

Agostino Tramontano



Anna Tramontano 1957–2017

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Anna Tramontano, who died unexpectedly in March 2017, was an Italian computational biologist of renown. Anna's work focused on protein structure and modeling studies, and she was a dedicated leader in the bioinformatics community, in her own country and worldwide. Anna was devoted to training in this emerging field, which lies at the interface of biology, chemistry, physics and computational sciences. She was not only a good scientist but also a great organizer, coordinator and colleague, and she mentored and inspired the next generation of scientists.

Anna trained as a physicist in her home town of Naples before being attracted by the exciting new developments in structural molecular biology. As a postdoc at the University of California, San Francisco, she authored a powerful graphics program to display protein structures, at a time when using computers to visualize 3D structure was still in its infancy. Uniquely for the time, the program allowed comparison of protein structures, an approach that has become the cornerstone of studies in protein evolution and function. The tool was later commercialized and became widely used by structural biologists.

In 1988, Anna moved on to join Arthur Lesk at the European Molecular Biology Laboratory (EMBL) in the Biocomputing Program in Heidelberg, where she started her best-known work, analyzing and predicting the structures of antibodies. Lesk had worked with Cyrus Chothia in Cambridge to interpret how the newly determined immunoglobulin fold recognizes a plethora of antigens through subtle changes in specific loops. Anna and Lesk went on to use this knowledge to predict structures of antibodies on the basis of sequence, using novel molecular modeling approaches. They developed a bespoke immunoglobulin modeling approach, which was based on careful analysis of the available structures and understanding the constraints imposed by the β -sandwich framework. Their work showed that it is possible to predict the structure of the antibody-binding site with high accuracy, on the basis of the principle that the loops responsible for antigen binding can assume only a limited number of conformations, depending on their length and the identity of residues at key positions both within and outside the loop. To quote Anna, this work "opened the road to the rational redesign of antibodies, especially for therapeutically important purposes."

At that time, EMBL was home to some of the most outstanding computational bioinformatics groups in the world. Those students and postdocs went on to lead many of the scientific developments in the field, both in Europe and beyond. One of these developments was the establishment of the International Society of Computational Biology (ISCB), of which Anna later became a Fellow and Vice President, and which today hosts the largest bioinformatics meeting (Intelligent Systems for Molecular Biology (ISMB)) in the world. Anna was also passionate about the European Conference on Computational Biology (ECCB), as an organizer and the chair of the steering committee, and was committed to helping young scientists to participate.

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Anna Tramontano and participants at the proteomics course in Nairobi, 2009.

Nelson Ndegwa

Retaining her life-long interest in the applications of molecular modeling for therapeutic targets, Anna returned to Rome as a group leader at the IRBM, a newly established research institute that was later acquired by Merck & Co, and she later became head of department. She continued to work on many potential drug targets, including the hepatitis C proteases and interleukin-6 in complex with its receptors. She was involved in developing many methods for inhibitor design, protein design and docking. In 2001, driven by her interest in the newly available genomic data, she returned to academia as a full professor at the Sapienza University of Rome. She continued to focus on structural bioinformatics, especially for proteins involved in biomedical problems, and also branched out to examining RNA molecules and their structures.

Determining the structure of a protein from its sequence has been a long-standing challenge, with implications for drug discovery and environmental interventions. Progress was initially slow, and one limitation in the early days of protein-structure prediction was that many papers had claimed substantial progress, yet it was difficult to judge whether real progress had actually been achieved. To address this problem, John Moult and colleagues established a biannual challenge, Critical Assessment of Structure Prediction (CASP), in which protein models built from sequence data are compared with the corresponding but not yet public experimental structures, through fully blinded methods testing. This series of experiments and associated conferences has profoundly affected the practice and assessment of structure prediction and modeling. Anna was always a major force in CASP, first as an influential participant, then as an assessor, and later as a long-standing member of the organizing committee. Anna served as the chief editor for CASP special issues in the journal *Proteins*, introduced rigorous statistics into model evaluation, pioneered new areas of evaluation, and organized many Europe-based planning workshops and international meetings. In all these efforts, she was always passionately concerned with two things:

maintaining the highest standards of scientific rigor, and mentoring, training and recognizing young scientists. She also added her critical approach to the assessment of the results of a newer initiative, Critical Assessment of Protein Function Annotation (CAFA).

Anna was a builder of bridges. She was deeply involved in many early European research projects aimed at integrating biological information and tools to describe protein structures and to predict structure, function and potential therapeutics by modeling. In particular, she was part of the small steering committee for BioSapiens, the EU FP6 project that for the first time brought together many nascent bioinformatics research groups across Europe to use computational approaches to ‘understand life’. In that role, Anna coordinated training and organized many workshops and popular training sessions. With great Italian flair, she hosted the project’s first all-hands meeting, setting the tone for the rest of the project and working tirelessly to ensure not only that the objectives were met but also, most importantly, that the attendees worked together to achieve common goals.

As the size and complexity of biological data increased, the need for a pan-European infrastructure for biodata and tools became apparent. Driven by the European Strategic Forum for Research Infrastructures (ESFRI) and building on previous European framework projects, the concept of the European Life-Science Infrastructure for Biological Information (ELIXIR) was developed. ELIXIR unites Europe’s leading life science organizations in managing and safeguarding the increasing volume of data generated by publicly funded research; it also sustains bioinformatics resources and enables users in academia and industry to access services. In its early days, it was challenging to establish a vision for ELIXIR and to engage funders and politicians, but Anna brought her broad experience, endless enthusiasm and dogged determination; she first led the efforts that ultimately resulted in Italy’s joining ELIXIR.

Anna was proud to be an Italian scientist and embraced her substantial teaching responsibilities, including lecturing undergraduates. She taught with great passion in fields including biochemistry and bioinformatics, training biomedicine and physics students. She created and directed a Master in Bioinformatics program at Sapienza, which has enabled many biologists, biotechnologists, physicists and chemists to enter the field. Her unique and catchy way of explaining difficult concepts, often with jokes, captured students’ attention. Her door was always open to students, who often turned to Anna for advice and support, and as a reference.

Anna had a long-standing history of participation and giving back to the community, as an alumna, collaborator, scientific advisor, councilor and friend. She served on innumerable scientific bodies, including the European Research Council (ERC), EMBL’s Scientific Advisory Council; the European Molecular Biology Organization (EMBO) Fellowship and Courses committees; and countless scientific review committees

worldwide. In those review roles, Anna was clear sighted and often critical and challenging, but always in a constructive way. Recently, Anna was a member of the National Board of Trustees Research (CNGR), an Italian ministerial body that sets general criteria for the selection and evaluation of research activities, chooses the scientists participating in selection committees and coordinates the activities of these committees.

Throughout her career, Anna extended her dedication to training young scientists with farther-reaching operations. Within ELIXIR, she led the training efforts and campaigned tirelessly for a bioinformatics training framework that could serve everyone in Europe. Anna’s model for the original BioSapiens summer schools deeply influenced the format of the EMBL–European Bioinformatics Institute (EBI) program. Cath Brooksbank, head of training at EMBL–EBI, said that Anna had “the perfect combination of leadership and listening skills” and was “so committed to her calling that nothing was too much work, and she fostered that commitment in those she worked with.” Importantly, she also dedicated herself to training programs for underrepresented scientists in challenging environments—work that took her to Cuba, Africa and most recently Saudi Arabia. Her influence was captured by Nelson Ndegwa, former president of the Regional Student Group of Eastern Africa in bioinformatics and computational biology, who recalled:

I first got in contact with Anna in 2007. We were interested in having ... courses, but we didn’t have resources to fund such activities. Anna, at the first request to give us a workshop, was very delighted to travel all the way from Italy to Nairobi and in addition was happy to sponsor some students from neighboring countries in the East African region to travel and attend the event, as travel scholarships are quite hard to come by. She gave a three-day proteomics course in Nairobi in 2009 [pictured]. She also generously sourced for [the] vast majority of the funding that went into supporting 52 students from Africa to attend the ISCB–ASBCB 2009 conference in Bamako, Mali. She connected many students to labs in Europe and beyond for various opportunities (study/internships). She was an academic mother to many of us in Africa, and our lives will forever be a testimony of her generosity and commitment.

Anna was loved by her close family, including her brother and his children, and all her scientific colleagues and friends around the world. Anna’s training of the next generation of scientists will be a great and persisting legacy. She was an exceptional mentor and promoter of young scientists, and she knew how to bring out the best in everyone. She will be deeply missed.

We thank many of those who shared their thoughts and memories with us here, especially Manuela Helmer Citterich, John Moulton and Nelson Ndegwa, as well as many other colleagues in Rome and worldwide.