Curriculum Anna Tramontano

Born in Naples 14/7/1957
Nationality: Italian
Present position: Chair Professor of Biochemistry
Sapienza University of Rome

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since 2001	Chair professor of Biochemistry, Sapienza University of Rome
2004-2011	Director of the Bioinformatics Program, CRS4, Pula (CA)
1996 - 2001	Director of the Computational Biology and Chemistry Department at IRBM (Merck Research Laboratories in Pomezia, Rome)
	The Department included three Units: Computational Biology (3 FTE), Computational Chemistry (3FTE) and Biotechnology (6 FTE)
in 1994/95	Director of Biocomputing Unit of IRBM
in 1990/93	Biocomputing Group Leader at IRBM
in 1988/90	Staff member of the European Laboratory for Molecular Biology in Heidelberg (D) in the Biocomputing Programme.
in 1987	Research fellow at International Institute of Genetics and Biophysics in Naples
in 1985/86	Staff scientist at Biosym Technologies Inc., San Diego, CA, USA
in 1984/85	Post-doctoral research fellow at the Department of Biochemistry and Biophysics of the University of California, San Francisco (USA)
in 1981/84	Research fellow at the International Institute of Genetics and Biophysics in Naples
in 1980	Laurea in Physics, summa cum laude, at the University of Naples

Scientific career

I was trained as a physicist but soon became fascinated by the complexity of biology and by the promises of computational biology and bioinformatics *ante literam*.

Since the beginning of my scientific activity, I used a multidisciplinary approach to address problems of biological and biomedical interest. I have both developed methods and applied them, often in close collaboration with biomedical colleagues.

My scientific career can be roughly divided into four phases.

After my degree in Physics and a period at the International Institute of Genetics and Biophysics in Naples, I moved to the USA as a **post-doctoral scientist at UCSF** in the Department of Biochemistry. In that period, I developed a system for the visualization and manipulation of protein structures called InsightII, later commercialized by Biosym first and Accelerys later. This is a user-friendly graphical molecular modeling that incorporates a variety of useful molecular modeling codes specifically designed for biological systems.
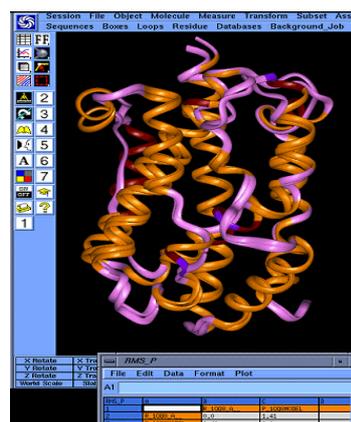
While a graphics program is rather easy to implement today, this was not the case at the time. Only two programs were available, MIDAS from UCSF and Frodo from Uppsala University. None of them could display more than one molecule at the time and both had serious limitations, due to the fact that even central computers had a memory smaller than that of any present desktop computer. Furthermore, the system had to run on two machines, a computational one and a graphics one (PS300 in that case) that had to communicate via a rather complex system of calls and message passing. The structure of the program I developed was very innovative and could solve these problems. Indeed, although modified for presently available hardware, the program is still sold and cited after more than 30 years and used in both academic and pharmaceutical company settings. Its structure has been a model for the development of several other graphics packages.

After a short period in Italy, I moved to the **EMBL** in the Biocomputing Program in the group of Prof. Arthur Lesk. There my main interest was the development of methods to analyse and predict the structure of antibodies, a very special class of molecules from both the functional and the structural point of view.
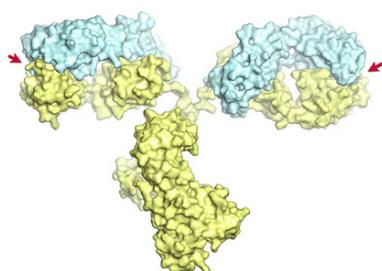
The prediction of an antibody structure from its amino acid sequence has several important applications. The models can be used in docking simulations to identify the epitope, i.e. the region of the antigen recognized by the antibody, can provide the basis for the rational design of selectable libraries, can help in engineering antibodies elicited in model systems for use in human therapy with the aim of reducing or abolishing unwanted and dangerous immunogenic responses. It also has implications for the redesign of biotechnologically useful antibodies adopted in a variety of experimental set-ups. We were able to develop a method, based on a careful analysis and interpretation of the available structures (rather few at the time), to infer the structure of this important class of molecules from their amino acidic sequence with high accuracy. The method is based on our finding that the loops responsible for antigen binding can only assume a limited number of conformations, and, more importantly, the particular conformation assumed by the loop depends only on its length and on the identity of specific amino acid residues located in key positions both within and without the loops. The method is still used today and the Nature paper reporting it has been cited more than 900 times and is still cited today (30 citations last year). It indeed opened the road to the rational redesign of antibodies, especially for therapeutically important purposes, such as, for example antibody humanization.

In 1990 I returned to Italy as group leader at **IRBM**, the research Institute of Merck & Co. near Rome. There I worked on several projects of pharmaceutical interest. For example, I built a model of the specificity pocket of the protease of hepatitis C virus on the basis of the known structures of trypsin-like serine proteases and of the conservation pattern of the protease sequences among various hepatitis C strains. The model allowed us to predict that the substrate of this protease should have a cysteine residue in its central position. This result provided

the basis for identifying the precise limits of the other proteins encoded by the viral polyprotein, allowed their cloning and characterization and therefore opened the road to the search for inhibitors. I also designed a 61-residue all-β protein using a portion of an immunoglobulin as a template, obtaining a molecule with a novel β-sheet topology and an engineered metal binding site. The protein was folded and compact and bound the metal, thus representing the first designed β-protein with a novel fold and a tailored function. By randomizing the sequence of two of its regions, we used it to construct a conformationally constrained peptide library displayed on phage. Furthermore, I predicted the structure of Interleukin-6 in complex with its receptors and engineering it as to act as an antagonist of the native protein.

During my time at IRBM, I was promoted Director of the Department of Computational Biology and Chemistry. The Department included three Units: Computational Biology (3 FTE), Computational Chemistry (3FTE) and Biotechnology (6 FTE).

In 2001, I moved back to the academic world. The main reason for this was the availability of the genomic data, a wealth of information that, at least at the time, did not raise much interest in the pharmaceutical companies and that I badly wanted to explore.

I became full professor of Biochemistry at the **Sapienza University** where I very rapidly established a very interdisciplinary group, all supported by my competitive funds. The group, on average, has been composed by two RTDs, 5-7 Post-docs, 3-7 PhD students including physicists, engineers, biologists, computational biologists, chemists and computer scientists (www.biocomputing.it).

The group has developed several methods for the analysis of antibody structures (taking advantage of the wealth of new information available), of genomic data and of protein-drug interactions. These have been applied to several relevant biomedical problems such as chronic lymphocytic leukemia, multiple acyl-CoA dehydrogenase deficiency, Down syndrome, respiratory defects, angiogenesis, splenic marginal zone lymphoma, Alzheimer's disease, Duchenne Muscular Dystrophy as well as to *Schistosoma mansoni*, *Plasmodium falciparum* and Cytomegalovirus infectious diseases.

Furthermore we are involved in several worldwide initiatives aimed at analyzing post-genomic biological data in order to improve our understanding of life at a molecular level. I co-organize CASP (the Critical Assessment of Techniques for Protein Structure Prediction international experiment), am involved in the assessment of the results of CAFA (the Critical Assessment of protein Function Annotation experiment) and have collaborated to

the analysis of the data produced by the ENCODE (Encyclopedia of DNA Elements) international initiative.

Bibliometric data (See also: http://www.researcherid.com/rid/D-5378-2009)

Editorial activities

Associate Editor of Bioinformatics (2006-)
Associate Editor of Current Opinion in Structural Biology (2012-)
Associate Editor of PLoS ONE (2011-)
Associate Editor of BBSRC (2011-)
Editorial Board The FEBS Journal (2002-2011)
Associate Editor of Proteins (2002-)
Advisory Editorial Board of EMBO Journal and EMBO Reports (2007-2008)

Major funding (partial list)

King Abdullah University for Science and Technology (KAUST) Award (2008-2016) 5,500 K$ (PI)
FIRB Italbionet (2004-2011) 500 K€ (PI)
PRIN (2012-2015) 168 K€ (PI)
FIRB Internazionale (2011-2014) 240K€ (PI)
Fondazione Banca di Roma (2010-2012) 1100 K€ (PI)
AIRC (2005-2010) 200 K€ (PI)
Italian Institute of Technology (IIT) Seed Projects (2010-2012) ~1,000 K€ (Co-PI)
Italian Institute of Technology (IIT) NanoBioTec project (2011-2016) ~4,000 K€ (PI)
EU: BioSapiens NoE (2005-2009) 500 K€ (Team leader)

Invited Seminars / lectures / conferences:

Argentina (Buenos Aires), Australia (Canberra, Lorne), Brasil (Rio de Janeiro), Canada (Québec), Croatia (Rovinj), Cuba (Havana), Denmark (Copenhagen), Finland (Turku, Tromso), France (Paris, Strasbourg), Germany (Munchen, Heidelberg, Braunschweig, Saarbrucken, Hamburg), Greece (Eraklion), India (Lucknow, Madurai), Israel (Eilat), Kenia (Nairobi), Mali (Bamako), Netherlands (Amsterdam, Njemegen), Norway (Oslo), Portugal (Oeiras), Russia (Moscow, Puschino), Saudi Arabia (Jeddah, Riyad), South Africa (Pretoria), Slovenia (Portoroz, Ljubjana), Spain (Madrid, Barcellona, La Coruna), Sweden (Stockholm, Uppsala), Switzerland (Ascona, Fribourg, Basel), Turkey (Istanbul, Antalya), UK (London, Oxford, Cambridge, Glasgow, Cardiff, Dover), Uruguay (Montevideo), USA (Asilomar, San Diego, Seattle, New York), Italy (most Universities and Research Institutes).

Managerial experience

As mentioned above, I coordinated the Department of Computational Biology and Chemistry at IRBM. The Department included twelve senior scientists and the members of their groups. The mission of the Department was to support the biology and chemistry effort of the site via the development and application of computational methods and to help in the design and set-up of innovative technologies (for example biological libraries for screening).

I have been part of the steering committee of the BioSapiens Network of Excellence, a large-scale, concerted effort to annotate genome data by laboratories distributed around Europe, using both informatics tools and input from experimentalists. We created a European Virtual Institute for Genome Annotation, bringing together many of the best laboratories in Europe (25 institutions based in 14 countries throughout Europe). An important accomplishment of the network was to achieve a closer integration between experimentalists and bioinformaticians, through a directed program of genome analysis, focused on specific biological problems. The annotations generated by the Institute are available in the public domain and easily accessible on the web. The Institute also established a permanent European School of Bioinformatics, of which I was responsible, to train bioinformaticians and to encourage best practice in the exploitation of genome annotation data for biologists.

In 2004 I was asked to organize and coordinate the Bioinformatics Program of the CRS4 Consortium in Sardinia. I hired the scientists and technicians of the Program, trained them, set-up the priorities and strategic directions of the laboratory and structured the services for external users. In 2011 the laboratory was fully functional and is now effectively managed by people working there full-time.

At Sapienza, as mentioned before, I coordinated a group of 15-20 people during the years. As expected, most of them left the lab for more permanent positions. Essentially all those who wanted to continue a career in science (the large majority) found very good positions in prestigious Institutions (EMBL, Imperial College, University of Basel, Technical University of Denmark, University of Southern Denmark, Albert Einstein College of Medicine, University of Innsbruck, II Universita' di Napoli, CNR, IIT, Universita' di Bologna, MRC Cambridge, University College etc.). From this point of view, I believe I created a school of computational biology in Italy that is now known and recognized in Europe and in the rest of the world.

I have been Vice-president of the International Society for Computational Biology (ISCB) (over 3,200 members) and am an elected member of its Board of Directors. I am also the chair of the ISCB nomination committee that manages the annual nomination process for the election of board members, officers, and student council. I also chair the steering committee of the European Conference in Computational Biology, the major European Computational Conference that is held every year in a different country and attracts more than 1,000 participants.

I have a long-standing experience in evaluating research at both the national and international level. I list here my most relevant activities in this area in the past few years.

Member of the **Scientific Council of the European Research Council** (2011 - 2014)
Chair of the ERC LS2 panel for Advanced Grants (2009-2011) (I resigned after having been selected by an independent international identification committee as member of the ERC Scientific Council)
Member of the **Scientific Advisory Boards** of:
    European Molecular Biology Laboratory (2006-2011)
    IIMCB Warsaw, chair (2008 -)
    Max Planck Institute for Molecular Genetics, Berlin, chair (2008 -)
    European Boinformatics Institute (EBI), chair (2005-2012)
    Centro Nacional de Biotecnología (2009 -)
    Institute Pasteur - Fondazione Cenci Bolognetti (2002 -)
    Centro de Regulacion Genomica (2011-)
    Swiss Institute for Bioinformatics (2009 -)
    Scuola Superiore Normale of Pisa ("Nucleo di Valutazione") (2011-)
    Max Delbruck Center for Molecular Medicine in Berlin (2014-)
    EMBO fellowship committee (2008 -2012)
    EMBO Course Committee (2004-2008)
    Chair of the Evaluation Committee for the FIRB (Future in Science) grants of the Italian Ministry (2012)
Evaluation of Italian Research (Member of the GEV Expert Group for the Life Sciences)

I have also served as **external evaluator** for several grant schemes, for example:
    EU FP6 and FP7
    ERC
    Vienna Science and Technology Fund (WWTF)
    Irish Research Council for Science, Engineering and technology
    Austrian Science Fund
    EMBO fellowship program
    University of Copenhagen
    University of Vienna
    Lundbeck Foundation
    Severo Ochoa Program, Spain
    Fundação para a Ciência e a Tecnologia, Portugal
    KAUST Competitive Research Grants
    PRACE

I have also been member of the **promotion committees** of several Universities (Vilnius University, Geneva University, University College London, Bar Ilan University, Hadassa University College, CNB Madrid, Chalmers University,

Missouri University, Haifa University, Koc University, University of Vienna, etc.) and **external examiner of PhD theses** in Cambridge, Paris, Uppsala, Switzerland, Finland, Denmark, Poland.