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Department: Chemistry, University of York
York Structural Biology Laboratory (YSBL)
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Date of appointment to the University: 1991
Present position: Professor in Structural Biology
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Previous posts:

1975-1979	Research Assistant, Dept. of Chemistry, **University of Lodz, Poland**.
1980-1982	Postdoctoral Research Fellow In **Max-Planck-Institute, Gottingen, Germany**
1983-1990	Lecturer, Dept. of Chemistry, **University of Lodz, Poland**
1989-1990	Postdoctoral Research Fellow, YSBL, **Dept. of Chemistry, University of York**
1991-1997	Research Fellow, YSBL, **Dept. of Chemistry, University of York**
1997-2002	Senior Research Fellow, YSBL, **Dept. of Chemistry, University of York**
2002-2012	Reader, YSBL, **Dept. of Chemistry, University f York**
2012-31.03.2026	Professor, YSBL, **Dept. of Chemistry, University of York**

Qualifications:

1972-1977	M.Sc. (with Medal) In Biology and Biophysics, University of Lodz, Poland
1977-1980	PhD (Protein Crystallography) (summa cum laude), University of Lodz, Poland

Funding (2015 – current):

BBSRC: Revealing Molecular Bases of Signal Transduction through Drosophila Insulin Receptor 01/08/2022-31/12/2025, £554,805.
Structural studies on human Insulin Receptor, Brzozowski A.M. 06/2019 – 12/2025. Novo Nordisk Guy Dodson Fund, £140,000.
MICA: A molecular dissection of the interplay between diabetes and cancer: an integrated, multidisciplinary approach. II. Brzozowski A.M., (PI), Jiracek J., (IOCB, Prague), 01/2018-12/ 2021, MRC, £840,000
A regional cryo-EM facility at the University of York. GJ Davies (PI) et al, AM Brzozowski (CoI), Wellcome Trust, 01/08/2017-31/07/2022, £1,601,545.
X-ray Diffraction Equipment for Macromolecular Crystallography at York GJ Davies (PI) et al, AM Brzozowski (CoI) BBSRC: 0018/09/20-17/09/21 £750,000.00, 18/09/20-17/09/2021
A molecular dissection of the interplay between diabetes and cancer: an integrated, multidisciplinary approach. Brzozowski A.M., (PI), Jiracek J., (IOCB, Prague), O'Connor R., (UCC, Cork), 2012-2017, MRC Programme Grant, 2012-2017, £1,800,000 (direct contribution to York - £996,680.00).

Key scientific achievements:

(i) The first structural evidence of semi-oxygenated human haemoglobin (Hb) trapped in the T state: the first structural evidence of mixed Koshland & MCW character of the allosteric oxygen binding to human Hb.

(ii) The first structural description of lipase and its serine-like proteases catalytic site. The first structural evidence of lipase:lipids complexes and elucidation of the mechanism of interfacial activation of lipases.

(iii) The first structure determination of the blue-multi Cu laccase: lignin synthesis and degradation.

(iv) The first structure of a free human Factor VIIa of the blood clotting cascade. This allowed elucidation of Factor VIIa activation, resulting in the design of more efficient Factor VIIa as a lifesaving drug.

(v) The structural description of human Insulin-like Growth Factor (hIGF-I) hormone: origins of functional specificity of hIGF-I and Insulin.

(vi) The first structure determination and description of the human Oestrogen Receptor (ER) and the hormone (oestradiol – E2) pharmacophore. This structure showed details of the E2 binding mode and indicated possible directions for rational design of E2 analogues.

(vii) The first structural evidence for molecular basis of agonism, partial- and full-antagonism in the Oestrogen receptor. This enabled rational drug design against breast, uterus and ovarian cancers and hormone therapy drugs. Determination of ER complexes with co-activators peptides.

(viii) The design and testing of new crystallization screens CSS-I/II, They have been widely used in many laboratories and are also commercially available. They link high efficiency and potential cryoprotection.

(ix) The introduction of mono-methyl-PEGs polymers suitable for macromolecules crystallization. Since then, hundreds of Nature, Science etc. structural papers used mmePEG-based screens.

(x) Proving that indolyl-3-acryloylglycine is not urine autism metabolite marker.

(xi) Use of protein and organic chemistry to semi-synthesise human insulin analogues that showed convergence of their active conformations, indicating insulin structure on human Insulin Receptor (IR). It was confirmed later in the crystal structure of insulin:IR complex.

(xii) Determination of the first human insulin:Insulin Receptor complex.

(xiii) Determination of the *Drosophila* (Dm) IMPL-2 protein responsible for regulation of bioavailability of insulins in the flies, which show novel, and very different to human IGFBPs fold and hormones binding modes.

(xiv) First confirmation of the crystalline storage form of insulin in live pancreatic beta-cells granules.

(xv) Determination of the first invertebrate Dm IR structure in the complex with Dm DILP5 insulin, showing very similar structural blueprint of the human and insect structures and hormones' binding modes. This is the first structural evidence of remarkable conservation of insulin signalling axis in the animal kingdom.

(xvi) Delivery of holistic hypothesis about signal transduction through Insulin Receptor.

Selected relevant publications:

1. The use of intuitive AF-based modelling for the understanding of activation and signalling through Insulin-like Receptors. AM Brzozowski et al. *Frontiers in Endocrinol*ogy (2025), 16, doi: 10.3389/fendo.2025.1633449

2. Structural Conservation of Insulin/IGF Signalling Axis at the Insulin Receptors Level in *Drosophila* and Humans Cristina M. Viola, et al. (2023) *Nature Comm*., **14**, 6271

3. Characterization of insulin crystalline form in isolated β-cell secretory granules Asai, S. et al (2022), *Open Biology*. 12, p., 220322.

4. Structures of insect Imp-L2 suggest an alternative strategy for regulating the bioavailability of insulin-like hormones. Kulahin Roed, N et al. (2018), *Nature Comm*, 9, 3860

5. Rational steering of insulin binding specificity by intra-chain chemical crosslinking. Viková, J. et al. (2016), *Scientific Reports (Nature),* 6, Article number: 19431,

6. How insulin engages its primary binding site on the insulin receptor. Menting, J. G. et al. (2012) *Nature,* **493**, 241-245

7. Implications for the active form of human insulin based on the structural convergence of highly active hormone analogues. Jiráček, J. et al. (2010) *PNAS*, 107, 1966-1970**.**

8. Is the presence of urinary indolyl-3-acryloylglycine associated with autism spectrum disorder? Wright, B. et al. (2005) *Developmental Medicine and Child Neurology*, 47, 190-192

9. Interaction of transcriptional intermediary Factor 2 nuclear receptor box peptides with co-activator binding site of Estrogen receptor alpha. Wärnmark, A. et al. (2002), *J. Biol. Chem*. 277, 21862-21863

10. Structural origins of the functional divergence of human Insulin-like Growth Factor-I and Insulin. Brzozowski, A. M. et al. (2002) *Biochemistry,* 41, 9389-9397

11. Structural insights into the mode of action of a pure antioestrogen. Pike, A. C. W., et al. *Structure* (2001), 9, 145-153

12. Clear Strategy Screens for macromolecule crystallisation. Brzozowski, A. M., Walton, J. *J. Appl. Cryst.* (2001), 34, 97-101

13. Structure of the ligand binding domain of the oestrogen receptor beta in the presence of partial agonist and full antagonist. Pike, A. C. W. et al. *EMBO Journal* (1999), 18, 4698-4618

14. Structure of human factor VIIa and its implications for the triggering of blood coagulation. Pike, A. C. W. et al. . *PNAS* (1999), 96, 8925-8930

15. Crystal structure of the type-2 Cu depleted laccase from *Coprinus cinereus* at 2.2 Å resolution. Ducros, V. et al. *Nature Structural Biology* (1998), 5, 310-316

16. Molecular basis of agonism and antagonism in the oestrogen receptor. Brzozowski, A. M. et al. *Nature* (1997), 389, 753-758

17. The structure of trp RNA-binding attenuation protein. Antson A. A. et al. *Nature* (1995), 374, 693-700

18. Poly(ethylene) glycol monomethyl ethers - an alternative to poly(ethylene) glycols in protein crystallisation. Brzozowski A. M. & Tolley S. P. *Acta Crystallographica* (1994), D50, 466-468

19. A model for interfacial activation in lipases from the structure of a fungal lipase-inhibitor complex. Brzozowski A. M. et al. *Nature* (1991), 351, 491-497

20. A serine protease triad forms the catalytic centre of a triacylglycerol lipase. Brady L et al. *Nature* (1990), 343, 767-770

21. Bonding of molecular oxygen to T state Human Haemoglobin. Brzozowski A. M. et al *Nature* (1984), 307, 74-76