BIOGRAPHICAL SKETCH

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NAME: Simon Justin GEORGE

eRA COMMONS USER NAME (credential, e.g., agency login): simonjgeorge

POSITION TITLE: Owner / Scientific Consultant

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
King's College, University of London	BSc (Hons)	09/1982	Chemistry
University of East Anglia	PhD	12/1986	Chemistry/Spectroscopy
University of East Anglia	PostDoc	09/1988	Chemistry/Spectroscopy

A. Personal Statement

I have the expertise, experience and motivation necessary to successfully carry out the proposed research. I am an experienced X-ray and Vibrational spectroscopist, and my career has specialized in the development of novel X-ray, Infrared and other techniques. That these have invariably been applied to problems in biological inorganic chemistry is notable, as these systems often have the dual challenges of dilute metal sites of interest, and limited amounts of material to study. My previous successes in building novel instrumentation for stopped-flow infra-red spectroscopy (SF-IR), soft X-ray spectroscopy, X-ray magnetic circular dichroism (XMCD) and as well as my history of working with EXAFS spectroscopy demonstrate my technical skills and knowledge. Similarly, the range and depth of my scientific publications, including 3 publications in *Science* and papers in *PNAS, Angewendte Chemie* and other first rank journals, demonstrate my abilities and expertise as a chemist.

After leaving the University of California in 2014, I took a 10 month break to focus on family issues and reflect on my career before establishing my company and starting work as a full time Scientific Consultant in mid 2015.

B. Positions and Honors

Positions and Employment

1988 – 1991 Staff Research Chemist, University of East Anglia, Norwich, UK
1990 – 1991 Visiting Scientist, National Synchrotron Light Source, Brookhaven National Lab., Upton NY.
1991 – 1993 Assistant Researcher, Department of Applied Science, University of California, Davis, CA.
1993 – 1998 Consultant, Stanford Synchrotron Radiation Laboratory, Stanford Linear Accelerator Center, Menlo Park, CA.
1994 – 1998 Scientist, Nitrogen Fixation Laboratory / Department of Biological Chemistry, John Innes Centre, Norwich UK.
1998 – 2003 Senior Scientist, Department of Biological Chemistry, John Innes Centre, Norwich UK.
1999 – 2006 Honorary Faculty, University of East Anglia, Norwich, UK.
2003 – 2009 Staff Scientist, Physical Biosciences Division, Lawrence Berkeley National Lab, Berkeley, CA.
2010 – 2014 Project Scientist, Department of Chemistry, University of California, Davis, CA.
2015 – Owner, Simon Scientific Inc., Berkeley CA

Professional Memberships

2000 – Member, Society for Biological Inorganic Chemistry
2003 – Member, American Chemical Society
2016 – Member, American Association for the Advancement of Science

C. Contribution to Science

My scientific career has always had two strands. First, I have always been interested in the development and use of novel spectroscopic techniques, and well as developing novel applications of existing techniques. Second, I have sought to apply these techniques to problems in inorganic chemistry of life; an interdisciplinary area which is sometimes called bioinorganic chemistry or biological inorganic chemistry. I am particularly interested in the structure-function relationships underpinning the functioning and biosynthesis of metal clusters and organometallic metal sites in biology, as well as the origin and fate of metals in biological systems.

1. My early career focused on the dynamic chemistry and biological function of iron-sulfur clusters in proteins, from simple ferredoxins to complex metalloenzymes such as the hydrogenases. Working in the group of Andrew Thomson (now OBE, FRS), I used the then novel technique of low temperature magnetic circular dichroism spectroscopy (MCD) (1) together with electron paramagnetic resonance (EPR) spectroscopy to study these materials. During this time, I worked with Fraser Armstrong at the University of Oxford (now FRS) on developing electrochemical approaches to preparing spectroscopic samples. Amongst my results that I achieved working with these colleagues included the characterizing the protonation (2,3) and cluster interconversion chemistry in ferredoxins (2-5); the electrochemical reduction and spectroscopic characterization of very low potential metal clusters (2-4) and probing the cluster chemistry of hydrogenase enzymes. I was also involved in the first measurements using immobilized thin film protein electrochemistry (3).

[1] Variable temperature magnetic circular dichroism
Thomson, A. J.; Cheesman, M. R.; **George, S. J.**, in *Meth. Enzymol,* **1993**, *225,* 199-232

[2] *Azotobacter chroococcum* 7Fe ferredoxin - 2 pH dependent forms of the reduced 3Fe cluster and its conversion to a 4Fe cluster
George, S. J.; Richards, A. J. M.; Thomson, A. J.; Yates, M. G. *Biochem. J.* **1984**, *224*, 247-25

[3] Investigation of metal-ion uptake reactivities of [3Fe-4S] clusters in proteins - Voltammetry of coadsorbed ferredoxin-aminocyclitol films at graphite electrodes and spectroscopic identification of transformed clusters
Butt, J. N.; Armstrong, F. A.; Breton, J.; **George, S. J.**; Thomson, A. J.; Hatchikian, E. C. *J. Am. Chem. Soc.* **1991**, *113*, 6663-6670

[4] Redox properties of *Azotobacter* 7Fe ferredoxin
Armstrong, F. A.; **George, S. J.**; Thomson, A. J.; Yates, M. G. *Biochem. Soc. Trans.* **1988**, *16*, 840-842

[5] Electrochemical and spectroscopic characterization of the conversion of the 7Fe into the 8Fe Form of ferredoxin III from *Desulfovibrio africanus* - identification of a [4Fe-4S] cluster with one non-cysteine ligand
George, S. J.; Armstrong, F. A.; Hatchikian, E. C.; Thomson, A. J. *Biochem. J.* **1989**, *264*, 275-284

2. When I first moved to the United States, I worked at Brookhaven National Laboratory at the NSLS synchrotron radiation facility. At this time, with Stephen Cramer, I applied the novel techniques of soft x-ray spectroscopy and X-ray magnetic circular dichroism to metalloenzymes, measuring the first spectra using these techniques on metalloproteins (1-4). I also measured my first EXAFS spectra, including a study on zinc figure structure which was published in *Science* (5). When I returned to the United States to work at Berkeley and Davis in 2002, these techniques were again in the forefront of my work, together another novel X-ray technique, nuclear resonance vibrational spectroscopy (NRVS), which is capable of measuring the element-specific vibrational structure of iron sites in proteins.

[1] L-edge x-ray absorption spectroscopy of *Pyrococcus furiosus* rubredoxin
George, S. J.; van Elp, J.; Chen, J.; Ma, Y.; Chen, C. T.; Park, J. B.; Adams, M. W. W.; Searle, B. G.; Degroot, F. M. F.; Fuggle, J. C.; Cramer, S. P. *J. Am. Chem. Soc.* **1992**, *114*, 4426-4427

[2] Soft x-ray magnetic circular dichroism - a probe for studying paramagnetic bioinorganic systems
Van Elp, J.; **George, S. J.**; Chen, J.; Peng, G.; Chen, C. T.; Tjeng, L. H.; Meigs, G.; Lin, H. J.; Zhou, Z. H.; Adams, M. W. W.; Searle, B. G.; Cramer, S. P. *Proc. Natl. Acad. Sci. U.S.A.* **1993**, *90*, 9664-9667

[3] Copper L-edge spectral studies - a direct experimental probe of the ground-state covalency in the blue copper site in plastocyanin
George, S. J.; Lowery, M. D.; Solomon, E. I.; Cramer, S. P. *J. Am. Chem. Soc.* **1993**, *115*, 2968-2969

[4] Molybdenum X-ray absorption edges from 200 – 20,000 eV, The benefits of soft x-ray spectroscopy for chemical speciation
George, S. J.; Drury, O. B.; Fu, J.; Friedrich, S.; Doonan, C. J.; George, G. N.; White, J. M.; Young, C. G.; Cramer, S. P. *J. Inorg. Biochem.,* **2009**, 103, 157–167

[5] Identification and characterization of zinc binding sites in protein kinase C
Hubbard, S. R.; Bishop, W. R.; Kirschmeier, P.; **George, S. J.**; Cramer, S. P.; Hendrickson, W. A. *Science* **1991**, *254*, 1776-1779

3. On my return to the United Kingdom in 1994, I worked as a Scientist, later Senior Scientist at the John Innes Centre in Norwich, the UK's premier plant science research center. There, with Roger Thorneley, I developed the novel technique of stopped-flow infra-red spectroscopy (SF-IR) and applied it to, amongst other systems, the binding of CO to nitrogenase, functional NO binding chemistry to metalloproteins as well as hydrogenase and nitrogenase (1-5). I later constructed a SF-IR system at Lawrence Berkeley Laboratory.

[1] Time-resolved binding of carbon monoxide to nitrogenase monitored by stopped-flow infrared spectroscopy
George, S. J.; Ashby, G. A.; Wharton, C. W.; Thorneley, R. N. F. *J. Am. Chem. Soc.* **1997**, *119*, 6450-6451

[2] Time-resolved infrared spectroscopy reveals a stable ferric heme-NO intermediate in the reaction of *Paracoccus pantotrophus* cytochrome cd_1 nitrite reductase with nitrite
George, S. J.; Allen, J. W. A.; Ferguson, S. J.; Thorneley, R. N. F. *J. Biol. Chem.* **2000**, *275*, 33231-33237 (correction, *J. Biol. Chem.* 2001, *276*, 47742)

[3] Six- to five-coordinate heme-nitrosyl conversion in cytochrome *c*' and its relevance to guanylate cyclase
Andrew, C. R.; **George, S. J.**; Lawson, D. M.; Eady, R. R. *Biochemistry* **2002**, *41*, 2353-2360

[4] The di-iron subsite of all-iron hydrogenase: Mechanism of cyanation of a synthetic {2Fe3S} - Carbonyl assembly
George, S. J.; Cui, Z.; Razavet, M.; Pickett, C. J., *Chem. Eur. J.* **2002**, *8*, 4037-4046

[5] Reactions of H_2, CO, and O_2 with active [NiFe]-Hydrogenase from *Allochromatium vinosum*. A stopped-flow infrared study
George, S. J.; Kurkin, S.; Thorneley, R. N. F.; Albracht, S. P. J. *Biochemistry* **2004**, *43*, 6808-6819

4. Much of my career has focused on the mechanism and biosynthesis of the nitrogenase and hydrogenase enzymes. For nitrogenase I have used the battery of techniques at my disposal, including EXAFS, to study the conformational changes of the FeMo-co active site on ligand and inhibitor binding (1,2). For hydrogenase, I worked with David Britt and James Swartz using SF-IR and EPR to study the biosynthesis of the H-cluster active site, producing two *Science* papers (3,4)

[1] Steric Control of the Hi-CO MoFe Nitrogenase Complex Revealed by Stopped-Flow Infra-red Spectroscopy
Yang, Z.-Y.; Seefeldt, L. C.; Dean, D. R.; Cramer, S. P.; **George, S. J.** *Angew. Chem. Int. Ed.*, **2011**, *50*, 272-275

[2] EXAFS and NRVS Reveal a Conformational Distortion of the FeMo-cofactor in the MoFe Nitrogenase Propargyl Alcohol Complex
George, S. J.; Barney B. M.; Mitra, D.; Guo, Y.; Igarashi, R. Y.; Dean, D. R.; Cramer, S. P.; Seefeldt, L. C. *J. Inorg. Biochem.* **2012**, *112*, 85-92

[3] A Radical Intermediate in Tyrosine Scission to the CO and CN^- Ligands of [FeFe] Hydrogenase
Kuchenreuther, J. M.; Myers, W. K.; Stich, T. A.; **George, S. J.;** NejatyJahromy, Y.; Swartz, J. R.; Britt, R. D. *Science* **2013**, *342*, 472-475

[4] The HydG enzyme generates an $Fe(CO)_2(CN)$ synthon in the biosynthesis of the FeFe hydrogenase H-Cluster
Kuchenreuther, J. M.; Myers, W. K.; Stich, T. A.; Suess, D. L. M.; Pelmentschikov, V.; Shiigi, S. A.; Cramer, S. P.; Swartz, J. R.; Britt, R. D.; **George, S. J.** *Science* **2014**, *343*, 424-427

5. Finally, I have a developing interest in the toxicology of lanthanides. It is now well-known that exposure to gadolinium based contrast agents (GBCAs) can, under certain circumstances, induce the disease Nephrogenic Systemic Fibrosis. With Stephen Cramer and Jerrold Abraham of Upstate Medical University, State University of New York (SUNY) I conducted a multi-technique X-ray imaging and EXAFS study which showed that the previously observed deposits in affected tissues comprised gadolinium phosphate-like materials. Since the Gd is no longer coordinated to the GBCA chelator this implied a direct link to GBCA exposure and the disease. This is an ongoing project.

[1] Synchrotron X-ray analyses indicate phosphate-bound gadolinium in nephrogenic systemic fibrosis
George, S. J.; Webb, S. M.; Abraham, J. L.; Cramer, S. P. *Brit. J. Dermatol.*, **2010**, *163*, 1077-1081

[2] Interaction of Gd-DTPA with phosphate and phosphite: Toward the reaction intermediate in Nephrogenic Systemic Fibrosis
Gao, S.; **George S.J.**; Zhou Z-H. *Dalton Trans.* **2016**, *45*, 5388-5394

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