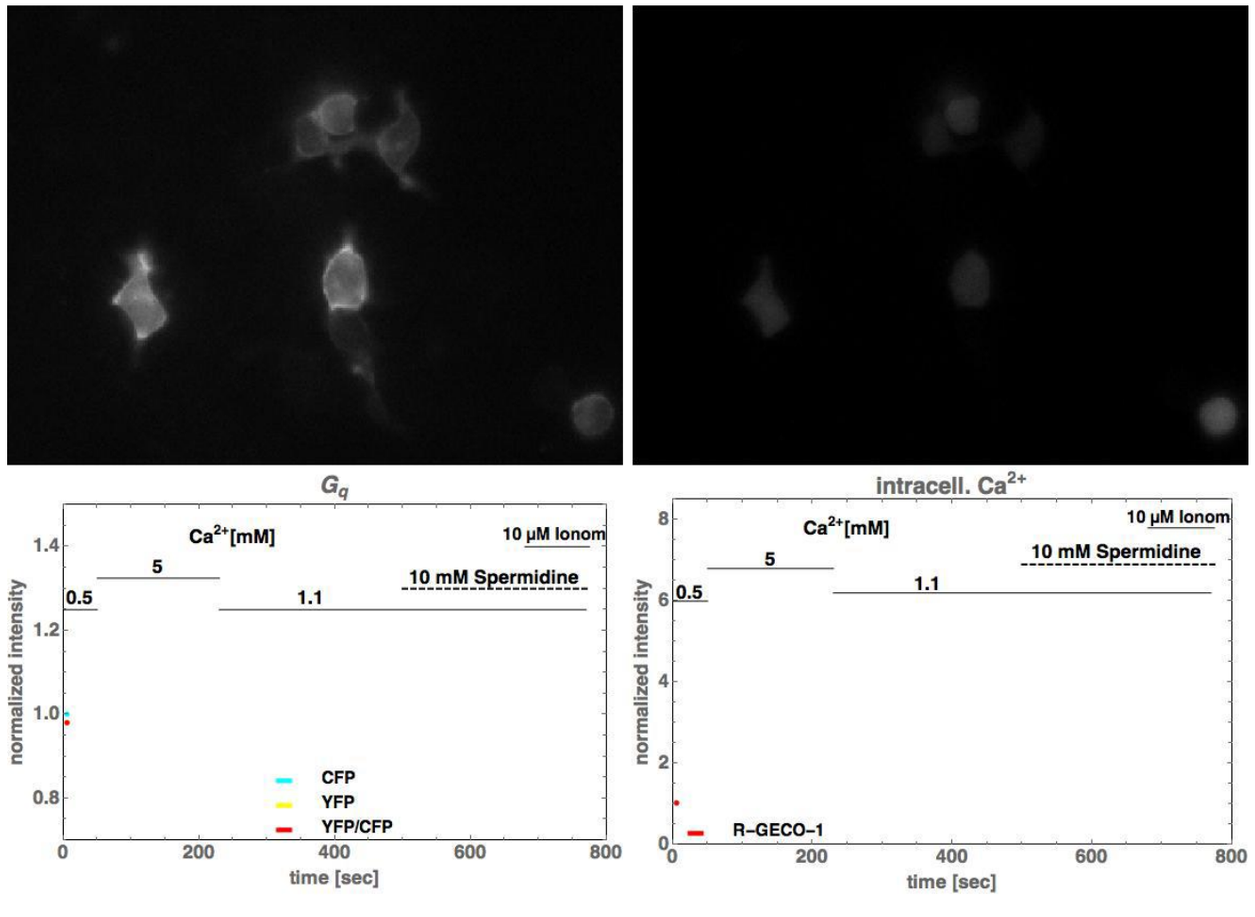
Susanne Roth

(now at Novonordisk, DK)



biophysical, GPCR conformation model and ligand bias, MWC based

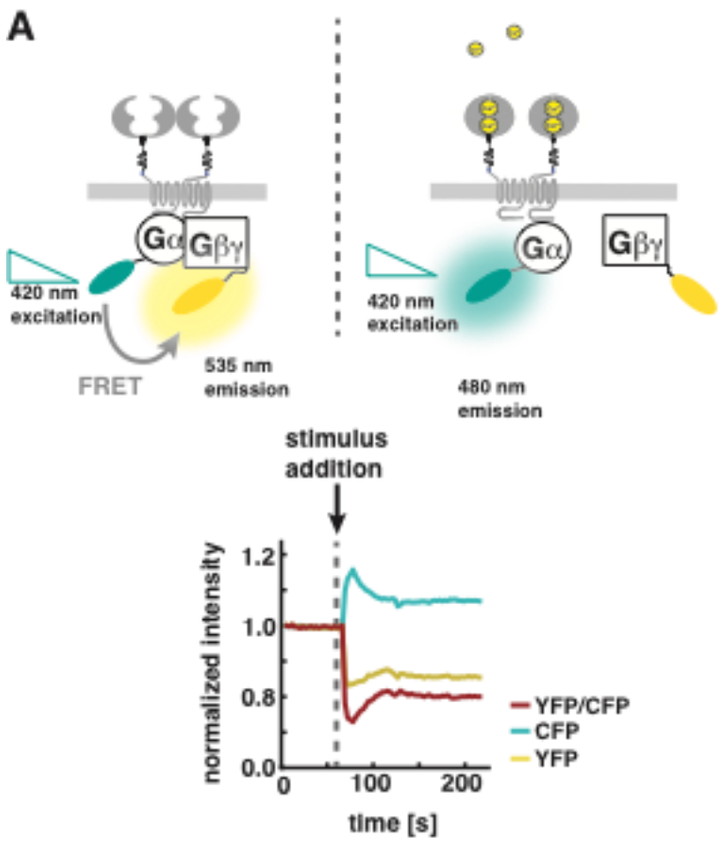


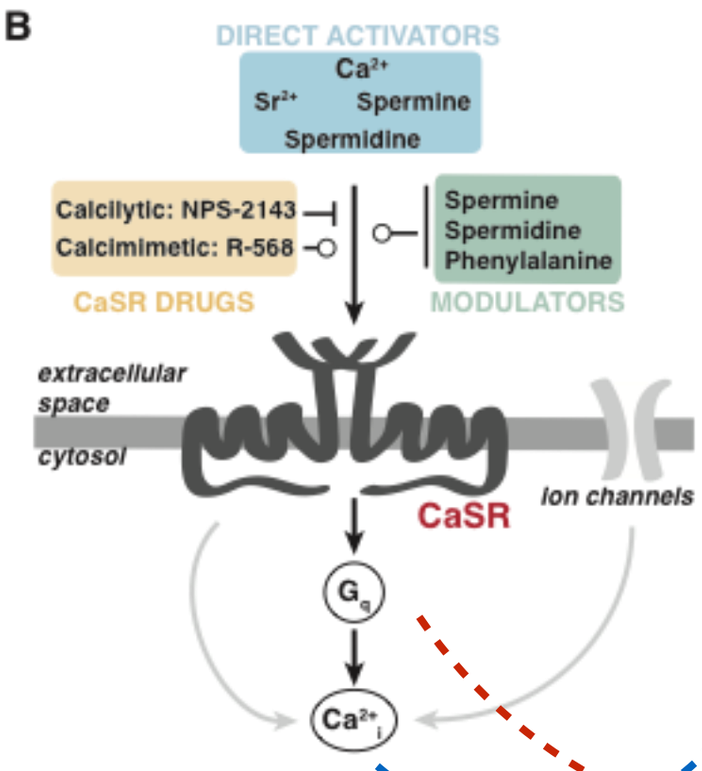


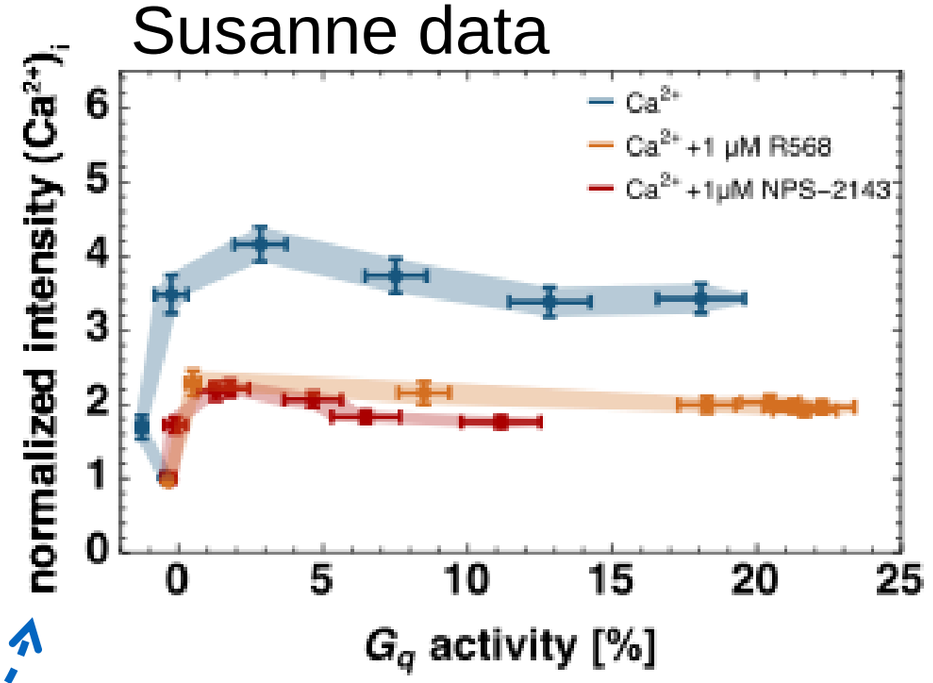
Gq FRET sensor and calcium sensor

Future CASR research

first was made by Susanne: multiplex signalling, network vs receptor bias



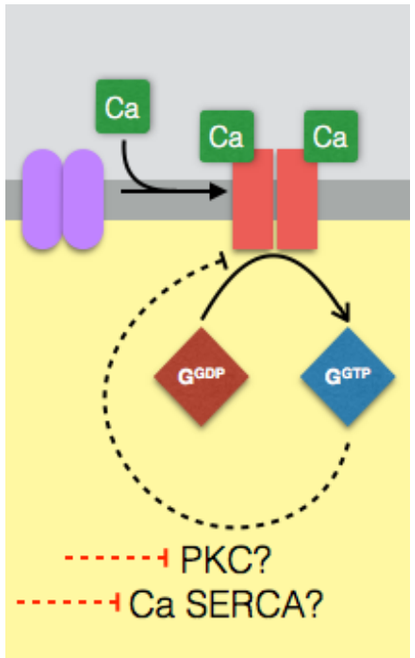




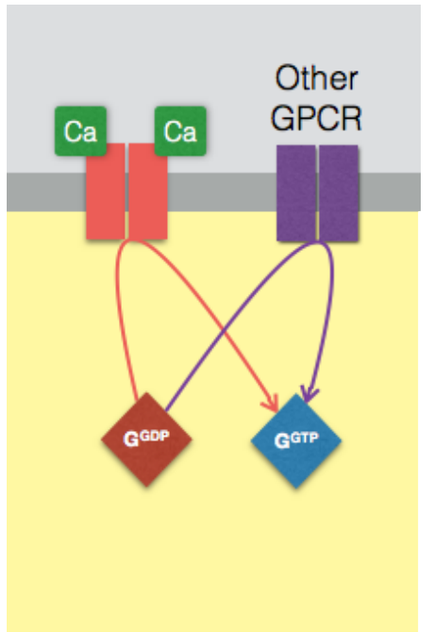
Diving deeper into the network,

using perturbations and multiple sensors

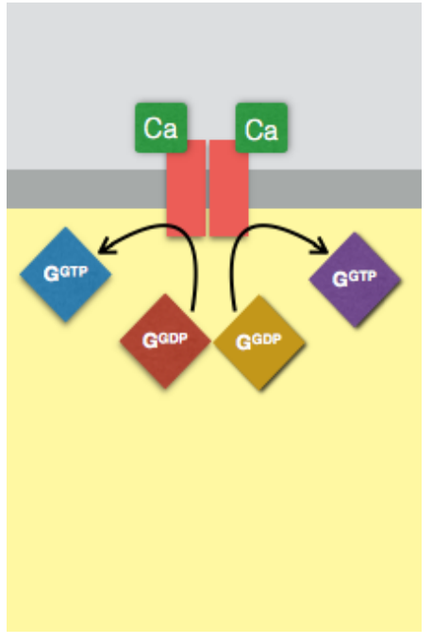
Intracellular control



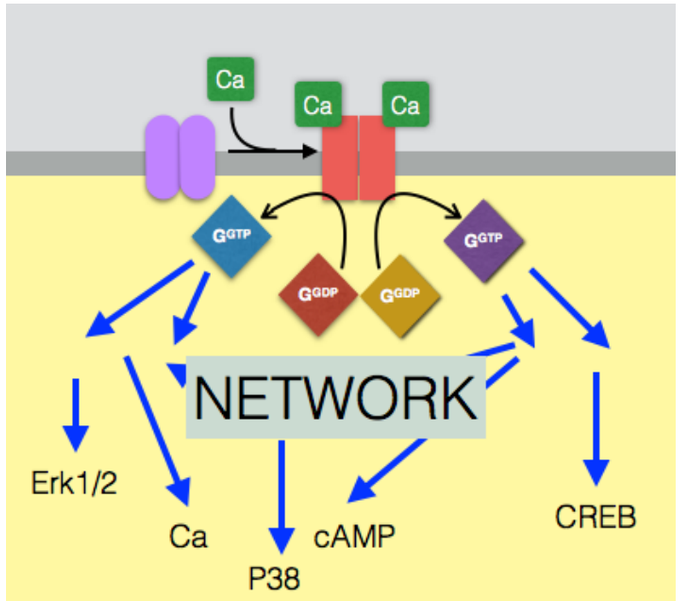
GPCR cross-talk



G-protein competition



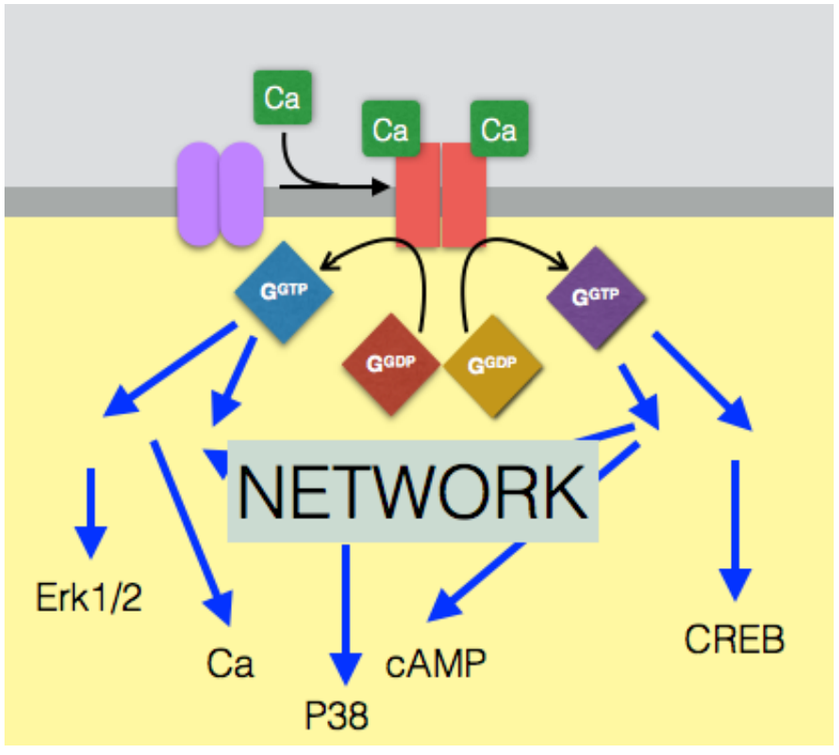
The downstream network



establish SOPs, establish G-protein FRET sensors, exchanging sensors, cell lines, discuss concepts (receptor bias, network bias,…), think more about dynamic phenomena (internalisation, G-protein competition), inside-out signalling, aiming for quantitative studies

Reaching an integrative understanding

of the role the CaSR in cell signalling and its cell-type dependence



We shall aim to make a biophysical/mathematical model of the receptor (Susanne started, unpublished). It is is based on conformation shift induced by ligand binding leading to altered activation of receptor binding proteins.

Then we need to go from receptor binding proteins to the cellular network. How to do this I am familiar with. But the question is: do we have the right and sufficient data and is a model what we really need? Perhaps we want a more coarse-grained network understanding, highlighting the role of particular mechanisms in network-bias and for cell-type differences.

We have only three years.