SILVIO AIME Curriculum Vitae

Academic achievements

1971: Laurea degree (cum laude) in Biological Sciences from the Faculty of Sciences of the University of Torino with a thesis on the biochemical effects in industrial waste from paper manufacturing industry;

1972: Research Fellow at the Institute of General Chemistry of the University of Torino;

1973: British Council Bursary at the School of Molecular Sciences of the University of East Anglia (UK);

1975-82: Research Fellow at the Institute of General Chemistry of the University of Torino;

1982-86: Associate Professor of General and Inorganic Chemistry at the Faculty of Sciences of the University of Torino (Courses: General Chemistry; Bioinorganic Chemistry);

1986-2000: Full Professor of General and Inorganic Chemistry at the Faculty of Pharmacy of the University of Torino (Courses: General and Inorganic Chemistry; Advanced Inorganic Chemistry; NMR Spectroscopy);

2000-2012: Full Professor of General and Inorganic Chemistry at the Faculty of Sciences of the University of Torino/Degree Course in Biotechnologies (Courses: General Chemistry; Supramolecular Chemistry; NMR Spectroscopy; Metals in Medicine; Molecular Imaging);

2013-2019: Professor of General and Inorganic Chemistry at the Department of Molecular Biotechnologies and Health Sciences/Degree Course in Biotechnologies (Courses: General Chemistry; Supramolecular Chemistry; NMR Spectroscopy; Molecular Imaging);

In 2007 SA moved to the Centre of Molecular Biotechnologies of the University of Torino. The Centre has the mission of developing research projects aimed at tackling important un-met medical needs with biotechnology-based approaches. SA's team contributes to this task with the development of probes and procedures in the fields of Molecular Imaging.

Since the starting of activities (1998) SA has coordinated the activities of the Integrated Laboratory for Innovative Methodologies at the Bioindustry Park "Silvano Fumero". The Laboratory has the mission of providing the industries of the Park with advanced services to support their research activities. In 2007 he started, thanks to the contribution of the regional government, the new industry-university laboratory dedicated to Preclinical Imaging equipped with the most advanced imaging technologies (MRI, PET/SPECT, Ultrasound, Optical Imaging). This laboratory is the core facility of the Regional Platform of Medical Imaging that gathers several industries active in Piedmont (Bracco, AAA, Im-3d, Ephoran, Invento srl, Cage- chemicals and Fluody).

SA had long standing collaborations with industries (regular consultant for Bracco Imaging) and his research work has led to 30 patent applications.

From his research group two start-up companies (Invento srl and Cage-chemicals) have been spinned-off.
SA is chairman of 2I3T that is the Society for the Incubator and the Technology Transfer of the University of Torino (47 new enterprises incubated since 2007).
From 2014 to 2019 SA was deputy-rector of the University of Torino with the commitment on matters related to Technological Transfer and Relations with the Regional Government.

Scientific Organizations

1980-84: President of the Italian NMR Discussion Group (1980-84);

1992-present: Vice-President of the Interuniversity Consortium of Research on Metals in Biological Systems (27 associated universities);

2000-05: Chairman of the EU COST Action D18 "Lanthanides in Diagnosis and Therapy" (55 teams);

2006-09: Chairman of the EU COST Action D38 "Metal-based Systems for Molecular Imaging" (48 teams);

2008-09: Secretary of the Council of the International Society of Molecular Imaging;

2008-10: Secretary of the Council of the European Society of Molecular Imaging;

2012-2013: President of the European Society of Molecular Imaging;

2011-2016: Chairman of the EU COST Action TD1004 "Theragnostics" (23 participating countries).

2008-2013: Chair of the WP "Molecular Imaging" in the prepatory phase of the ESFRI Large Scale Facility "EurobioImaging".

2009-2015: Associated to The Istituto di Biostrutture e Bioimmagini (IBB) of CNR and Head of the IBB research unit c/o the Molecular Biotechnology Center of the University of Torino.

2013-present: Italian delegate to the interim board of the EU-LSF "EurobioImaging".

Along the years SA has served in several EU panels for the evaluation of R&D projects. From 2007 to 2010 SA has been member of the ERC "Material and chemical sciences" panel (PE 4) for the Starting Grants programme.

Journals

Member of the Editorial Board of: Journal of Biological Inorganic Chemistry, Magnetic Resonance in Chemistry, Journal of Bioinorganic Chemistry and Applications and of the Journal of Molecular Imaging.

2006-2015 Editor in-chief of "Contrast Media and Molecular Imaging" (Wiley)

Awards

1987: Nasini Medal from the Italian Chemical Society;
1996: Medal from the Italian NMR Discussion Group;
2000: Sapio Prize;
2004: European Magnetic Resonance Foundation Award;

2010: Award from the European Soc. Magnetic Resonance in Medicine and Biology;
2010: Doctor honoris causa from the University of Debrecen;
2011: Honorary Doctorate from Eindhoven Technical University;
2011: Hans Fisher Senior Fellow, Institute of Advanced Study, Technical University Munich;
2013: Distinguished Professor at the Eindhoven Technical University;
2013: World Molecular Imaging Society 2013 Gold Medal Award;
2013: Fischer Award for Contrast Media Research;
2014: Amedeo Avogadro Award from the Italian Chemical Society.
2016: Member of the "Accademia dei Lincei"

Research Activities

Along his career SA has published ca. 600 peer-reviewed papers and 30 patents.
From Scopus, SA has an h-index of 73.

Most of the achievements deal with the applications of MRI/NMR. He was introduced to NMR spectroscopy in 1973, when he spent a year in the laboratory of Prof. R.K.Harris (University of East Anglia, UK) to work on the analysis of complex NMR spectra of organophosphorous compounds. Back to Torino, he started the NMR laboratory and, for some years, his work was mainly devoted to the study of Metal Carbonyl derivatives that was the main topics at the Institute of General Chemistry in those years. Much work has addressed the characterization of the stereochemical non-rigidity of Metal Carbonyls identifying several pathways for the intramolecular exchange of carbonyls, hydrides and organic moieties coordinated to the metal centres. The most studied systems were represented by polymetallic substrates as they were thought to mimic what happens on the surface of heterogeneous catalysts (cluster-surface analogy). Beyond the study of the fluxional behaviour, important contributions were brought to assess structural parameters in solution thanks to the measurement of the relaxation times, for instance to determine H,H distances in Hydrides containing systems. Finally the advent of multidimensional NMR prompted a number of investigations aimed at assessing the structural and dynamic properties of this class of molecules in solution in order to get more insight into the understanding of the key steps of their reactivity. Then, the multi-nuclear, multi-parametric studies of Metal carbonyls were extended to the solid state by applying both Magic Angle Spinning and Wide Line techniques. Important results on the occurrence of solid state dynamics were obtained.
In the early eighties the huge impact of NMR on biological systems prompted to start new lines of activities. One dealt with the study of melanin pigments for which solid state NMR techniques appeared particularly competitive to characterize systems that are black, insoluble, irregular...
This research line gave particularly interesting results in the study of neuromelanin and of the role of metal ions in the ethiology of Parkinson disease. Years later (2001-2006) this work on melanin pigment has been re-addressed (thanks to a pluriannual grant from the Japanese KAO company) to study hair melanin and to find a catalyst for hair bleaching.
The second line of activities dealt with the exploitation of the peculiar magnetic properties of Lanthanide ions to tackle biological problems either *in vitro* and *in vivo* (MRI applications). The most significant scientific results are the following:
a) Assessment of the in solution structure and dynamics of isomers of Ln(III)-DOTA and of Ln(III)-DTPA complexes and their derivatives; syntheses of new structures endowed with improved relaxometric properties.
b) Elucidation of the relationships between solution structure and exchange rate of the coordinated water molecule in Ln(III) chelates and relative insights for the design of systems endowed with high relaxivities for MRI applications.
c) Synthesis of Gd(III) complexes functionalized with moieties interacting with serum albumin; characterisation of their binding affinity at the light of designing "Blood Pool Agents" for MR

Angiographic applications. Systems binding to the glycation sites of proteins have also been investigated.
d) Synthesis and characterisation of systems responsive to the oxygen partial pressure depending on the recognition of the conformational variation (T to R) of hemoglobin or on the formation of supramolecular adducts with poly-beta-cyclodextrins and porphyrins containing MnII/III ion.
e) Set-up of systems based on autoassembling of Lanthanide chelates, functionalized with different substituents and interacting groups in order to accumulate, at the sites of interest, a large number of MRI Contrast Agent units.
f) Cellular Labelling (e.g. stem cells, tumor cells, insule, ...) with Gd(III) complexes, by pinocytosis, electroporation, hypo-osmotic shock and receptor mediated endocytosis, for MRI applications and elucidation of the relationships between intracellular localization of the paramagnetic agents and observed relaxation enhancements.
g) Targeting of cancer cells by paramagnetic complexes through a variety of transporting/receptor systems (e.g. Glutamine transporters, adhesion cells, LDL-, Folate-, Integrins-receptors).
h) Set-up of a new class of MRI Contrast Agents based on the transfer of Saturated Magnetization to the water resonance (CEST agents, Chemical Exchange Saturation Transfer). As their effects is dependent upon the irradiation frequency at the resonance of the exchangeable protons, their use opens the possibility (forbidden for the relaxation based MRI agents) of detecting more than one MRI agent in the same region of interest. Further improvements have led to the new class of high sensitive LipoCEST agents based on the use of Liposome technology.
i) Design of a number of MRI Contrast Agents whose relaxation enhancement or Magnetization Tranfer properties are responsive to a specific parameter of the biological microenvironment (pH, temperature, enzymatic activity, metabolites' concentration).
l) Use of nano-sized carriers (from endogenous systems to liposomes, dendrimers.etc.) loaded with imaging reporters for diagnostic and "teranostic" applications. The nanocarriers have been designed in order to release their payload in response to endogenous (pH, specific enzymatic activity) or external stimuli (e.g. UltraSound).
m) Finally, the search for enhancing the sensitivity of MR probes for Molecular Imaging applications has led to tackle the field of hyperpolarized molecules. The approach is based on the addition of a para-Hydrogen molecule to a C-13 labelled substrate and the detection of the resulting C-13 image thanks to a procedure that transfers the spin order of the para-Hydrogen molecule into net C-13 magnetization. This line of research is very interesting, not only for its MRI objectives, but for its implications to lead the researcher into the not yet explored world of spin isomers. Recent work in this field (Nature Commun. 2015) has shown that, by merging the chemical design and a fine control of the conditions for generating net C-13 magnetization, it is possible to expand markedly the number of substrates hyperpolarizable by the p-H_2 route (including pyruvate and lactate, currently accessible only by the complex and expensive DNP route).

Overall these research activities have provided an important contribution to the development of the field of Molecular Imaging. It is expected that Molecular Imaging protocols, based on the visualization of molecules or molecular events that are the "signature" of a given pathology, will profoundly innovate the *in vivo* diagnostic procedures in providing early diagnoses and efficient monitoring of the therapeutic treatments. Entering the domain of Molecular Imaging has led to the introduction of other Imaging modalities besides MRI in our work. Thus, in the last decade, our lab has been equipped with PET, SPECT, OI, CT and US scanners and it is now common practice the design and testing of multi-modal probes. Moreover skills in microscopy/histological validation of the *in vivo* imaging results have also been acquired.