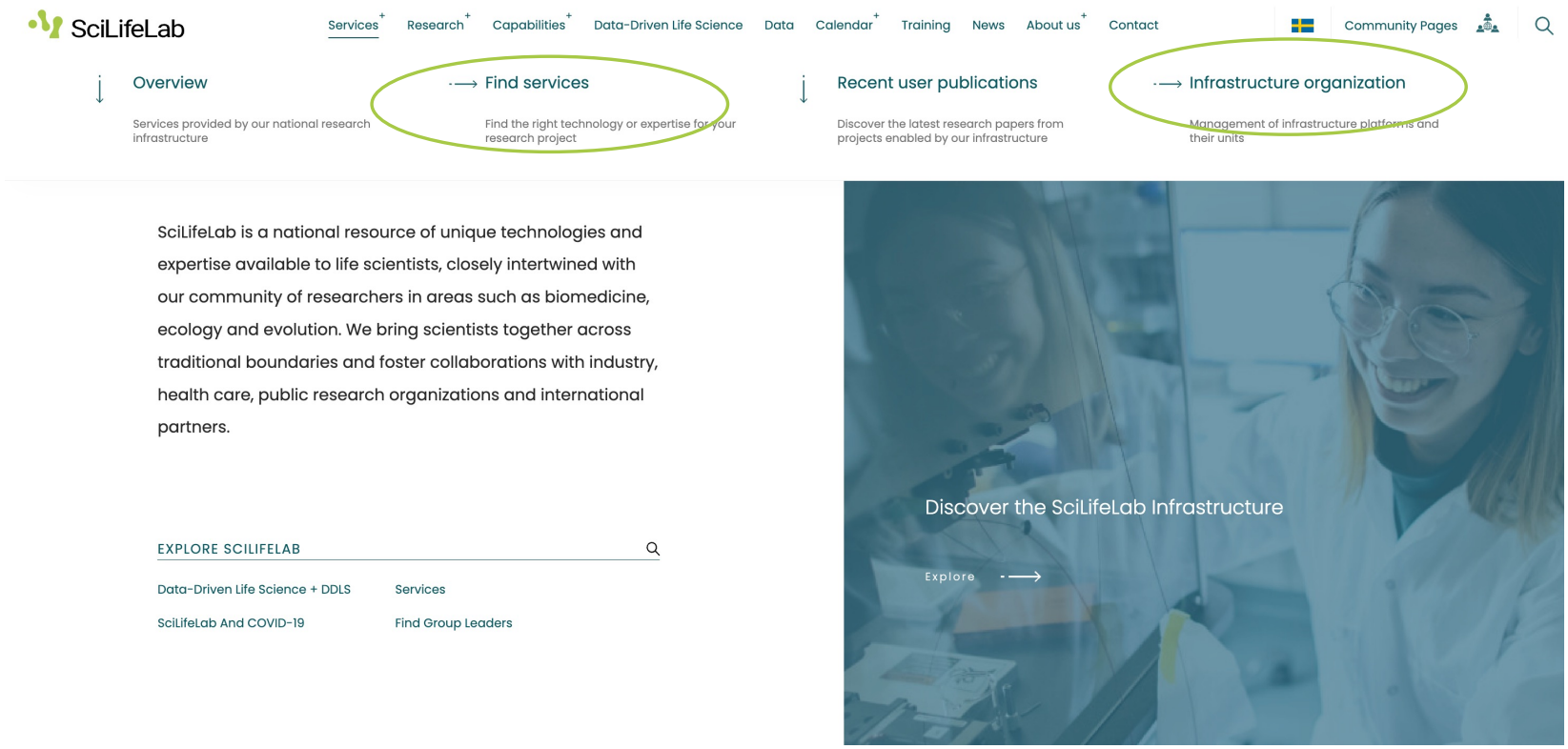
Cecilia Persson – coordinator for Integrated Structural Biology in Sweden
cecilia.persson@nmr.gu.se
Facility manager at the Swedish NMR Centre

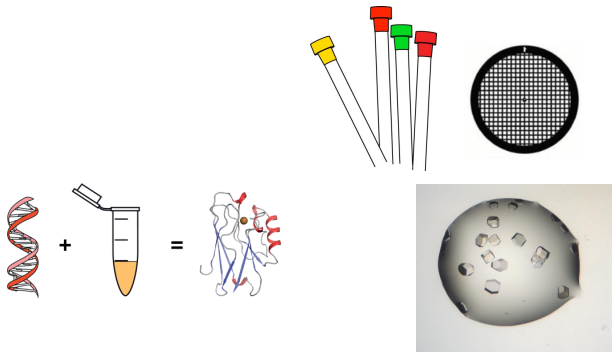
scilifelab.se



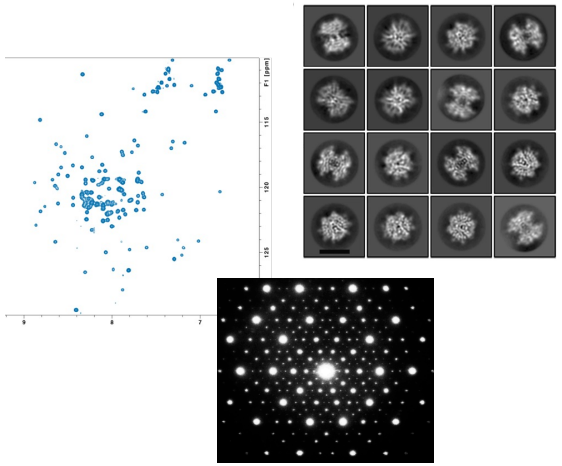
Integrated Structural Biology

Scientific questions answered at the atomic level - including dynamics from sub-nanoseconds to hours

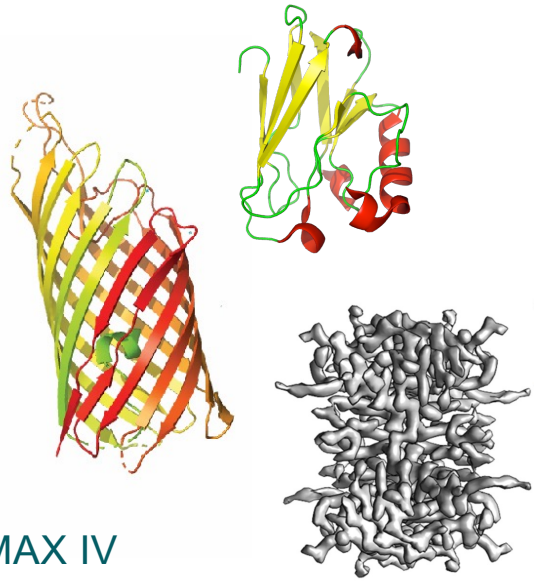
From gene to 3D structure



Protein production - PPS
Biophysical characterisation - ProLinC



Structural Proteomics
Swedish NMR centre
Cryo-EM

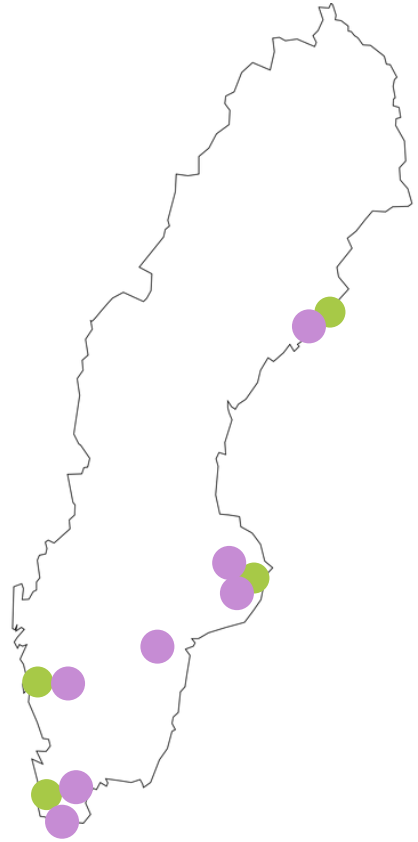


MAX IV
ESS

AlphaFold – collaboration with NBIS on how to verify computational result with experimental data

Integrated Strutural Biology platform

- Swedish NMR Centre @ UmU
- Swedish NMR Centre @ UoG
- Structural Proteomics, LU
- Cryo-EM, SU
- Cryo-EM, UmU
- Protein Production Sweden, PPS, VR-RFI
- ProLinC, LiU biophysical characterization, EU-infrastructure
- MAX IV, Lund
- ESS, Lund
- InfraLife, Stockholm, Lund



Access to infrastructures

Structural Proteomics – Simon Ekström

www.bioms.se
https://www.scilifelab.se/units/structural-proteomics/
Continuous project application

Swedish NMR Centre – Cecilia Persson

https://www.gu.se/en/nmr
https://www.scilifelab.se/units/swedish-nmr-centre/
Cecilia Persson
nmraccess.se
Continuous project application

Cryo-EM – Marta Carroni

www.scilifelab.se/facilities/cryo-em
www.emhub.cryoem.se
-BAG applications evaluated once a year
-RA applications evaluated continuously

ProLinC

dean.derbyshire@liu.se

PROTEIN PRODUCTION SWEDEN
National Research Infrastructure

www.pps.gu.se

NBIS – Claudio Mirabello

https://nbis.se/get-support

ess EUROPEAN SPALLATION SOURCE

MAX IV

Five universities
Six expression systems

PROTEIN PRODUCTION SWEDEN
National Research Infrastructure

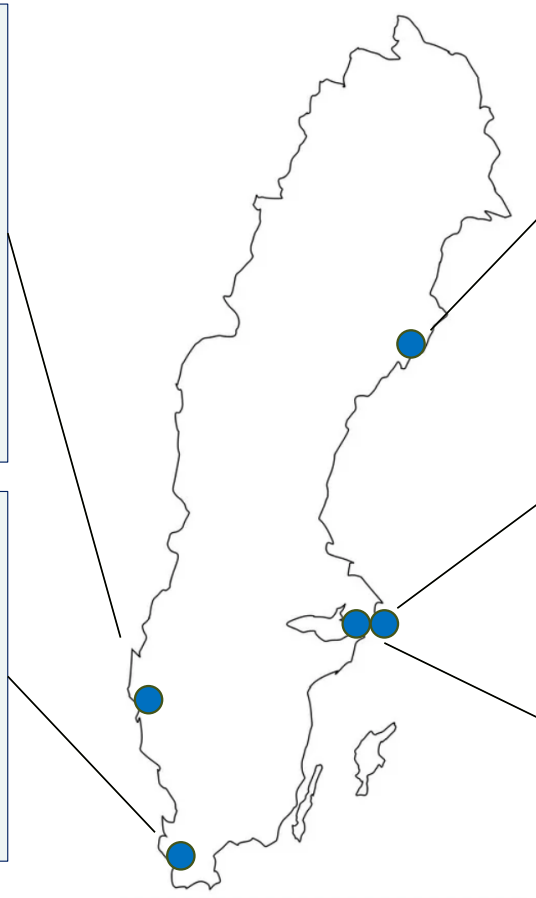
www.gu.se/pps

UNIVERSITY OF GOTHENBURG

Mammalian Protein Expression (MPE)
- HEK cell expression

Yeast Protein Production Platform
- *Pichia pastoris*

Swedish NMR Center (SNC)
- Cell free protein expression



LUNDS UNIVERSITET

Lund Protein Production Platform (LP3)
- Insect cells, BEVS
- Deuterized proteins for neutron scattering
- Molecular chaperones for MX

UMEÅ UNIVERSITET

Protein Expertise Platform (PEP)
- *E.coli*
- Plant cells

Karolinska Institutet

Protein Science Facility (PSF)
- *E.coli*

KTH VETENSKAP OCH KONST

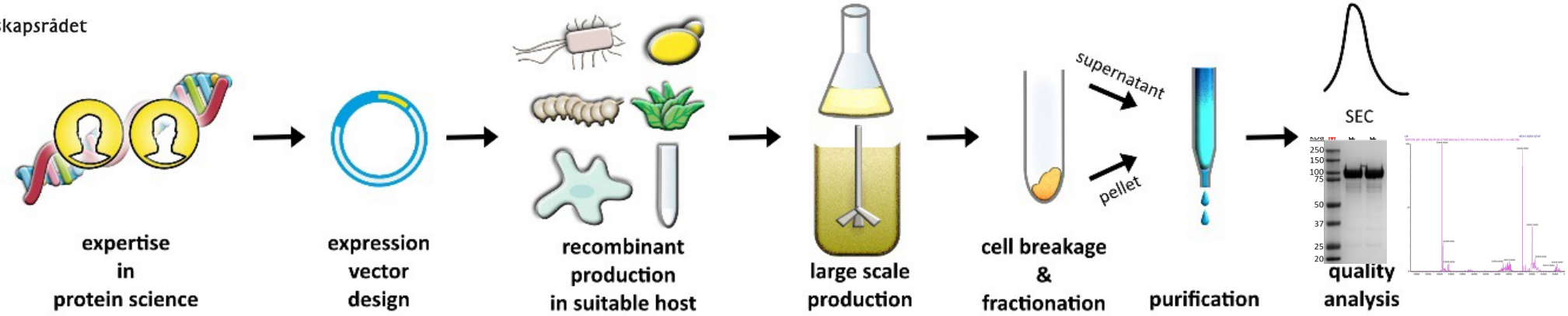
KTH Protein Factory
- CHO cells, secretory expression

Vetenskapsrådet

PROTEIN PRODUCTION SWEDEN
National Research Infrastructure

Vetenskapsrådet

PPS performs all steps within protein design, expression and purification, to generate proteins for all researchers in Sweden!



Expression system and protocol are decided in discussion with the research users.

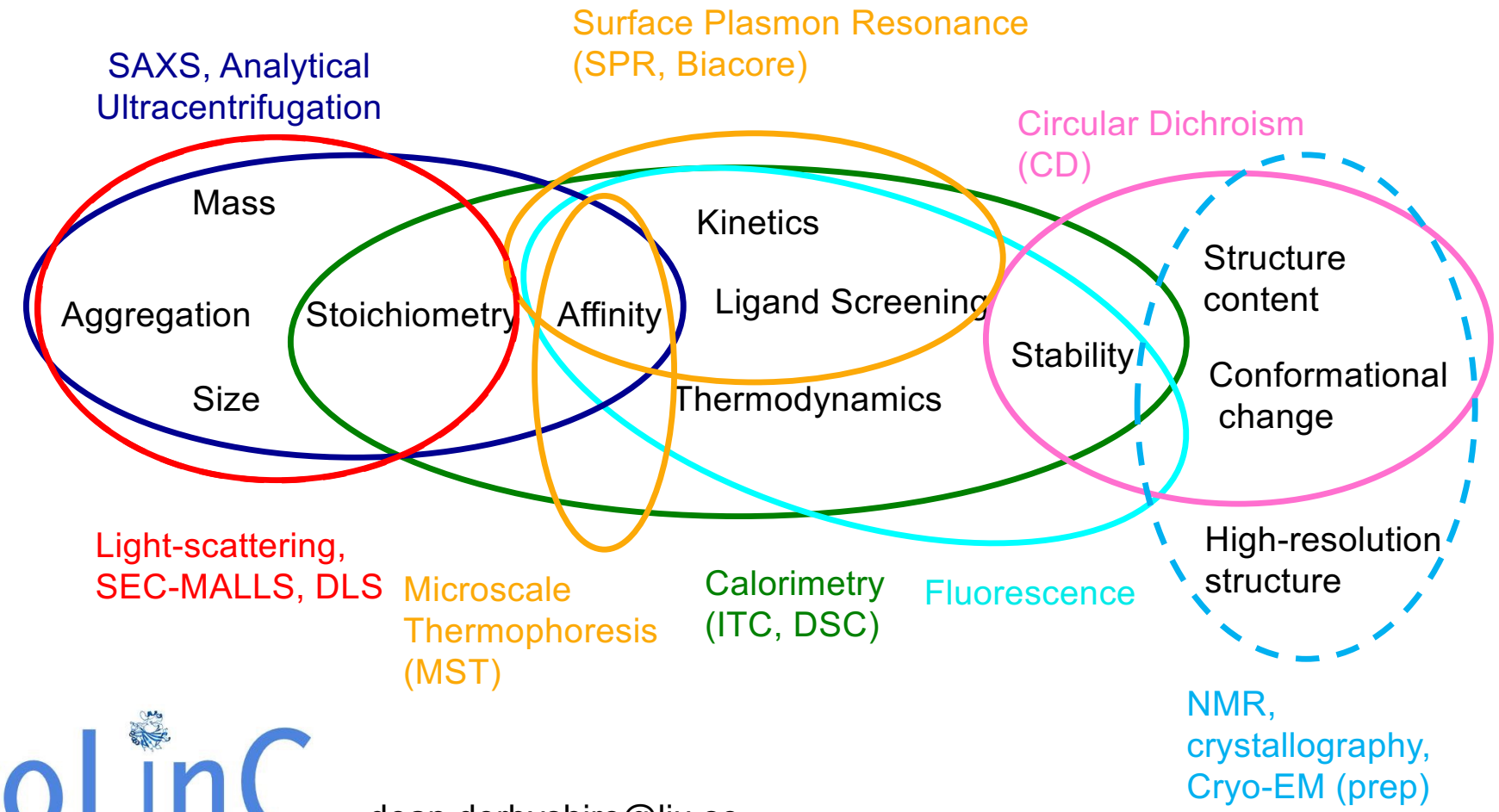
Fee-for-service of agreed work at subsidized cost.

- Bacteria, *E.coli*
- Yeast, *P.pastoris*
- BEVS/insect cells
- Mammalian cells
- Plant cells
- In vitro/cell free

Results:
Purified protein along with documentation, QC analysis is handed over to the user.

Always available for discussion!

Biophysical and structural characterisation in ProLinC



ProLinC

dean.derbyshire@liu.se

Swedish NMR Centre – Cecilia Persson

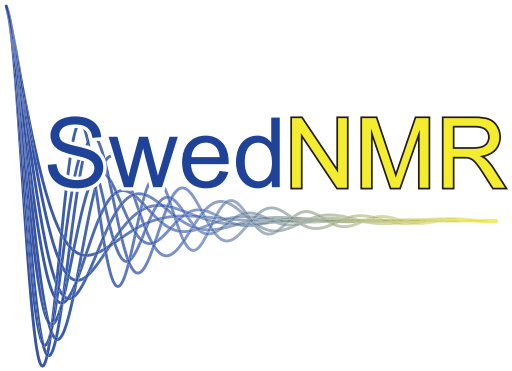
https://www.gu.se/en/nmr
https://www.scilifelab.se/units/swedish-nmr-centre/
www.nmraccess.se
Continuous project application

NMR in different areas at the Swedish NMR centre

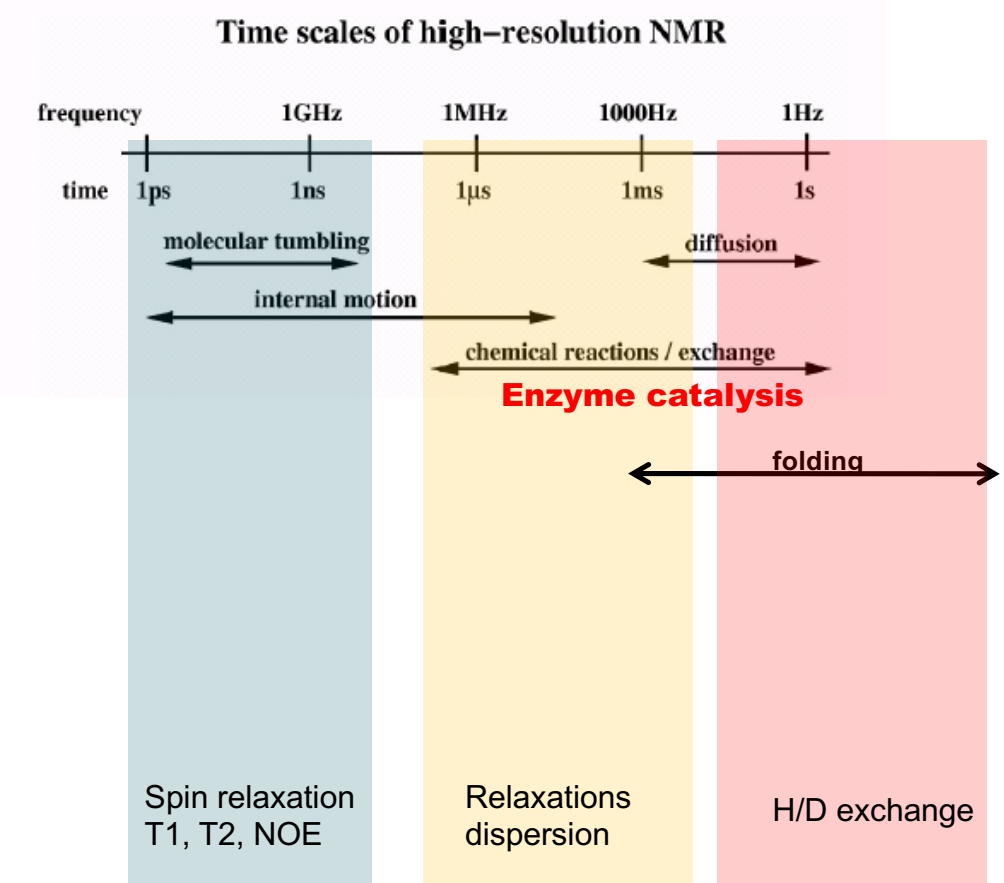
Structural Biology
Small molecules
FBS
Metabolomics
DNP

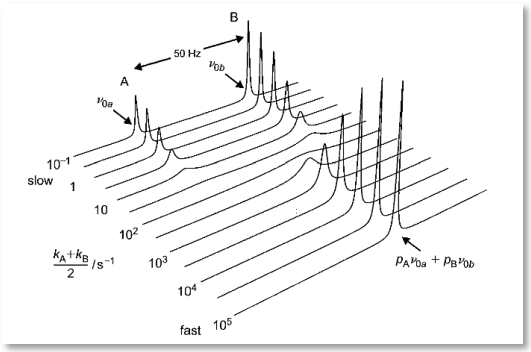
Structural Biology – different types of questions

- Structure determination
- Dynamics – requires backbone assignment and can then be used together with structure from another techniques
- Interaction – CSP (chemical shift dispersion) - requires backbone assignment and can then be used together with structure from another techniques
- Screening for binding – FBS, is done with unlabelled protein
- General assessment of folded state IDP/Folded/aggregated – Can be done with unlabelled sample as a first measurement



NMR – Not only structural determination also DYNAMICS!





Special experiments designed to be sensitive for internal motions

Solid state NMR
Magic Angle Spinning - MAS

Seeks to reintroduce averaging process through mechanical rotation:

7 mm – 7 kHz
3.2 mm – 24 kHz
0.7 mm – 111 kHz (almost 7 000 000 rpm)

Sample rotors (Varian)

Structural Proteomics – Simon Ekström

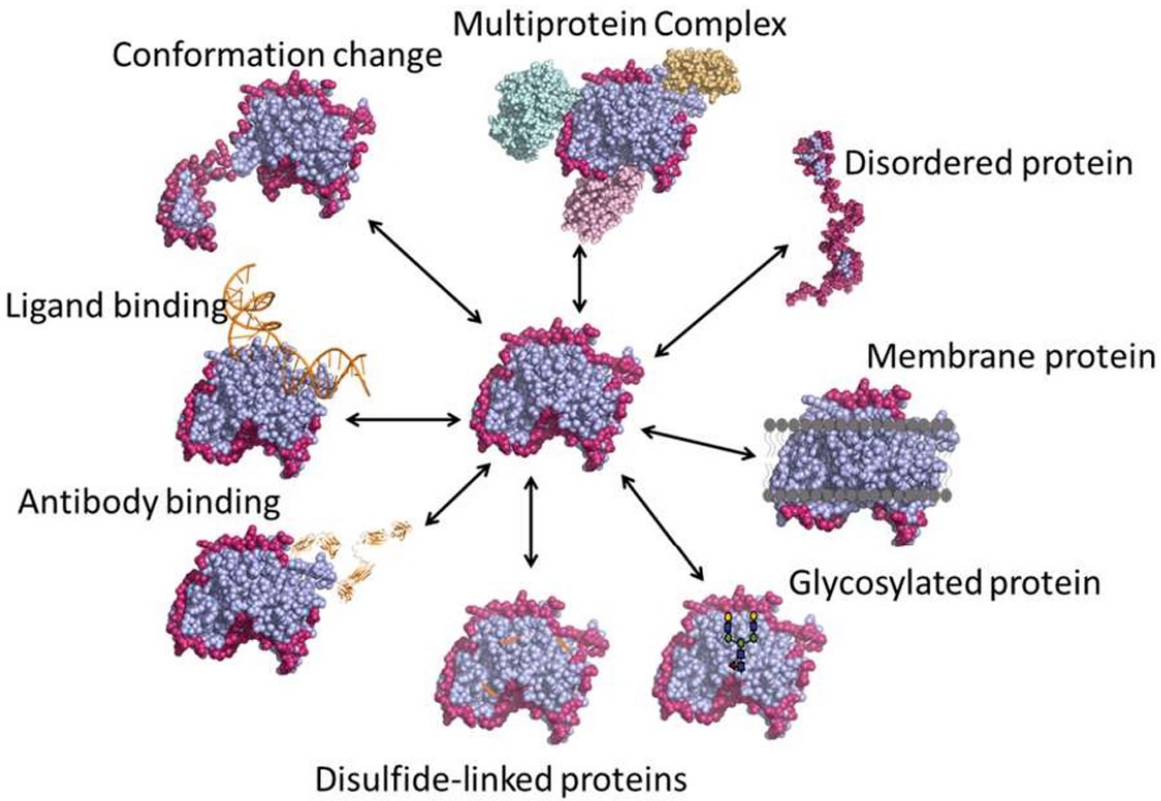
www.bioms.se

https://www.scilifelab.se/units/structural-proteomics/

Continuous project application

The **proteome** is the entire set of proteins produced or modified by an organism or system at a specific time point or state.

Proteomics is the large-scale experimental analysis of proteins and proteomes.



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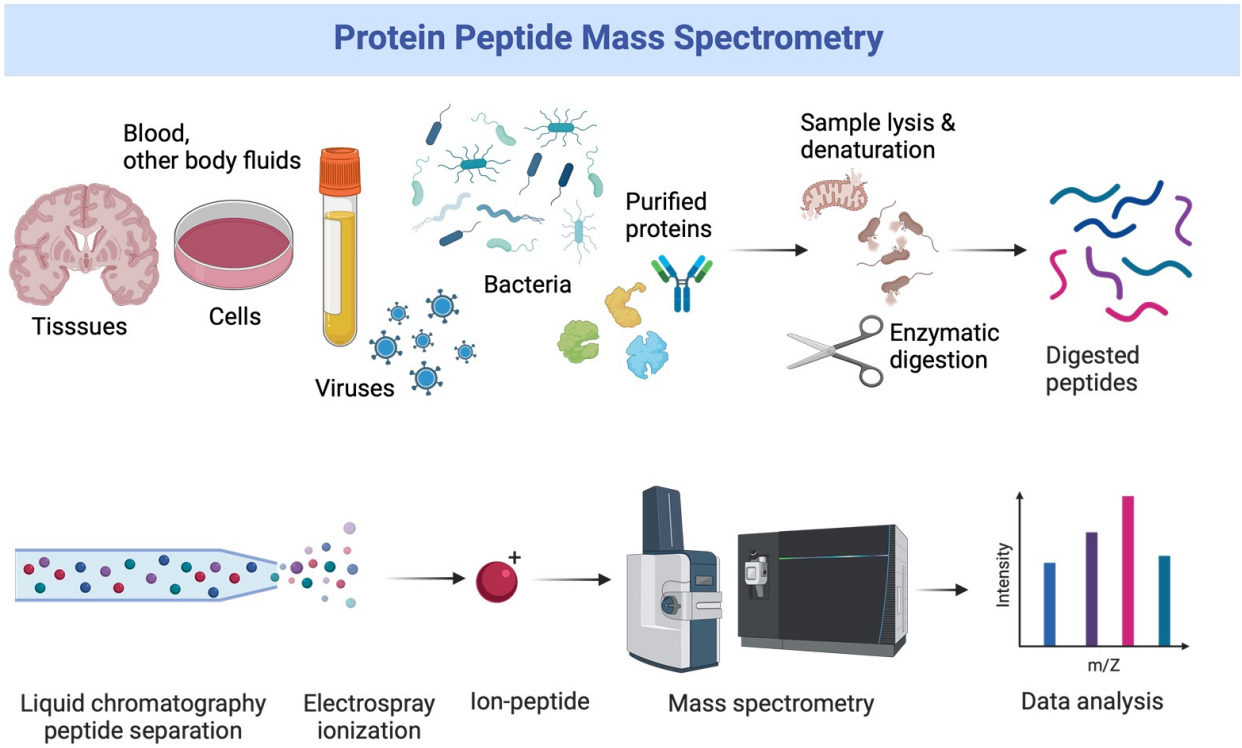
Continuous project application

MS-based proteomics approaches – workflow overview



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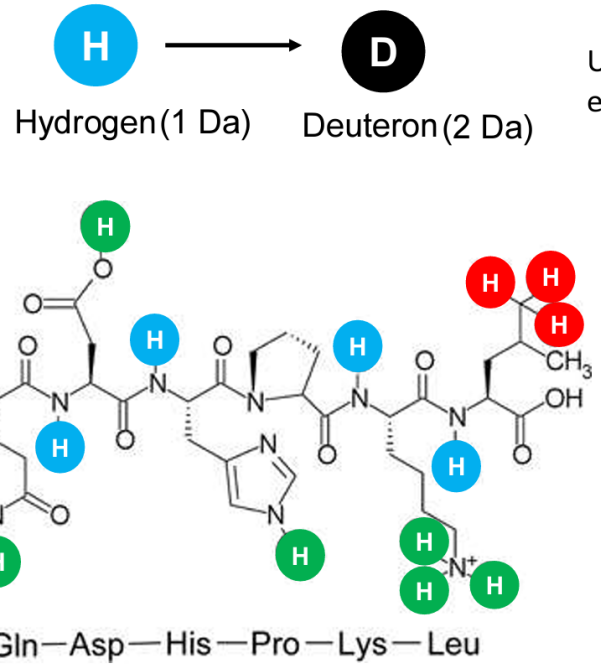
Continuous project application



Under physiological conditions the exchange rates for fully exposed amide hydrogens range from 10^1 to 10^3 s^{-1}.

H/D exchange rates

- **To fast** exchangeable hydrogens
- **Medium** backbone amide hydrogens
- Non-exchangeable hydrogens bonded to carbon

https://en.wikipedia.org/wiki/Hydrogen%E2%80%93deuterium_exchange

http://www.labspaces.net/blog/1225/Quick_and_Dirty_Intro_to_Mass_Spectrometry

Cryo-EM – Marta Carroni

www.scilifelab.se/facilities/cryo-em

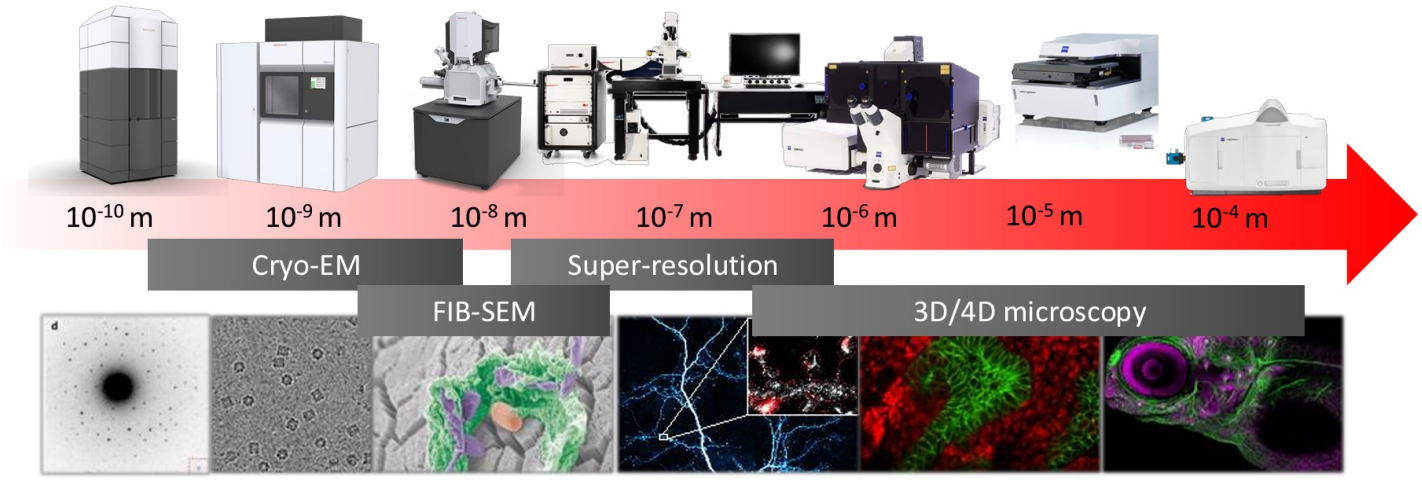
www.emhub.cryoem.se

-BAG applications evaluated once a year

-RA applications evaluated continuously

Imaging across scales – micro and nano

The cellular and molecular imaging (CMI) platform enables research that requires *imaging on various spatial scales*, from the atomistic to organismal levels, leveraging and integrating advanced *fluorescence* and *electron* microscopy methods not generally accessible to individual research groups or local facilities.



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www.scilifelab.se/facilities/cryo-em

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-BAG applications evaluated once a year

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Single particle analysis

Intergration of AlphaFold and Cryo-EM

nature communications

Article

https://doi.org/10.1038/s41467-024-52951-w

Unmasking AlphaFold to integrate experiments and predictions in multimeric complexes

Received: 13 May 2024

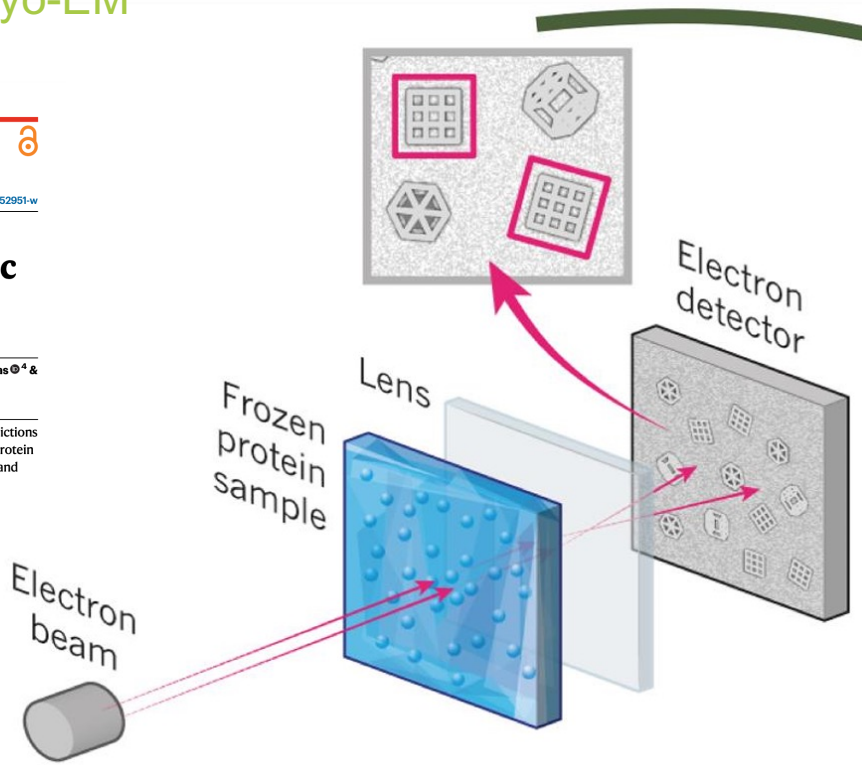
Accepted: 26 September 2024

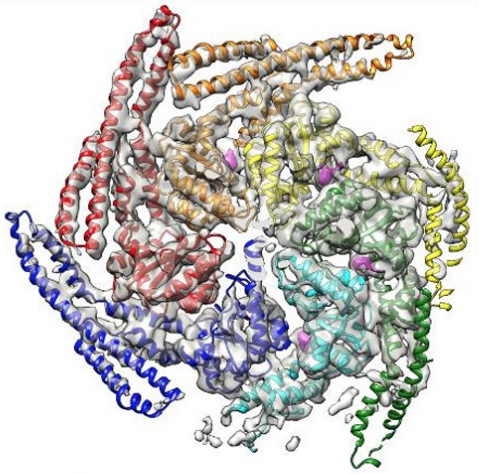
Published online: 09 October 2024

Check for updates

Claudio Mirabello[1], Björn Wallner[2], Björn Nystedt[3], Stavros Azinas[4] & Marta Carroni[4]

Since the release of AlphaFold, researchers have actively refined its predictions and attempted to integrate it into existing pipelines for determining protein structures. These efforts have introduced a number of functionalities and



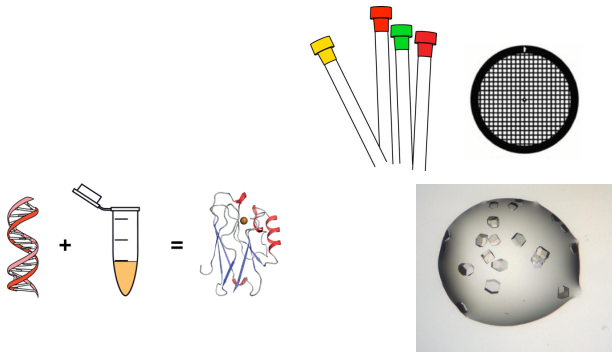


Structure

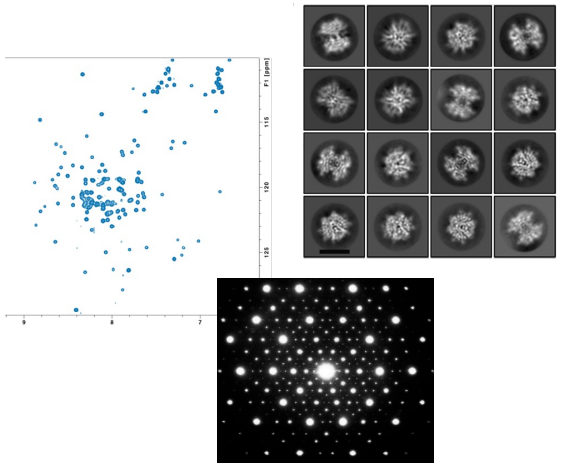
Integrated Structural Biology

Scientific questions answered at the atomic level - including dynamics from sub-nanoseconds to hours

From gene to 3D structure



Protein production - PPS
Biophysical characterisation - ProLinC



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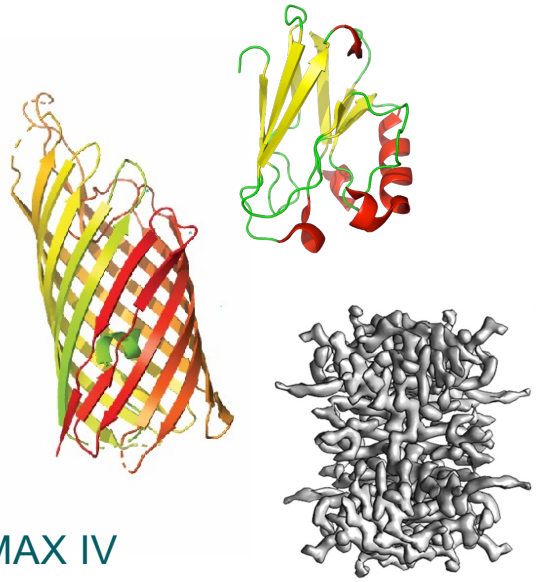

MAX IV
ESS

AlphaFold – collaboration with NBIS on how to verify computational result with experimental data

Integrated Structural Biology

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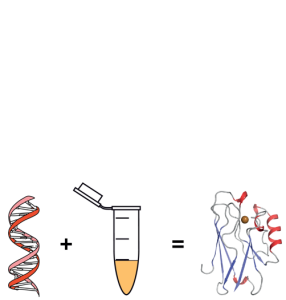
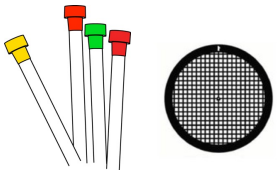
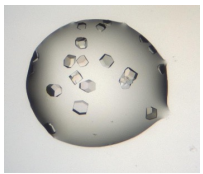






Protein production - PPS
Biophysical characterisation - ProLinC

Structural Proteomics

Insights at peptide levels
Very small amounts needed
Probing dynamics on the scale of a few seconds

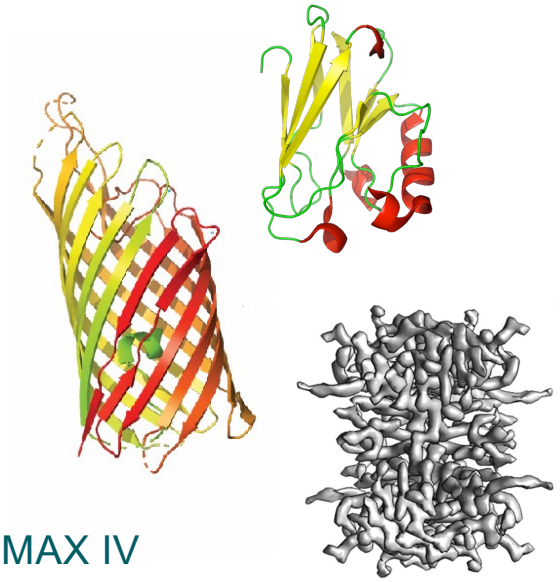
Swedish NMR centre

Atomic level information
Dynamics on ps to second timescale
Fairly large amounts of material
Isotope labeling

Cryo-EM

Small amounts of material needed
“Small” proteins not in reach (yet)
A few ångström resolution

Microscopy is the bridge to in situ structural biology



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