

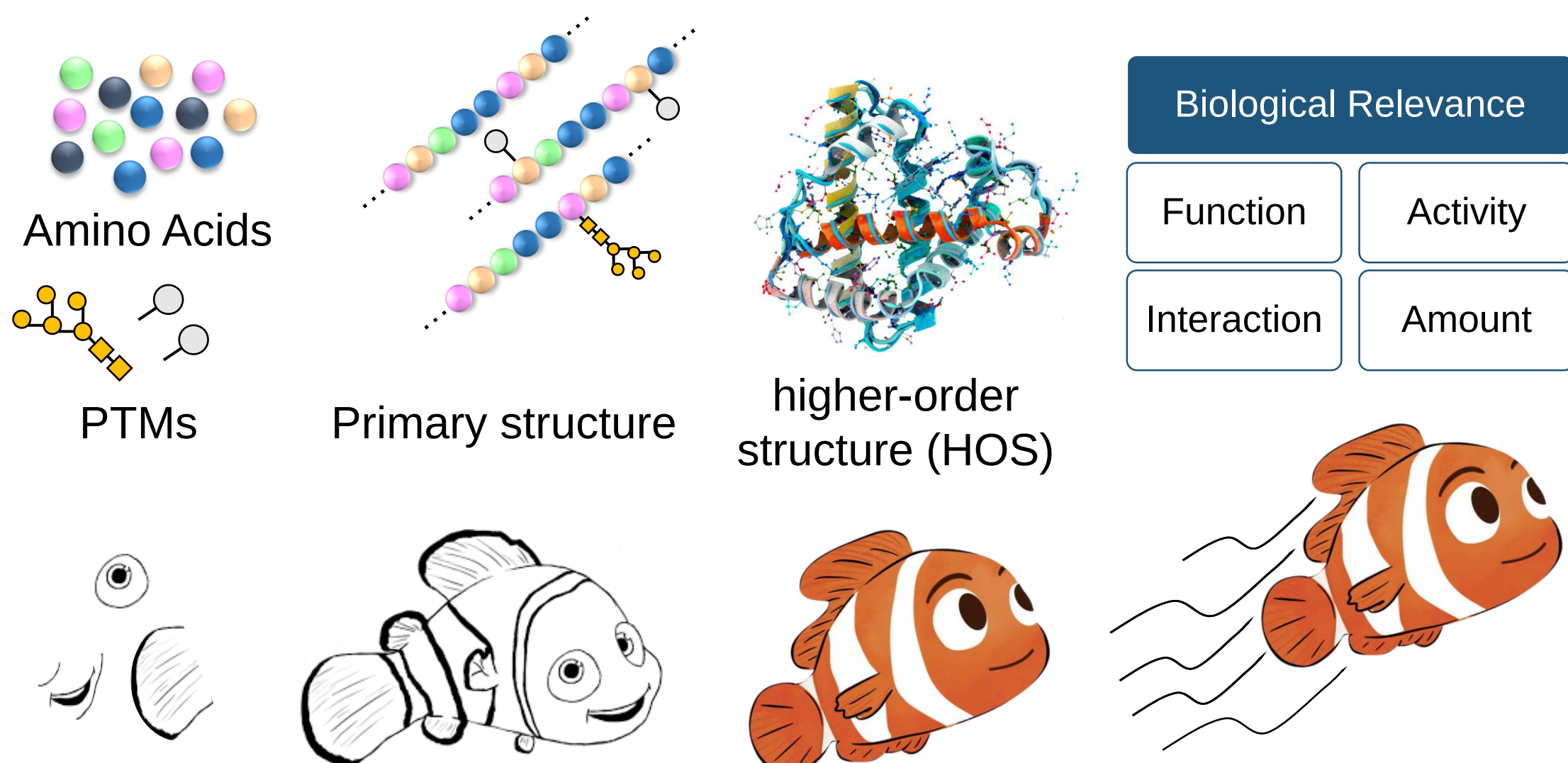
ProMET project: Fundamental protein metrology towards a better definition of the measurand

Amandine Boeuf¹, Cristian Arsene², Laura Cavallarin³, Sarah Cianférani⁴, Christa M. Cobbaert⁵, Declan Cook⁶, Vincent Delatour¹, Elena Dominguez-Vega⁵, Chiara Giangrande¹, Santosh L. Gande⁷, Maria Gabriella Giuffrida³, Oscar Hernandez-Alba⁴, Ibolya Kepiro⁸, Cristina Lamberti³, Luise Luckau⁹, Paul Matejtschuk¹⁰, Gavin O'Connor², Merve Öztuğ¹¹, Chiara Portesi¹², Francesco Romaniello¹², L. Renee Ruhaak⁵, Tim Rudd¹⁰, Max Ryadnov⁸, Evren Saban¹¹, Consolato Schiavone¹², Harald Schwalbe⁷, Sridhar Sreeramulu⁷, Claudia Swart², Konstantinos Thalassinou⁶, Hélène Vaneckhoutte¹, Leopold Walzel¹³, Michael G. Weller¹³

1-Laboratoire national de métrologie et d'essais (LNE), Paris, France; 2-Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, Germany; 3-Consiglio Nazionale delle Ricerche (CNR), Turin, Italy; 4-Centre National de la Recherche Scientifique (CNRS), Strasbourg, France; 5-Leids Universitair Medisch Centrum (LUMC), Leiden, Netherlands; 6-University College London (UCL), London, UK; 7-Johann Wolfgang Goethe-Universität Frankfurt am Main (GUF), Frankfurt, Germany; 8-National Physical Laboratory (NPL), Teddington, UK; 9-UK's National Measurement Laboratory (NML) hosted by LGC, Teddington, UK; 10-Medicines and Healthcare Products Regulatory Agency (MHRA), South Mimms, UK; 11-Türkiye Bilimsel ve Teknolojik Arastirma Kurumu (TUBITAK ÜME), Gebze, Turkey; 12-Istituto Nazionale di Ricerca Metrologica (INRiM), Turin, Italy; 13-Bundesanstalt für Materialforschung und -prüfung (BAM), Berlin, Germany

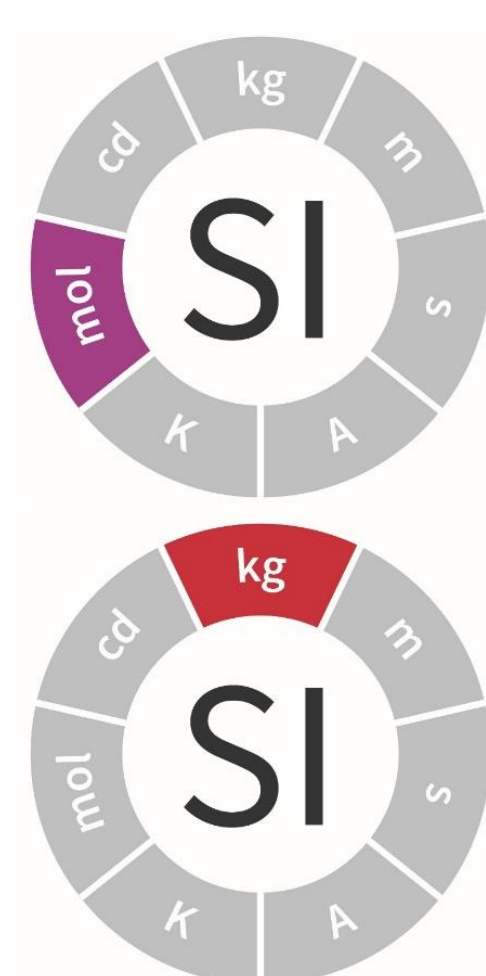
Proteins

- **Dynamic, heterogeneous and large biomolecules** (~10nm) with **biological relevance**
- Constituted of building blocks (~few Å): **amino acids**



Proteins & Metrology

- Protein measurements: **new area in metrology** (~10 years)
- Quantification currently **based on protein primary structure**
→ Black and white picture!
- **Traceability** of measurement results to the SI for **small unmodified protein**¹:
 - Purity assessment
 - Quantification in matrices
- **Lack of comparability** of results between different measurement principles highlighted for protein quantification^{2,3}



Protein Structure & Activity

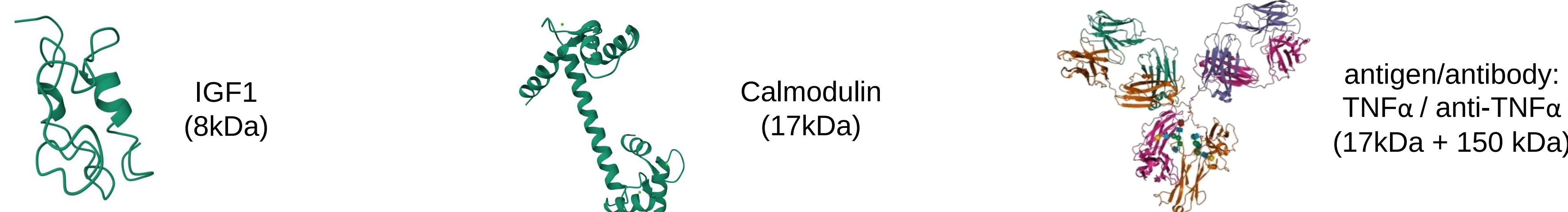
- Variations in the primary structure naturally occur (truncation, amino acid deletion/substitution, post-translational modifications PTMs)
→ **One protein represented by a complex mixture of modified proteins: proteoforms**
- Variations can affect the HOS and biological relevance
→ **Impact on quantitative measurements**

Needs to ensure accurate and comparable protein measurements

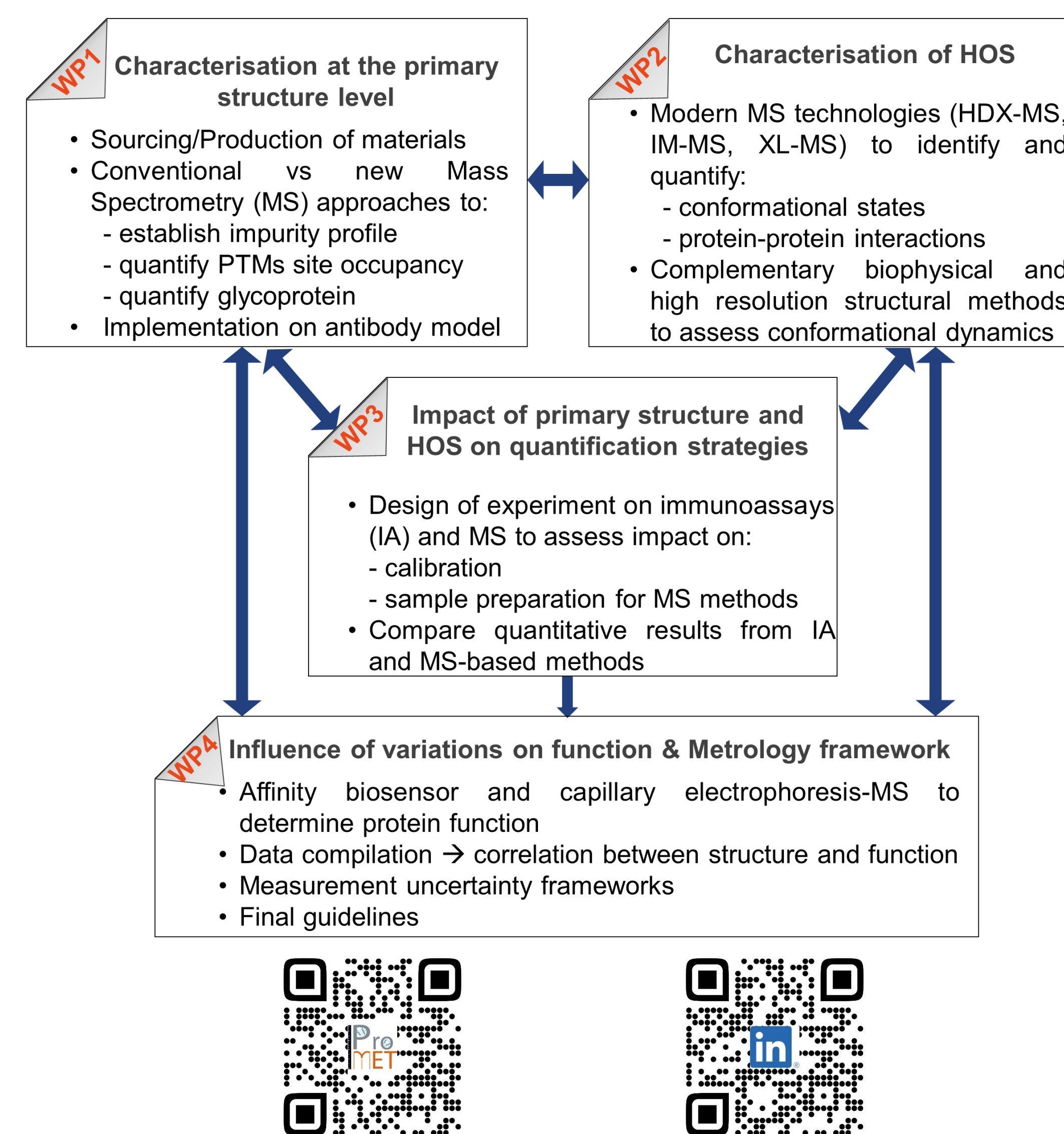
- Extend **SI-traceable** purity assessment and quantification in matrices of **large and modified proteins**
- Unravel protein overall structures, interactions, and their relationship to function
- Consider a **holistic approach** by evaluating additional physical units (units of time or length) and develop **metrological references** with **fit-for-purpose uncertainties and SI-traceability**
- Provide recommendations to **better define the measurand** by considering the complexity, heterogeneity, and overall structure of proteins

ProMET to address fundamental metrology challenges

- Project, **gathering NMIs/DIs and the academic community** from proteomics, structural and systems biology to **address needs and initiate the future of protein metrology**



- Investigate the **influence of primary sequence variants and PTMs** of proteins on the assessment of the chemical purity (WP1)
- Develop **fit-for-purpose strategies for the characterisation and quantification of HOS** using structural mass spectrometry (MS) combined with other biophysical approaches and existing computational techniques (WP2)
- Investigate the **impact of structure heterogeneities on protein measurements and protein function** (reference measurement procedures and routine methods) (WP3 & 4)
- Fill the gap by **developing a metrology framework and guidelines** to better define the measurand for protein (WP4)



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EUROPEAN PARTNERSHIP

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METROLOGY PARTNERSHIP

EURAMET

Impact

Improve accuracy and comparability of protein measurements
→ access to **more reliable data/results**

Contribution in different areas:

- New tests toward **precision medicine**
- Access **therapies** at lower costs
- Safety of the **food** chain and consumer protection
- Better **doping** assays
- New **environmental** applications



¹Josephs R D. et al. Metrologia, 2019. <https://doi.org/10.1088/1681-7575/ab27e5>

²Huynh et al. Anal Bioanal Chem, 2021. <https://doi.org/10.1007/s00216-021-03361-0>

³Giangrande C et al. CCLM, 2023. <https://doi.org/10.1515/cclm-2022-1250>

Corresponding author: amandine.boeuf@lne.fr