Moscow Institute of Physics and Technology
Research Center for
MOLECULAR MECHANISMS
of Aging and Age-Related Diseases

JOINT INSTITUTE
FOR NUCLEAR RESEARCH

1930
РОСБИОТЕХ
РОССИЙСКИЙ
БИОТЕХНОЛОГИЧЕСКИЙ
УНИВЕРСИТЕТ

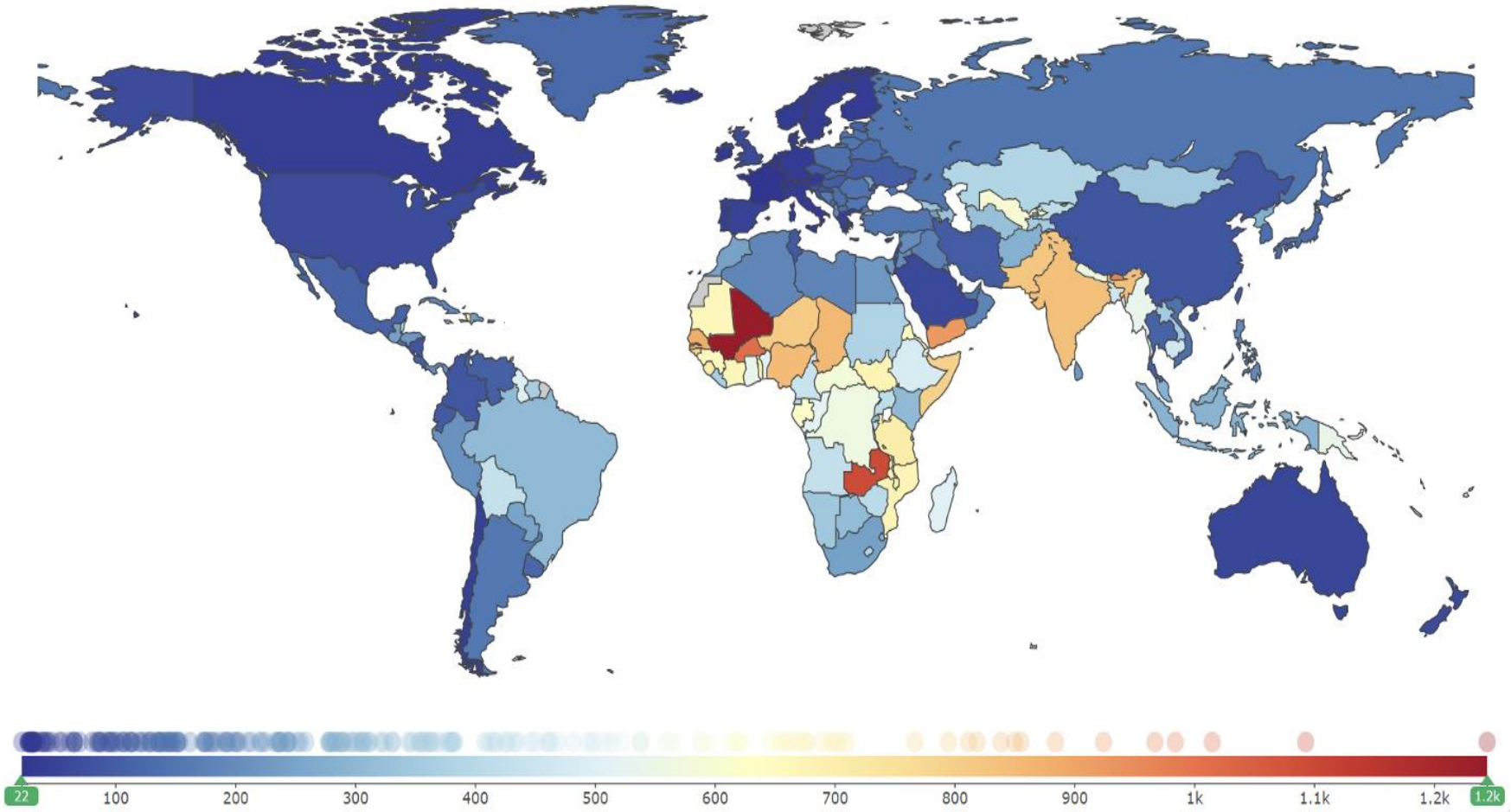
Efficient Iron Loading of Ferritin Produced in *E. coli*

ASSOCIATION OF YOUNG
SCIENTISTS AND SPECIALISTS OF JINR

30.10.2024

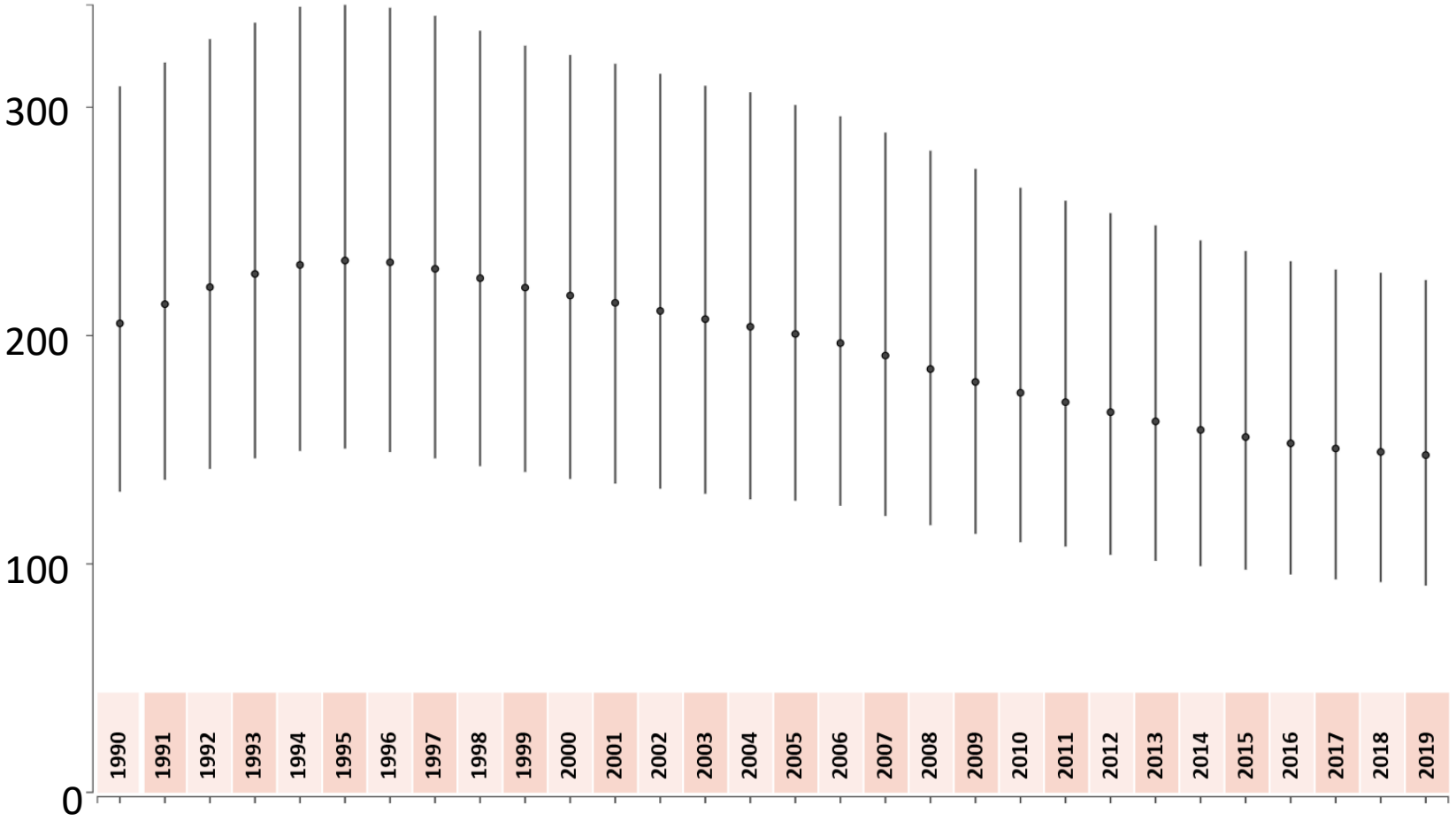
Dr. Alexey Vlasov

Iron deficiency worldwide



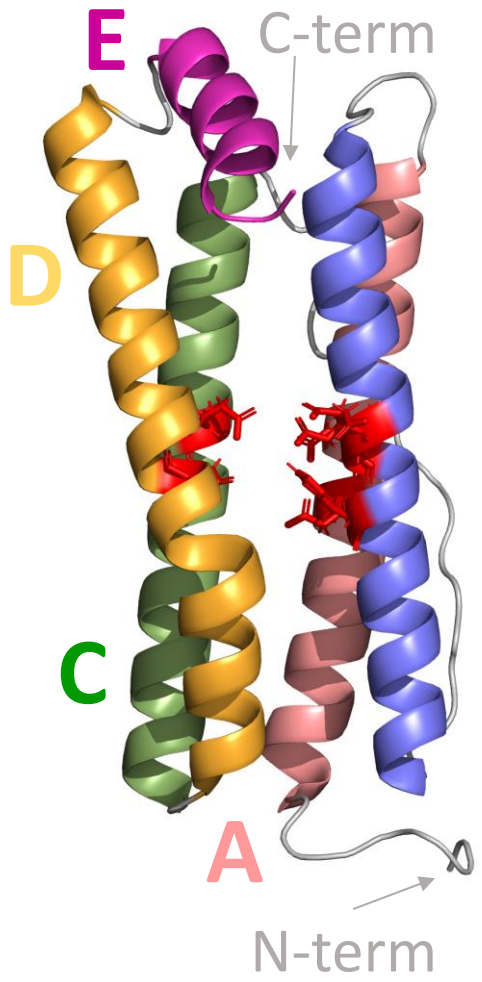
Iron deficiency in the population's diet for 2019. The sample is presented for all ages, for both sexes, the values of reported cases of iron deficiency in each country are normalized per 100,000 people. Data obtained using the Global Burden of Disease service (https://vizhub.healthdata.org/gbd-compare/).

Iron deficiency in Russia (1990 – 2019)

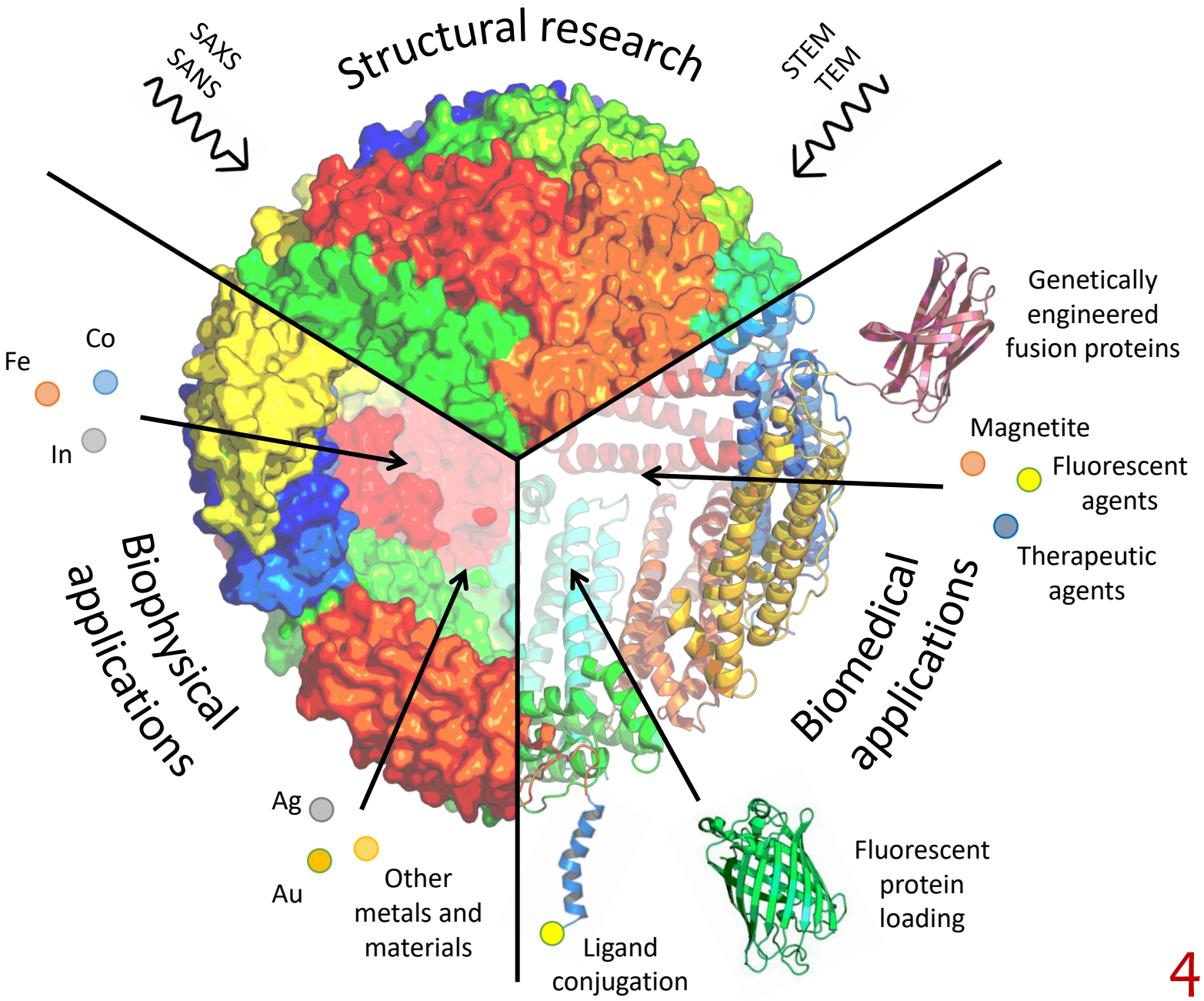


Iron deficiency in the diet of the population of the Russian Federation from 1990 to 2019. The sample is presented for all ages, for both sexes, the values of reported cases of iron deficiency in each country are normalized per 100,000 people. Data obtained using the Global Burden of Disease service (https://vizhub.healthdata.org/gbd-compare/).

Background



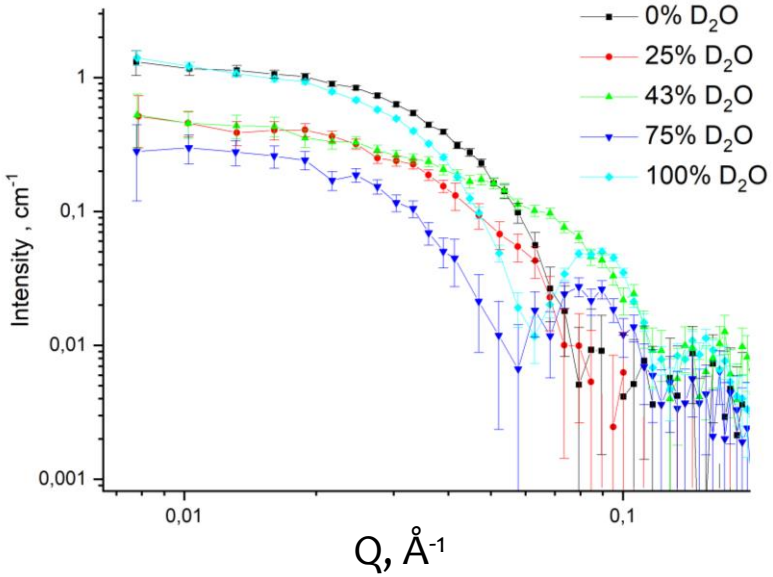
(Sudarev *et al.* 2023)

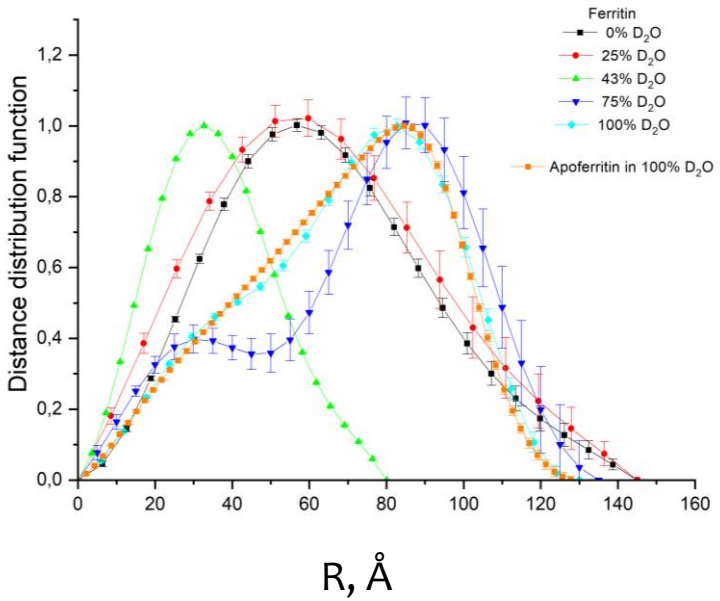


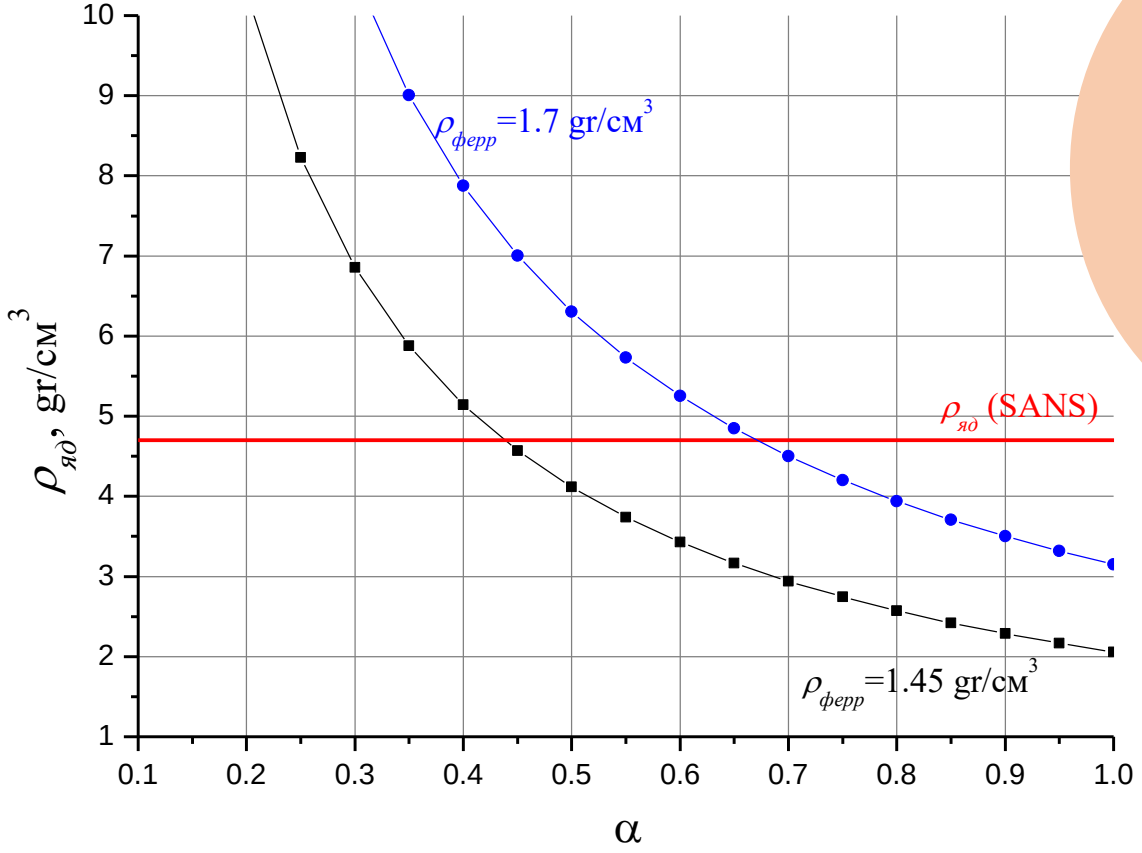
R&D landscape

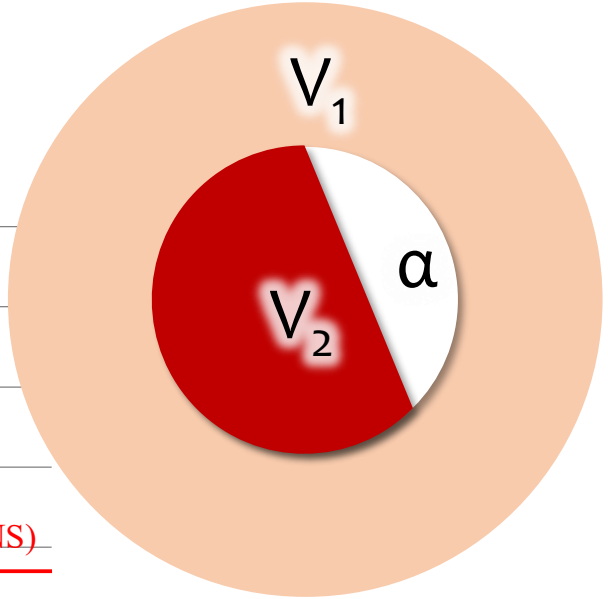
- …
- Ferritin iron loading
- Iron metabolism
- …

SANS studies of ferritin





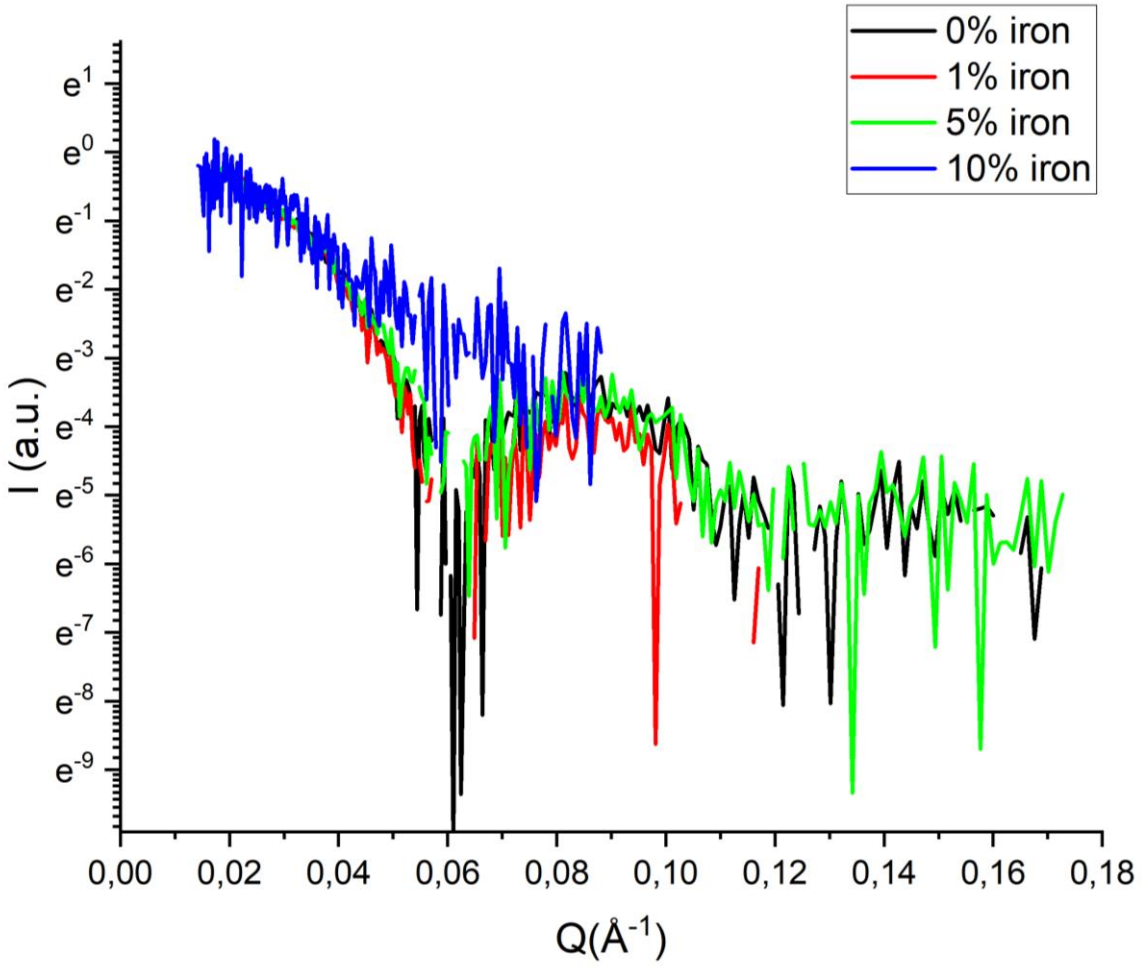


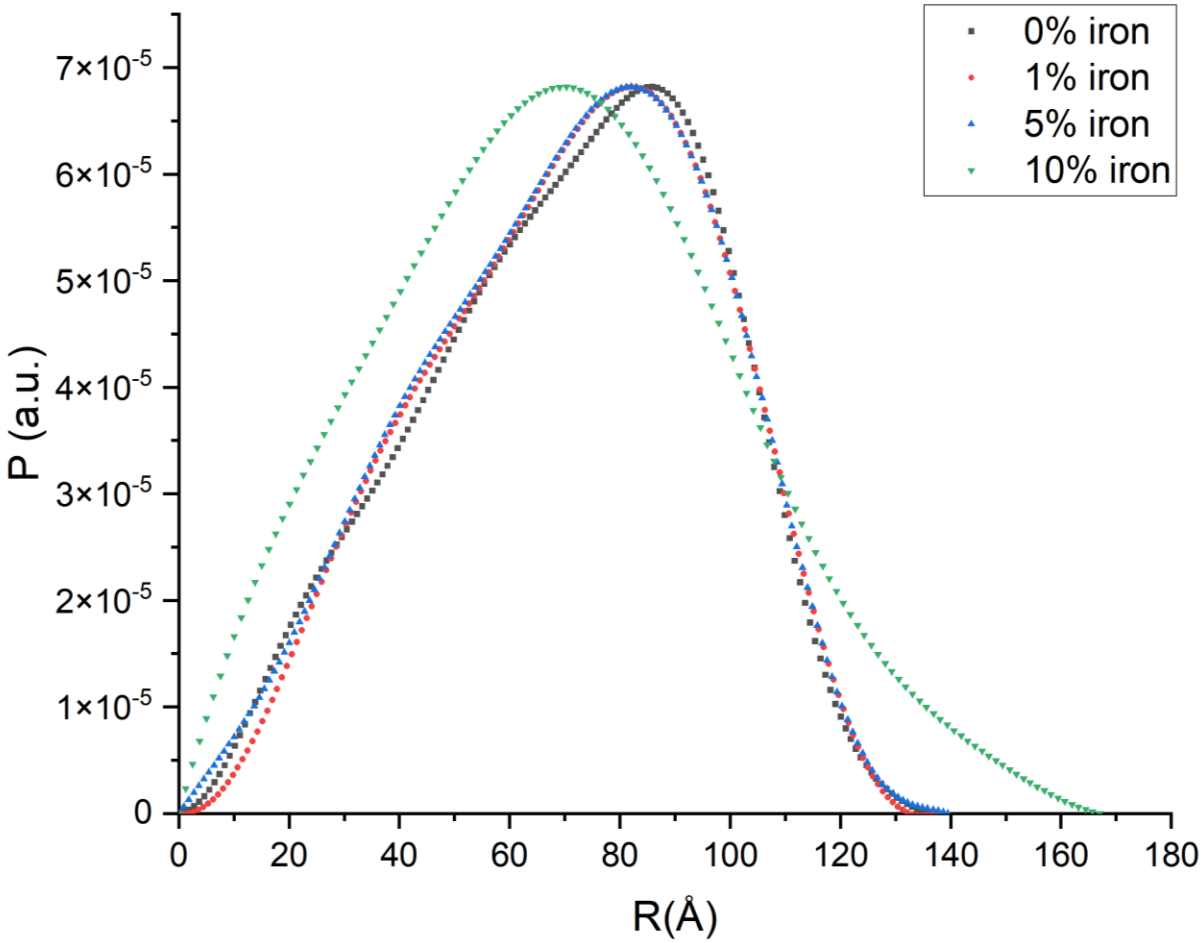


$[FeO(H)]_8[FeO(HPO_4)]$

$$\rho_{core} = \frac{1}{\alpha}\left(\rho_{ferr}\left(1+\frac{V_1}{V_2}\right)-\rho_{apof}\frac{V_1}{V_2}\right)=\rho_{ferr}\left(1+\frac{R_1^3}{R_2^3}\right)-\rho_{apof}\frac{R_1^3}{R_2^3}=\mathbf{4.7\ g/cm^3}$$

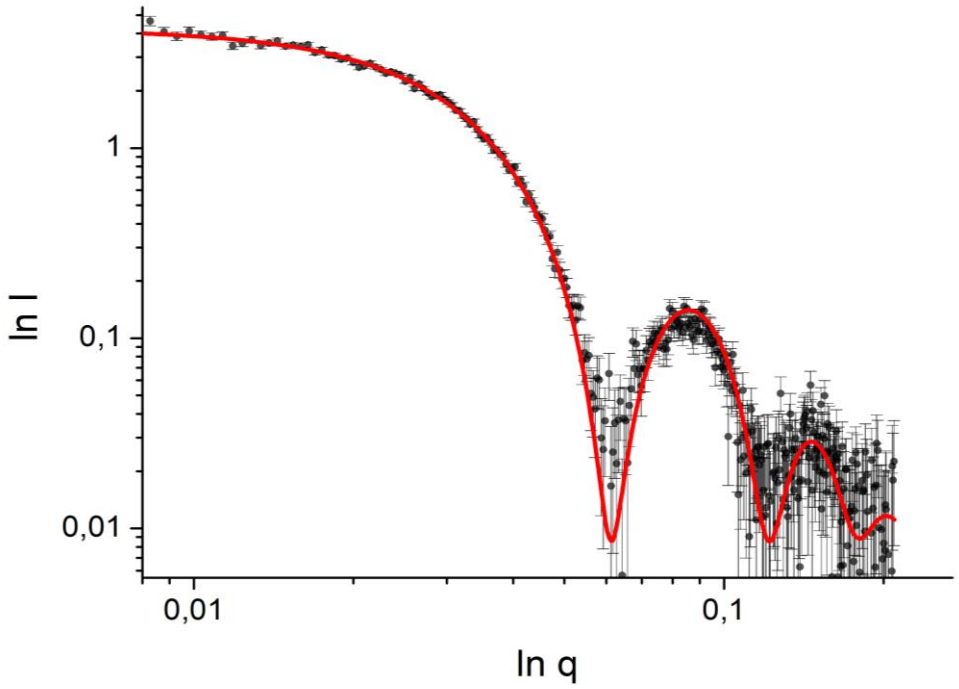
SAXS studies of ferritin

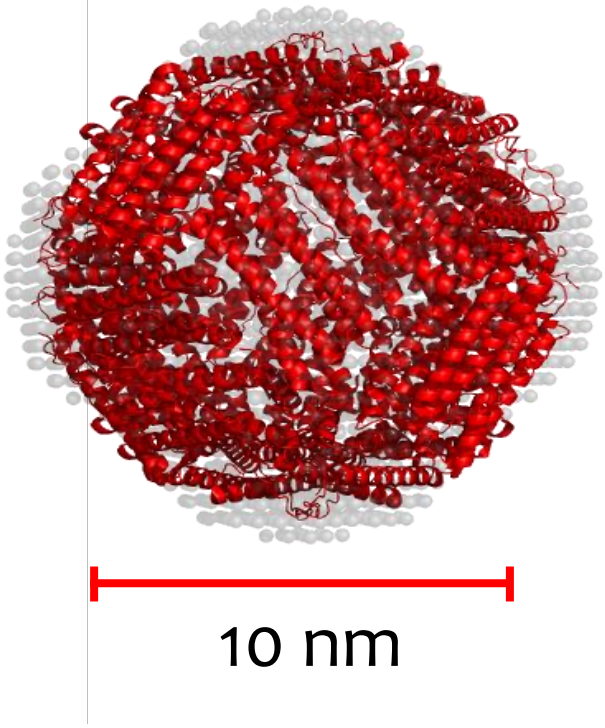


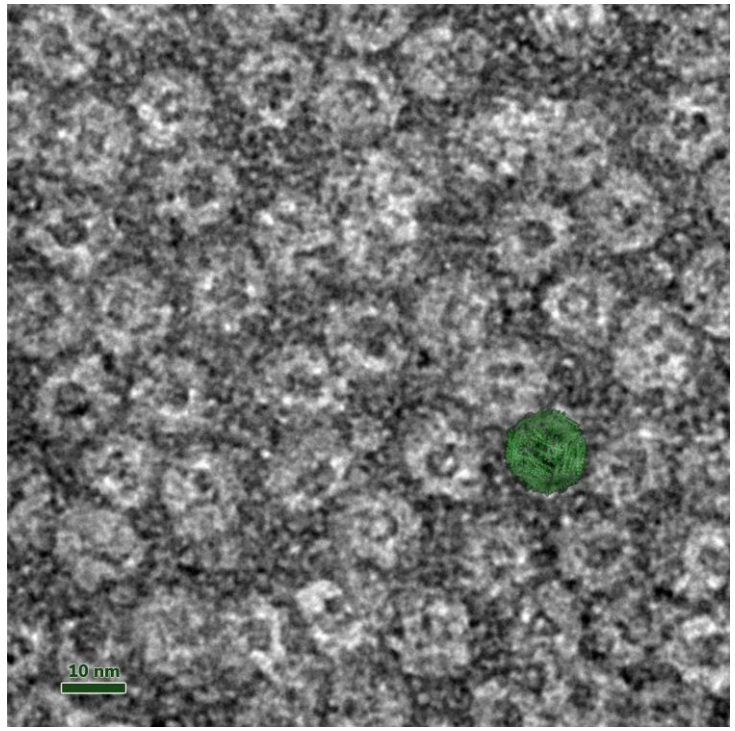


Checking the assembly

24 x His Ferritin

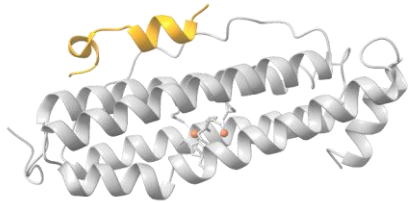






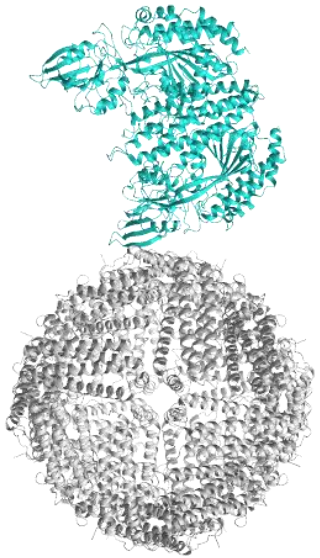
Iron metabolism

NCOA4

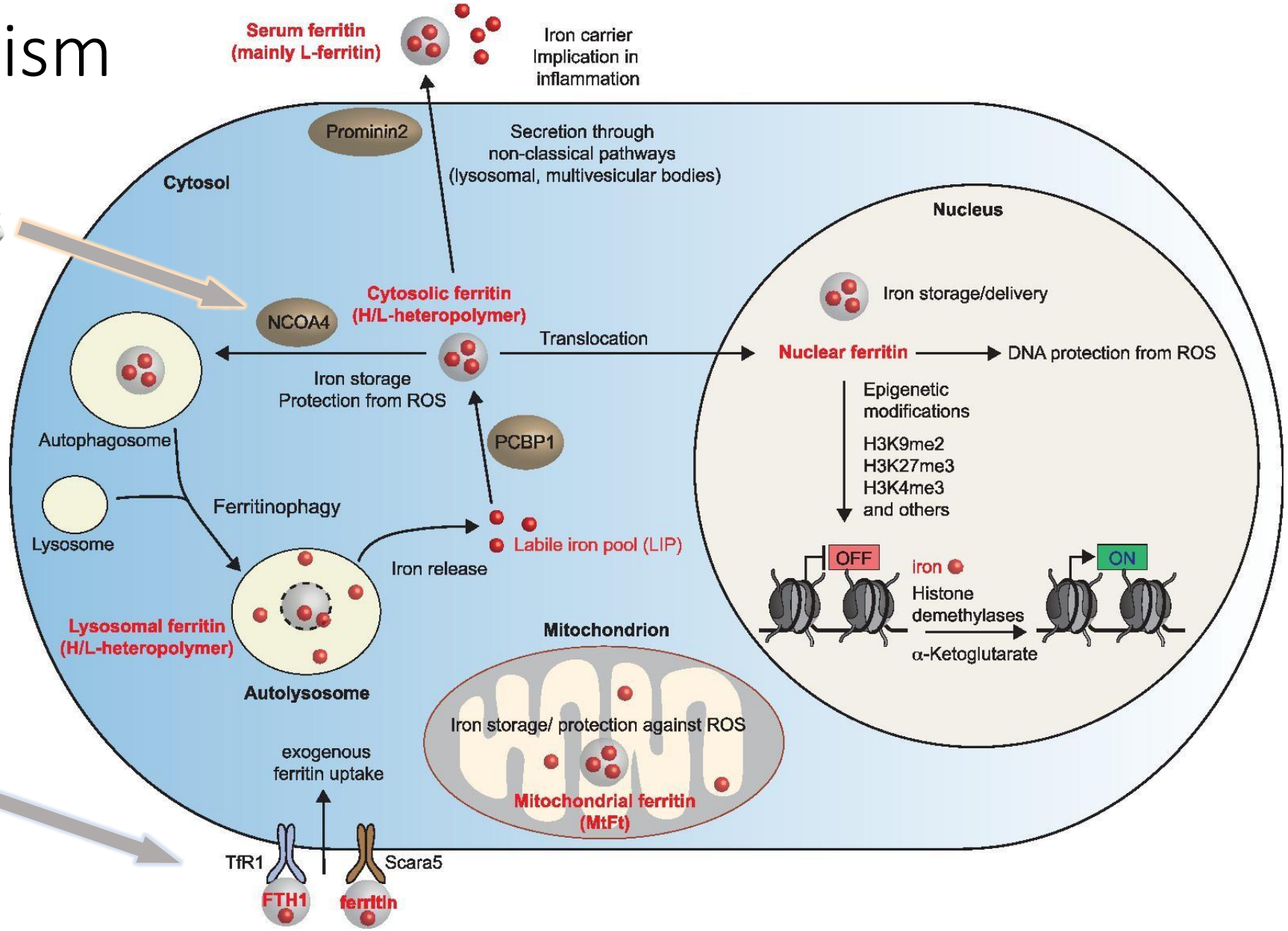


PDB ID: 8QU9

TFR1



PDB ID: 6GSR



Plays *et al.*, Metallomics, 2021

Ferritin-based dietary supplements

Bovine spleen ferritin

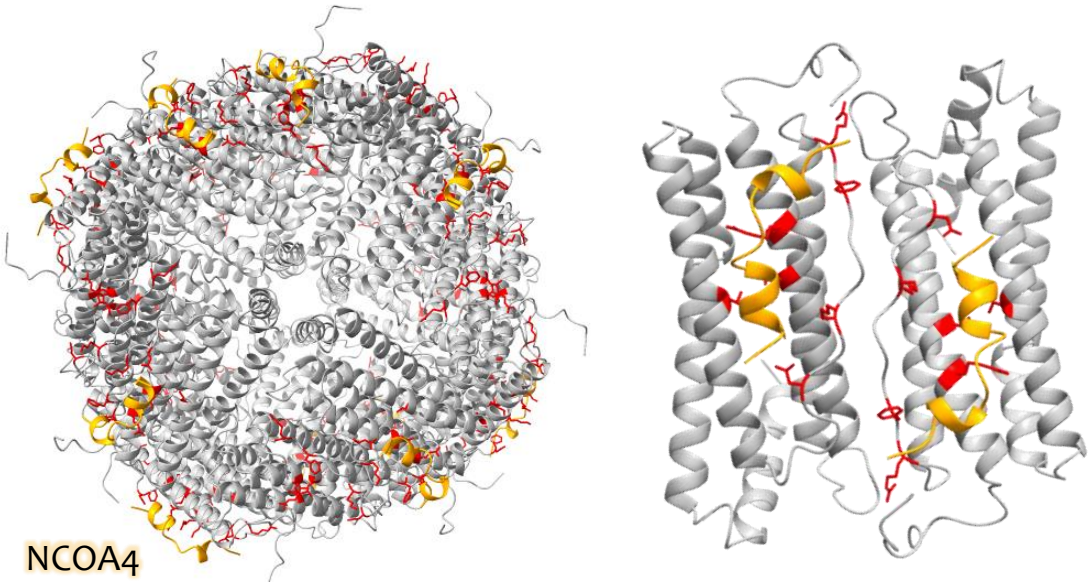
- One pill contains 30% of daily dose of iron
- Bioavailable iron

Pea seed ferritin

- One pill contains ~110% of daily dose of iron
- Bioavailable iron (?)
- Vegan

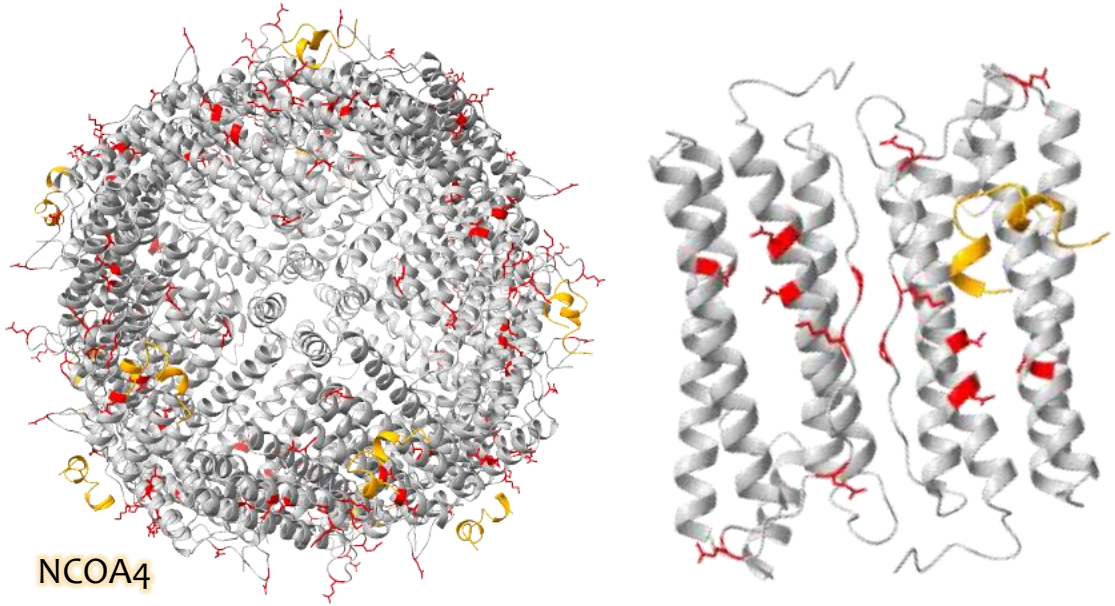
AF-predicted interactions with NCOA4

Bovine spleen ferritin




```
Score:889, Identities:169/183(92%), Positives:177/183(96%), Gaps:1/183(0%)

Query  1    MTTASTSQVRQNYHQDSEAAINRQINLELYASYVYLSMSYYFDRDDVALKNFAKYFLHQS  60
            MTTA  SQVRQNYHQDSEAAINRQINLEL+ASYVYLSMS+YFDRDDVALKNFAKYFLHQS
Sbjct  1    MTTAFPSQVRQNYHQDSEAAINRQINLELHASYVYLSMSFYFDRDDVALKNFAKYFLHQS  60

Query  61   HEEREHAEKLMKLQNQRGGRIFLQDIKKPDCDDWESGLNAMECALHLEKNVNQSLLELHK  120
            HEEREHAEKLMKLQNQRGGRIFLQDIKKPD DDWE+GL AMECALHLEKNVN+SLLELHK
Sbjct  61   HEEREHAEKLMKLQNQRGGRIFLQDIKKPDQDDWENGLKAMECALHLEKNVNESLLELHK  120

Query  121  LATDKNDPHLCDFIETHYLNEQVKAIKELGDHVTNLRKMGAPESGLAEYLFDKHTLGDSD  180
            LATDKNDPHLCDF+ETHYLNEQVKAIKELGDHVTNLR+MGAPESG+AEYLFDKHTLG+ D
Sbjct  121  LATDKNDPHLCDFLETHYLNEQVKAIKELGDHVTNLRRMGAPESGMAEYLFDKHTLGECD  180

Query  181  NES  183
              ES
Sbjct  181  -ES  182
```

Pea seed ferritin

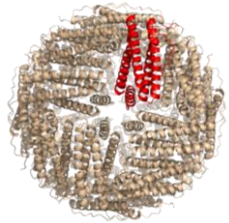


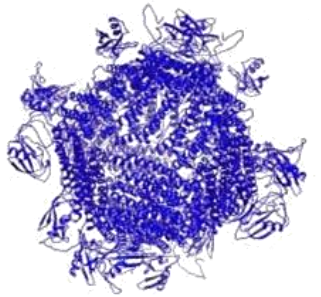

```
Score:151 bits(381), Expect:1e-50,
Method:Compositional matrix adjust.,
Identities:87/175(50%), Positives:110/175(62%), Gaps:7/175(4%)

Query  6    TSQVRQNYHQDSEAAINRQINLELYASYVYLSMSYYFDRDDVALKNFAKYFLHQSHEERE  65
             S  RQN+  + E+ IN QIN+E  ASYVY S+  YFDRD+VALK FAK+F   S E RE
Sbjct  76   VSLARQNFADECESVINEQINVEYNASYVYHSLFAYFDRDNVALKGFAKFFKESSEEHRE  135

Query  66   HAEKLMKLQNQRGGRIFLQDIK--KPDCDDWESG--LNAMECALHLEKNVNQSLLELHKL  121
            HAEKLMK QN RGGR+ L  IK    + +  E G  L AME AL LEK  N+ LL +H +
Sbjct  136  HAEKLMKYQNTRGGRVVLHPIKDVPSEFEHVEKGDALYAMELALSLEKLTNEKLLNVHSV  195

Query  122  ATDKNDPHLCDFIETHYLNEQVKAIKELGDHVTNLRKMGAPESGLAEYLFDKHTL  176
            A   ND  +  FIE  YL EQV+AIK++ ++V  LR++G    G   + FD+  L
Sbjct  196  AERNNDLEMTHFIEGEYLAEQVEAIKKISEYVAQLRRVG---KGHGVWHFDQRLL  247
```

Conclusions

- Ferritin might be potentially used as a dietary supplement against iron deficiency and anemia
- SAS & EM can be efficiently used for checking the ferritin iron loading and assembly
- Bovine spleen ferritin has clear and proven molecular mechanisms of entrance in the cells and autophagosomes
- Pea seed ferritin mechanisms of entrance in the cells and autophagosomes are unclear. Do they really exist?

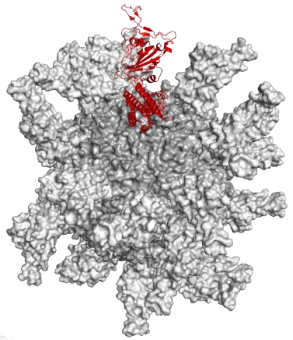
Collaboration invitation

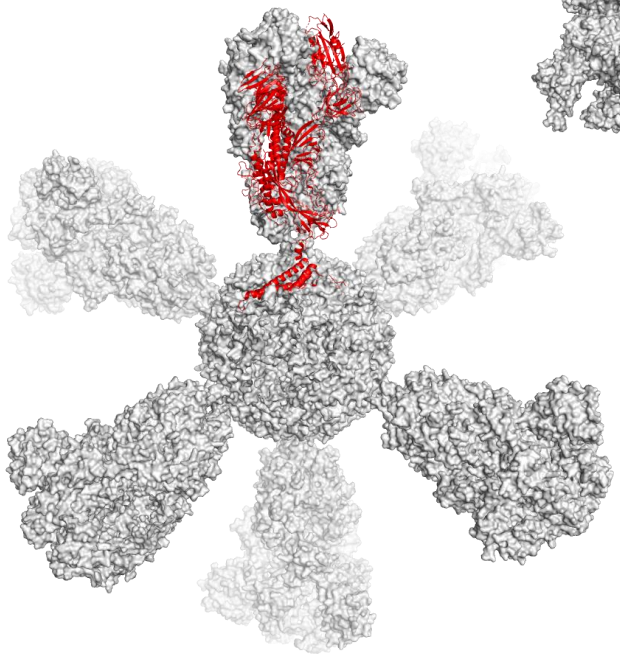




- Elemental particles
- Small molecules
- Nanoparticles (d < 8 nm)
- …

- Ferritin
- Ferritin-(fusion protein)
- …





Contacts

Dr. Alexey Vlasov

E-mail: vavplanet@gmail.com

Tel: +7 (926) 043-41-43

Acknowledgements

- Ms. Margarita Gette
- Ms. Oksana Tilinova
- Mr. Vsevolod Sudarev
- Mr. Nikolay Bondarev
- Dr. Yury Ryzhykau
- Dr. Sergei Bazhenov
- Dr. Ilya Manukhov
- Dr. Alexander Kuklin

JOINT INSTITUTE FOR NUCLEAR RESEARCH

FLNP

Funding

Ministry of Science and Higher Education of the Russian Federation, project FSMF-2023-0010; “Integrated structural biology and genetics for the production of protein preparations and biologically active substances as new food and non-food products.”.

MIPT MOSCOW INSTITUTE OF PHYSICS AND TECHNOLOGY

Moscow Institute of Physics and Technology
Research Center for
MOLECULAR MECHANISMS
of Aging and Age-Related Diseases

1930 РОСБИОТЕХ
РОССИЙСКИЙ БИОТЕХНОЛОГИЧЕСКИЙ УНИВЕРСИТЕТ

Thank you for attention