160 DE ANI
UNIVERSITATEA DIN BUCUREȘTI
330 DE ANI DE TRADIȚIE ACADEMICĂ

UNIVERSITATEA DIN BUCUREȘTI

PAOLO CARLONI

Doctor Honoris Causa

Universitatea din București
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PAOLO CARLONI
DOCTOR HONORIS CAUSA

Laudatio | Paolo Carloni

Domnule Profesor Paolo Carloni,
Domnule Profesor Marian Preda, Rector al Universității din București,
Domnule Profesor Claudiu Buglea, Președintele Senatului Universității din București,
Stimați invitați, colegi și studenți,

Este o onoare pentru mine să prezint astăzi în fața dumneavoastră câteva aspecte ale activității prodigioase desfășurate de Profesorul Paolo Carloni, directorul Institutului de Biomedicină Computațională de la Centrul de Cercetări din Jülich, Germania, profesor titular la Universitatea RWTH din Aachen și co-director al Institutului JARA de Neuroștiințe moleculare și imagistică.

Centrul de Cercetări din Jülich este o instituție națională de cercetare cu activitate într-o paletă largă de domenii, precum energia, teoria informației sau bioeconomia. Centrul din Jülich este printre cele mai importante în Europa și în lume în dezvoltarea infrastructurii de calcul, inclusiv a sistemelor de calcul integrate exascale și a celor cuantice.

Institutul de Biomedicină Computațională, condus de Profesorul Paolo Carloni, dezvoltă și aplică metodologii avansate pentru simulări moleculare, bioinformatică structurală și biologia sistemelor, cu scopul de a înțelege procesele neurobiologice fundamentale și de a dezvolta biomarkeri și agenți terapeutici pentru boli neurologice. Institutul este implicat direct în dezvoltarea metodologiilor computaționale care pot fi utilizate în centrul de calcul exascale de ultimă oră, aflat în prezent în curs de dezvoltare la Centrul de Cercetări din Jülich. Profesorul Carloni este co-dezvoltator al MiMiC, un cod scalabil pentru calcule masive – calcule numerice combinate de mecanică cuantică și dinamică moleculară – tipul de calcule utilizate pentru a putea descifra reacțiile chimice în sistemele biologice. Contribuțiile profesorului Carloni în domeniul simulărilor moleculare au fost deja distinse cu premii și recunoașteri prestigioase. Printre acestea se numără titlul de **Ambasador în științe chimice din Franța, obținut în 2024** de la CNRS

Chemistry, un program inaugurat în 2019 pentru a atrage cercetători străini de prestigiu în chimie computațională în laboratoarele franceze; **Premiul Zimmer International Scholar Award 2021 de la Universitatea din Cincinnati, SUA**, ca o recunoaștere a contribuțiilor importante în chimia computațională și biofizică; **Membru străin al Academiei de Științe din Bologna, Italia**, (2019) pentru contribuțiile sale la dezvoltarea biologiei computaționale (ca o remarcă suplimentară, Academia de Științe din Bologna a fost înființată în 1690).

Născut la Florența, Profesorul Carloni a urmat **studii de licență în Chimie la Universitatea din Florența**. În 1994 a obținut **titlul de Doctor în Științe la Universitatea din Florența**, unde a lucrat cu Lucia Banci și Per Luigi Orioli, precum și cu Michelle Parrinello (laboratorul de cercetare IBM Zürich, Elveția). Subiectul tezei de doctorat a fost studiul unor metaloproteine, enzime care folosesc ioni metalici pentru a cataliza reacții chimice.

Din 1990 până în 1991 a efectuat un **stagiu de cercetare la Laboratorul de Cercetări al IBM din Kingston**, SUA, iar din 1992 până în 1994 un alt **stagiu la Laboratorul de Cercetări al IBM din Zürich** cu Michele Parrinello. În 1994, domnul Carloni a devenit profesor asistent la Universitatea din Florența, timp în care a mai efectuat un stagiu la **Laboratorul de Cercetări al IBM din Zürich** pentru încă doi ani. În această perioadă s-a concretizat studiul său din 1995 privind structura și legarea cisplatinei, un compus utilizat pe scară largă în tratamentul cancerului ovarian. Cinci ani mai târziu, în 2000, profesorul Carloni și grupul său au folosit o metodă a mecanicii cunatice, teoria funcționalei de densitate, pentru a caracteriza interacțiunile dintre cisplatină și ADN.

În 1998 a devenit **profesor asistent în Chimie la Școala Internațională de Studii Avansate (SISSA) din Trieste** și coordonatorul grupului de lucru pentru biofizică al Rețelei Europene de Structură Electronică Psi-k. În 1999, cu mult înainte ca evoluțiile în biologia structurală, metodologiile computaționale și infrastructura de calcul să facă din studiul canalelor

ionice o cercetare de rutină, profesorul Carloni și grupul din Trieste au publicat simulări de dinamică moleculară ale mecanismului prin care ionii de potasiu și sodiu se leagă de canalul ionic de potasiu.

În 2000 a fost promovat **profesor asociat la SISSA Trieste**, în 2003 a devenit șef al grupului de cercetare în biofizică și **șef al Secției de Statistică și Biologie la SISSA Trieste**, iar în 2004 a fost promovat profesor titular la SISSA Trieste. Din 2006 până în 2009, profesorul Carloni a fost responsabil pentru SISSA în cadrul Proiectului de neuroștiință și robotică al Institutului Italian de Tehnologie din Trieste, Italia. În 2009, a acceptat oferta pentru un **post de profesor titular la Universitatea RWTH din Aachen și la Institutul de Cercetări din Jülich**, pentru ca, în 2012, să devină director al Institutului de Biomedicină Computațională. Din 2016 este **co-director al Institutului de Neuroștiințe Moleculare și Neuroimagistică JARA și co-director** (part-time) **al Laboratorului Universității Naționale din Vietnam pentru Simulări Multi-Scală ale Sistemelor Complexe.** Din 2018 profesorul Carloni este **co-director al Centrului JARA pentru Simulări numerice și Știința datelor**, iar din 2024, este **liderul secțiunii din Germania pentru EBRAINS**, o infrastructură europeană dedicată cercetării creierului.

Cercetările din laboratoarele pe care le conduce sau pe care le-a condus au fost susținute de granturi de cercetare de la agențiile naționale și europene de finanțare, inclusiv, în ultimii ani, granturile Uniunii Europene "Proiectul creierului uman", "EBRAINS 2.0: O infrastructură de cercetare pentru a promova neuroștiința și sănătatea creierului" și "Calcul avansat, algoritmi cuantici și abordare bazată pe date pentru știință, tehnologie și inginerie".

De-a lungul anilor, Profesorul Paolo Carloni a coordonat numeroși tineri cercetători, doctoranzi și studenți post-doctoranzi, unii dintre ei devenind ulterior profesori în instituții prestigioase, precum Școala Politehnică Federală din Lausanne sau Universitatea RWTH din Aachen. De asemenea, a fost examinator extern pentru mai mulți doctoranzi la

EPFL Switzerland, Institutul Karolinska din Stockholm și alte instituții de cercetare prestigioase; în plus, profesorul Carloni a făcut parte din comitetul de angajare pentru posturi de profesor la universități din Germania, Austria și Danemarca. Începând cu anul 1998, Profesorul Carloni a organizat sau co-organizat în mod regulat conferințe sau ateliere științifice – el este, de exemplu, implicat în activitățile CECAM (Centre Européen de Calcul Atomique et Moléculaire). A susținut sute de lecții și seminarii invitate. Profesorul Carloni este evaluator pentru agențiile naționale și europene de finanțare a cercetării și editor pentru revistele Protein, Structure, Function, Bioinformatics și PLoS One.

Până în prezent, **a publicat peste 350 de lucrări**. Titlurile publicațiilor sale dezvăluie **amploarea intereselor de cercetare interdisciplinare**, care reunesc fizica, chimia, biologia și informatica.

Suntem privilegiați să avem în Profesorul Paolo Carloni **un prieten al Universității din București**. Ca parte a misiunii Centrului de Cercetări din Jülich de a promova dezvoltarea calculului masiv pe sisteme exascale pentru științele vieții și la invitația Platformei Diasporei Academice (Ambasada României, Berlin), profesorul Carloni a vizitat în 2022 câteva instituții de cercetare și dezvoltare din România, inclusiv Universitatea din București. Suntem recunoscători pentru implicarea domnului Dr. Iulian Costache (Ambasada României, Berlin) și profesorului Sorin Costreie (Universitatea București și Consilier de Stat) în organizarea acelei vizite. Îi suntem foarte recunoscători Profesorului Carloni pentru sprijinul continuu acordat grupului de Biofizică computațională din Facultatea de Fizică, doctoranzii având acum acces la o infrastructură puternică de calcul.

Domnule Profesor Paolo Carloni, în calitate de Decan al Facultății de Fizică, aș dori să vă urez bun venit la Universitatea din București. Titlul de *Doctor Honoris Causa* reprezintă o recunoaștere simbolică a contribuțiilor dumneavoastră la dezvoltarea științei.

Prof. univ. dr. Lucian Ion
Decanul Facultății de Fizică

Dear Professor Paolo Carloni,
Your excellency, Professor Marian Preda, Rector of the University of Bucharest,
Your excellency, Professor Claudiu Buglea, President of the Senate of the University of Bucharest,
Dear Guests, Colleagues and Students,

I am honoured to have the privilege to introduce to you today Professor Paolo Carloni, the Director of the Institute for Computational Biomedicine at the Forschungszentrum Jülich, Jülich, Germany, Full Professor at the RWTH Aachen University, and Co-Director of the JARA-Institute Molecular Neuroscience and Imaging, Forschungszentrum Jülich.

Forschungszentrum Jülich (FZJ), The Research Center Jülich, is a national research institution pursuing research on broad fields such as energy, information, bioeconomy. Forschungszentrum Jülich is a leader in the development of computing infrastructure, including exascale and quantum computing. The Institute of Computational Biomedicine, led by Professor Carloni, develops and applies advanced methodologies for molecular simulations (structural bioinformatics and complex biological systems), with the aim of understanding fundamental neurobiological processes and to develop biomarkers and therapeutical agents for neurological diseases. The Institute led by Professor Carloni is directly involved in the development of computational methodologies that can be used with the cutting-edge exascale computing center currently being developed at the Forschungszentrum Jülich. Professor Carloni is a co-developer of MiMiC, a massively scalable code for combined quantum mechanical/molecular dynamics computations – these are the type of computations one uses to be able to decipher chemical reactions in biological systems, for example.

Professor Carloni's contributions to the field of molecular simulations have already been distinguished with prestigious awards and recognitions. These include **the 2024 Ambassadorship in Chemical Sciences in France, from CNRS Chemistry**, a programme inaugurated in 2019

to attract prestigious foreign researchers in computational chemistry to visit French laboratories; **the 2021 Zimmer International Scholar Award, from the University of Cincinnati, USA**, as a recognition for distinguished contributions in computational chemistry and biophysics; **2019, Foreigner Member of the Bologna Academy of Sciences, Bologna, Italy**, for his contributions to the development of computational biology (as a note, the Bologna Academy of Sciences was established in 1690).

Born in Florence, Professor Carloni pursued his **undergraduate studies ('Laurea') in Chemistry at the University of Florence**. In 1994 he obtained his **PhD from the University of Florence**, where he worked with Lucia Banci and Per Luigi Orioli (University of Florence), and Michelle Parrinello (IBM Zürich Research Laboratory, Rüshlikon, Switzerland). For his PhD Professor Carloni worked on metalloproteins, enzymes that use metal ions to catalyze chemical reactions.

From 1990 to 1991 he was a **visiting scientist at the IBM Research Laboratory in Kingston**, USA, and from 1992 to 1994 he was first a **visiting scientist and then post-doctoral researcher at the IBM Zürich Research Laboratory** working with Michele Parrinello. In 1994 Professor Carloni became assistant professor at the University of Florence, from where he took a leave and went to the **IBM Zürich Research Laboratory** for two more years. From these years arose for example his 1995 study on the structure and bonding of cisplatin, a compound widely used in the treatment of ovarian cancer. Five years later, in 2000, Professor Carloni and his group used quantum mechanics (density functional theory) to characterize interactions between cisplatin and DNA.

In 1998 he became an **assistant professor in Chemistry at the International School for Advanced Studies (SISSA) in Trieste**, and the coordinator of the biophysics working group of the Psi-k European Electronic Structure Network. In 1999, long before developments in structural biology and computational methodologies and infrastructure made it almost a routine to study ion channels, Professor Carloni and his laboratory in Trieste published molecular dynamics simulations of the

mechanism by which potassium and sodium ions bind to the potassium ion channel.

In 2000 he was promoted to **associated professor** at SISSA Trieste, in 2003 became Head of Research Line in Biophysics and **Head of the Statistical and Biological Sector at SISSA Trieste**, and in 2004 he was promoted to **full professor at SISSA Trieste**. From 2006 to 2009 Professor Carloni was responsible for SISSA of the Project on Neuroscience and Robotics of the Italian Institute of Technology Trieste, Italy. In 2009 he accepted the offer for a **full professorship (W3) at the RWTH Aachen University and the German Research School of the Forschungszentrum Jülich**, where he then in 2012 became director of the Institute for Computational Biomedicine. Since 2016 he became a **co-director of the JARA-Institute of Molecular Science and Neuroimaging**, Forschungszentrum Jülich, and **co-director** (part-time) **of the Vietnam National University Key Laboratory Multi-Scale Simulations of Complex Systems**. Since 2018 Professor Carloni is **co-director of the JARA Center for Simulation and Data Science**, and since 2024, he is **Germany's Node Leader for EBRAINS**, an European Research Infrastructure for Brain Research.

The research in the laboratories he is leading or has led has been supported by research grants from National and European Funding Agencies, including, in the recent years, the European Union Grants 'Human Brain project', 'EBRAINS 2.0: A research infrastructure to advance neuroscience and brain health', and 'Advanced computing, quantum algorithms, and data-driven approaches for science, technology, and engineering'.

Over the years Professor Paolo Carloni has supervised numerous young researchers, doctoral and post-doctoral students, some of which went on to become themselves professors in prestigious institutions, including EPFL Switzerland and RWTH Aachen University. He was also an external examiner for several doctoral students at the EPFL Switzerland, the Karolinska Institute in Stockholm, and other prestigious research institutions; moreover, Professor Carloni was part of the hiring committee for professorship positions at universities

in Germany, Austria, and Denmark. Since 1998 Professor Carloni has regularly organized and co-organized scientific meetings – he is, for example, very supportive of CECAM (Centre Européen de Calcul Atomique et Moléculaire). He gave, we estimate, hundreds of invited talks and seminars. Professor Carloni is a reviewer for National and European research funding agencies, and an editor for the journals Protein, Structure, Function, Bioinformatics, and PLoS One.

The pages of this booklet include Professor Carloni's CV and publication list. To date, he has **published over 350 papers**. We could only mention here a few of his studies. Perusing just the titles of the his publications reveals the breadth of his **highly interdisciplinary research interests**, which bring together physics, chemistry, biology, and computer science.

We are indeed privileged to think of Professor Paolo Carloni also as a **friend of the University of Bucharest**. As part of the mission of the Forwschungszentrum Jülich to promote the development of exascale computing for life sciences, and at the invitation of the Academic Diaspora Platform (Embassy of Romania, Berlin), in 2022 Professor Carloni visited Research and Development Institutions in Romania, including the University of Bucharest. We are most grateful here to Dr. Iulian Costache (Embassy of Romania, Berlin) and Professor Sorin Costreie (University of Bucharest and State Councelor) for making possible the meetings that took place on the occasion of the visit to Bucharest in 2022. We are also most grateful for Professor Carloni for his continuous support of computational biophysics at the Faculty of Physics, where young doctoral students now have the chance to do their research using a powerful super-computing infrastructure.

Professor Paolo Carloni, as the Dean of the Faculty of Physics I would like to welcome you to the University of Bucharest. The Doctor Honoris Causa title recognizes your distinguished contributions to the pursuit of science.

Prof. dr. Lucian Ion
Dean, Faculty of Physics

Curriculum vitae | Paolo Carloni

PERSONAL DATA

Prof. Paolo Carloni, Ph.D.
Date and place of birth: August 26, 1963, Florence (Italy)
Nationality: Italian
Gender: Male
Mandatory Civil Service: 1988–1989

CURRENT POSITION

Professor at RWTH Aachen University, Aachen, Germany (W3) and Director of the Computational Biomedicine section (INM-9/IAS-5) of the Institute for Neuroscience and Medicine (INM) and Institute for Advanced Simulation (IAS) at Forschungszentrum Jülich GmbH, Jülich, Germany
www.fz-juelich.de/en/ias/ias-5
Co-Director of the JARA-Institute Molecular Neuroscience and Neuroimaging (INM-11), Forschungszentrum Jülich GmbH, Jülich, Germany
https://www.fz-juelich.de/en/inm/inm-11

CONTACT DATA

Forschungszentrum Jülich GmbH
INM-9/INM-11
Wilhelm-Johnen-Straße
52428 Jülich, Germany
Phone: +49 2461 61-8941 / +49 151 46740839
Fax: +49 2461 61-4823
Web: *www.fz-juelich.de/en/ias/ias-5*
E-Mail: p.carloni@fz-juelich.de

EDUCATION

1982: Diploma (Maturità Scientifica) with 60/60.
1990: Graduation ('Laurea') in Chemistry at the University of Florence (Italy) with 110/110. Supervisors: Ivano Bertini, Pier Luigi Orioli.
1990–1994: Ph.D. in Chemistry (majoring computational biophysics), from the University of Florence. Title of the Thesis: 'Theoretical Studies on Metalloproteins'. Supervisors: Lucia Banci, Pier Luigi Orioli (University of Florence), Michele Parrinello (IBM Zurich Research Laboratory, Rüschlikon, Switzerland).
1990–1991 Visiting scientist at the IBM Research Laboratory, Kingston, NY, USA, with Prof. E. Clementi.

1992 Visiting scientist at the IBM Zurich Research Laboratory, Department of Computational Physics, Rüschlikon, Switzerland, with Dr. Michele Parrinello.

PROFESSIONAL EXPERIENCE

1993–94 Postdoc at the Department of Chemistry, University of Florence (Italy) and visiting scientist at the Zurich IBM Research in the Lab of M. Parrinello (Rüschlikon, Switzerland).
1994 Assistant professor in Chemistry at the Department of Chemistry, University of Florence (Italy).
1995–1997 On leave at the University of Florence – Visiting Scientist at the IBM Zurich Research Lab, Rüschlikon, Switzerland.
1998–2000 Assistant professor in Chemistry at the International School for Advanced Studies (SISSA), Trieste, Italy.
1998–2008 Responsible for the Biophysics working group of the Psi-k European Electronic Structure Network (www.psi-k.org).
2000–2003 Associate professor in Chemistry at SISSA.
2003–2009 Head of the Research Line in Biophysics of the Democritos center for simulations in Trieste. Head of the Statistical and Biological Physics Sector in SISSA.
2004–2009 Full professor in Chemistry at SISSA.
2006–2009 Responsible for SISSA of the Project on Neurosciences and Robotics of the Italian Institute of Technology (www.iit.it), Trieste, Italy.
2009–2014 Full Professor (W3) in Theoretical Biophysics at the German Research School (GRS) of Forschungszentrum Jülich GmbH, Jülich, and RWTH Aachen University, Aachen, Germany.
2012– Director of the Institute for Computational Biomedicine (IAS-5), Institute for Advanced Simulation, Forschungszentrum Jülich, Germany.
2013– Director of the Institute for Computational Biomedicine (INM-9), Institute for Neuroscience and Medicine, Forschungszentrum Jülich, Germany.
2014– Full Professor (W3) in Theoretical Biophysics at RWTH Aachen University, Aachen, Germany.
2016– Co-Director of the JARA-Institute Molecular Neuroscience and Neuroimaging (INM-11), Forschungszentrum Jülich GmbH, Jülich, Germany.
2016– Co-Director of the VNU Key Laboratory on "Multi-scale Simulation of Complex Systems" (part time) at the VNU – University of Science, Hanoi, Vietnam.
2018– Co-Director of the JARA Center for Simulation and Data Science (JARA CSD), Research Center Jülich and RWTH Aachen University.

2024– EBRAINS (https://www.ebrains.eu/) Germany Node Leader. EBRAINS is an European Research Infrastructure for brain research.

RESEARCH INTERESTS

For more than three decades, Paolo Carloni has developed and used multiscale methods in molecular simulation (from quantum to coarse grain) aimed at understanding structure/function of biomolecules and their complexes. He has contributed to the modeling of metal ions in biological systems, to the understanding of reaction mechanism of enzymatic superfamilies (such as that of the proteases), to molecular mechanisms of drug resistance, to the investigation of RNA/ligand interactions, and, more recently to providing insight on the function and the signaling cascades of neuroreceptors. For the last years, he has been largely involved in molecular simulation projects in molecular neurobiology exploiting high performance computing and machine learning.
h-index (Google): 67
Google Scholar: https://scholar.google.com/citations?user=G2R_F1sAAAAJ&hl=en

MEMBERSHIPS

American Chemical Society
Biophysical Society
German Biophysical Society
JARA-HPC, JARA-Brain (Jülich Aachen Research Alliance)

REFEREE FOR

Journals: Science, Nature Journals, PNAS, J. Am. Chem. Soc. and other ACS Journals, Phys. Rev. Lett. and other APS journals, Biophys. J, Plos Computational Biology.

EDITORIAL EXPERIENCE

Editorial Manager for the Journals: Proteins: Structure, Function, Bioinformatics, PlosONE.

GRANT REVIEWER EXPERIENCE

ERC grants, EU grants, ESF grants, BMBF grants, grants from the Swiss, Italian, European, German, Dutch Science Foundations, Humboldt grants, Research Council of KU Leuven.
JARA, PRACE, JSC, GCS/NIC, CINECA, RWTH grants for CPU time.

AWARDS

2024 Ambassador in Chemical Sciences in France, from CNRS Chemistry
The program was initiated in 2019 to give prestigious foreign researchers the opportunity to visit French laboratories that are active in their respective field, thereby establishing preliminary contacts and fostering international collaboration.
2021 Zimmer Int'l Scholar Award, University of Cincinnati, Cincinnati, USA
The award was given for my contributions in computational chemistry and biophysics. The Hans and Marlies International Scholar Program supports research projects between the University of Cincinnati and scientists from around the world.
2019 Foreigner Member of the Bologna Academy of Science, Bologna, Italy
The academy is an institution founded in 1690 to bring together scientists working in the different branches of knowledge, divided into "Physical Sciences" and "Moral Sciences". The Members are appointed for their scientific merits. I was awarded in the Physical Sciences Class (Biological Sciences Section) for my contributions to the development of computational biology.
2013 Distinguished Professorship, Vietnam National University, Ho Chi Minh City, Vietnam. The professorship was given in recognition of my contributions to the development of a computational biophysics line of research in Vietnam.

FUNDED GRANTS

1998: Quantum description of H-bonding in biological systems: € 100,000. Grant from the Italian Region Friuli Venezia Giulia.
2001: Structural inorganic biology in the post-genomic era: methodologies and "targeting": € 28,000: Grant of the Italian University Minister and SISSA.
2002: 'Molecular modeling of anti-Alzheimer's targets' € 40,440. Grant from the Biotechnological company Lay-Line Genomics, Rome (Italy).
2003: Role of Zn in enzymatic systems and in protein-protein interactions investigated by molecular dynamics simulations: € 31.300. Grant of the Italian University Minister and SISSA.
2003: "Structural inorganic biology in the post-genomic era: methodologies and targeting": € 28,000: Grant of the Italian University Minister and SISSA.
2003: "Computer Modeling of the Wild-type and Mutated HCN Ion Channels: Structure and Function": € 32,300. Grant from Glaxo-Wellcome, Stevenange, UK.
2004: "Interaction between HIV-1 Tat and its molecular targets: Molecular modeling and in vivo experiments" € 44,400. Grant from the Regione Friuli Venezia Giulia.
2004: "A new approach to drug design": € 30,000 from the Grant of the Italian University Minister.

2004: Two grants for PhD students (€ 60,000) given by the Italian Minister of Education for "Theoretical Investigation of Drug/Target interactions".
2005 'Theoretical Investigation of proteins involved in Alzheimer's Disease', Grant of the Italian University Minister (€ 200,000).
2005: Grant for mobility between Italy and Argentina: "Theoretical Investigations on Metallo Beta-Lactamases" (€ 10,000).
2005: GRAND grant for "Molecular simulation of neurodegenerative diseases" (€ 60,000).
2006: Telethon Grant for investigation of Parkinson's'' Disease: € 60,000.
2006–2008: Grant from the "Instituto Italiano di Tecnologia (IIT)" (€ 120,000) for investigation of neurodegenerative disease and of the molecular mechanism of the olfaction.
2006 Grant from the region Friuli-Venezia Giulia for "Action of Anticancer agents" (€ 10,000).
2006 Grant from the region Friuli-Venezia Giulia for "Action of beta-lactamases" (€ 10,000).
2007 Grant from the Illy-Coffee Company on the "Molecular basis of Olfaction and Taste" (€ 30,000).
2009 Grant from the Italian Ministry of Education on "Investigation of neurogenerative diseases" (€ 30,000).
2010–2013 DFG Grant for "Ion Permeation in the Single Channel of the Bacterial Porin NanC: an integrated in silico and in vitro approach" (€ 326,000).
2011 Grant from the Italian Ministry of Education on "Targeting HIV transcription to control infection and to purge post-integrative latency" (€ 30,000).
2010–2011 Nano Cancer Grant for "Investigating proteins involved in human tumors" (€ 30,000).
2011–2012 DFG International Cooperation Grant for the "Molecular basis of odorant ligands recognition: a computational study" project in collaboration with Prof. Hoang Zung, Director of the Institute for Science and Technology, Vietnam National University, Ho Chi Minh City (Vietnam) (€ 19,000).
2011–2013 BMBF grant for "International Co-operations between Germany and Argentina" (€ 8,400).
2012–2013 Grant from the Italian Ministry of Education on 'Cellular events in HIV-1 attack: a multi-disciplinary approach' (€ 60,000).
2012–2014 Grant from Illy-Coffee "In Silico Toxicology: Inhibiting Acrylamide Action" (€ 44,000).
2012–2015 DFG Grant for "Prediction of structural properties of cisplatin/protein adducts from QM/MM methods" (€ 159,500).

2013–2016 Human Brain Project grant: Molecular Dynamics Simulations" (€ 486,550).
2013–2016 DFG Grant for "Copper binding to the physiological form of the alpha-synuclein protein" (€ 166,350).
2013–2016 Human Brain Project for "Drug Design" (€ 250,000).
2014–2017 DFG Grant for "Computer-aided design of immunotoxins for a potential anti-cancer therapy" (€ 147,550).
2014–2017 DFG Grant ERA-Chemistry for "Design and synthesis of biologically inspired ion-conducting nanopores" (€ 168,680).
2015–2021 Grant from the Fondazione E. Illy for the "Computational Science of Coffee" (€ 250,000).
2015–2018 EU Grant, HPC-LEAP, "High Performance Computing in Life sciences, Engineering and Physics" (€ 428,559).
2015–2018 EU Grant for the BioExcel Center of Excellence in Computational Biology (€ 259,774).
2017–2020 DFG Research Group "Funktionale Dynamik von Ionenkanälen und Transportern – DynIon" (€ 319,200).
2017–2019 BMBF "Dual 2 Pet" grant (€ 155,984).
2017: "Development of software for multi-scale DNA simulation for application in drug-design and computational biomedical physics", Funding agency: Vietnam National University (€ 17,796). 2017: "Investigation on structures and physico-chemical characteristics of the gel network applied for topical cream formulations", Funding agency: NAFOSTED, (€ 56,834).
2017: Title: "Computational study of strong electrostatics interactions among DNA molecules inside DNA viruses in the presence of multivalent counterions", Funding agency: NAFOSTED, Grant number: 103.02-2012.75, Invested amount: (€ 25,386).
2017–2019: Development of NeuroDrug Design web-portal for design and synthesis of ligands for brain imaging and drug leads for neurodegenerative diseases, FIRST Project, MOST 13/FIRST/1.a/VNU1 (€148, 428).
2018–2021: EU ITN Grant, "Stimulate" (€ 498,432).
2018–2020: "Human Brain Project" grant: (€ 523,133).
2018–2023: DFG, "MultiSenses-MultiScales: Neue Ansätze zur Aufklärung neuronaler multisensorischer lntegration" (€ 433,618).
2019–2021: EU Grant, BioExcel-2 Center of Excellence for Computational Biology (€ 178,443).
2019–2022: BMBF, "PaTOR – Molecular simulation-based rational design of Painkillers targeting the Opioid Receptor" (€ 235,021).

2017–2019: EU Grant, HPC-LEAP, "High Performance Computing in Life sciences, Engineering and Physics" (€ 240,217).
2020–2022: HGF Grant, "Helmholtz European Partnering" (€ 750,207).
2020–2023: DFG Grant, "Functional dynamics of ion channels and transporters – DynIon – "for the subproject TP 06 "Proton transfer and substrate recognition in SLC17 transporters", DYNION-2 (€ 5,500).
2020–2023: EU-Grant, "Human Brain Project" (€ 497,850).
2020–2021: H2020-SC1-PHE-CORONAVIRUS-2020: Advancing knowledge for the clinical and public health response to the 2019-nCoV epidemic – EXaSCale smArt pLatform Against paThogEns for Corona Virus) (€ 96,250.00).
2021–2023: BMBF Grant: "Innovationspoolprojekt des Forschungsbereichs Information" (collaboration with JSC) (€ 39,185.50).
2023–2027: EU Grant: "Advanced computing, QuanTum algorIthms and data-driVen Approaches for science, Technology and Engineering (AQTIVATE)" (€ 521,078.40).
2023–2024: HGF Grant: Helmholtz European Partnering (HEP) (€ 500,000, INM-9 und INM-5).
11/2023–10/2025: HGF Grant: "Al- and HPC-based Design of Synthetic Receptor Assays for Continuous Metabolite Sensing" (AI-Receptor) (€ 125,000).
2024–2026: EU Grant: EBRAINS 2.0: "A Research Infrastructure to Advance Neuroscience and Brain Health" (€ 37,187).
2024–2026: HMC Grant: "Metadata Enrichment for SupraBank (MetaSupra)" (€ 95,202).

ORGANIZATIONAL EXPERIENCE

1. ICTP workshop on Structure and Function of Biomolecules, Trieste, Italy, 1998.
2. INFM National Meeting on Computational Methods in Biological Systems, Catania, Italy, 1999.
3. CECAM – PsiK workshop on Ab-initio modelling in the biological sciences, Lyon, France, 2001.
4. ICTP Conference on Interaction and Assembly of Biomolecules, Trieste, Italy, 2001.
5. ICTP College on Biophysics: From Molecular Genetics to Structural Biology, Trieste, 2001.
6. CECAM workshop on 'Ion Channels: from Biology to Physics', Lyon, France, 2002.
7. ICTP-INFM Conference on 'New Frontiers in Nano-Biotechnology: Monitoring Protein Function with Single-Protein Resolution', Trieste, Italy, 2003.

8. Psi-k Workshop on 'Ab Initio Modelling in Biological Systems', Trieste, Italy, 2004.
9. 'Biophysics Symposium' of the Psi-k conference, Schwäbisch Gmünd, Germany, 2005.
10. ICTP Conference on “Drug development for the third world", Trieste, Italy, 2006.
11. Psi-k workshop on ab initio modelling of biomolecules: methods and applications, Leiden, The Nederland, 2006.
12. CECAM workshop in Hybrid Atomistic Methods for Materials and Biological Systems, Lyon, France, 2006.
13. CECAM workshop on DNA: From Quantum to Coarse Grain, Lyon, France, 2006.
14. CPMD2008 ICTP conference on modeling and computation of structure and dynamics of condensed phase systems, Trieste, Italy, 2008.
15. Ab Initio Modelling in Applied Biosciences: Structure, Dynamics and Function, Uppsala University, Uppsala, Sweden, 2008.
16. International Workshop on Computational Biophysics (IWCBP-1), Ho Chi Minh City, Vietnam, 2010.
17. Workshop on Computational Modelling and Simulation of Biological Systems, Unidad de Gestión Cientifica, Institut Pasteur Montevideo, Uruguay, 2010.
18. Summer School on Atomistic Simulation Techniques for Material Science, Nanotechnology and Biophysics (CECAM Conference), SISSA, Trieste, Italy, 2010.
19. Conference on Molecular Aspects of Cell Biology: A Perspective from Computational Physics, ICTP Miramare, Trieste, Italy, 2010.
20. Workshop on Large-Scale Computer Simulation, German Research School Jülich / Aachen, Germany, 2011.
21. Workshop on “From Computational Biophysics to Systems Biology 2011”, FZJ, Jülich, Germany, 2011.
22. CPMD 2011 “Extending the limits of Ab initio Molecular Dynamics Simulations for Chemistry, Materials Science and Biophysics”, Barcelona, Spain, 2011.
23. “International Conference in Computational Medicine inside The 4th International Conference on the Development of Biomedical Engineering in Vietnam (BME4)”, Ho Chi Minh City, Vietnam, 2012.
24. CECAM Workshop at EPFL: Molecular Simulations of Membrane Proteins: From Biophysics to Pharmacological, Lausanne, Switzerland, 2012.

25. Workshop – Oak Ridge National Laboratory (Joint Institute for Computational Sciences (JICS) German Research School (GRS) Joint Workshop on Large Scale Computer Simulation), Knoxville, Tennesse, USA, 2012.
26. CPMD-Meeting 2013, Matter, life, light from ab initio molecular dynamics simulations, Leipzig, Germany, 2013.
27. CECAM Workshop – Forschungszentrum Jülich: Frontiers of computational biomolecular spectroscopy and mass spectrometry, Jülich, Germany, 2013.
28. CECAM Workshop – Forschungszentrum Jülich: "1198. Computational approaches to chemical senses", Jülich, Germany, 2015.
29. CECAM Workshop – Forschungszentrum Jülich: "Extended software development workshop", Jülich, Germany, 2015.
30. HPC-LEAP School – Forschungszentrum Jülich: "High Performance Computing in Life sciences, Engineering and Physics", Germany, 2016.
30. HPC-LEAP conference – Hybrid Methods in Molecular Simulation, Cagliari, 2017.
31. CECAM Workshop – Physiological role of ions in the brain: towards a comprehensive view by molecular simulation, Pisa, Italy, May 2018.
32. BME7 2018m KeyLab Workshop on "Recent computational and experimental advances in molecular medicine", International University Ho Chi Minh City, June 2018.
33. German workshop on structural predictions of membrane proteins, Jülich, November 2019.
34. CECAM Flagship Workshop – Scuola Normale Superiore: "15. Innovative strategies for neurodegenerative diseases: a perspective from molecular simulation, machine learning and experiment", Pisa, Italy, September 2021
35. FZJ INM&IBI Retreat 2021, Jülich, October 2021.
36. CECAM Flagship Workshop – Scuola Normale Superiore: "1063. Recent Advances in Machine Learning Accelerated Molecular Dynamics", Pisa, Italy, March 2022.
37. CECAM Flagship Workshop – "Ions, membrane and channels: Multiscale simulations from quantum to coarse-grain. A symposium in honor of Mike Klein.", Rome, Italy, October 2022.
38. 2nd German workshop on structural predictions of membrane proteins, Jülich, February 2023.
39. CECAM Flagship Workshop – "Biomolecular simulation and machine learning in the exascale era: first applications and perspectives", Pisa, Italy
40. Helmholtz European Partnering Workshop, Genoa, Italy, July 2023.**41.**

3rd German workshop on structural predictions of membrane proteins, Jülich, February 2024.

42. CECAM Flagship Workshop – "Towards quantitative cell biology through AI-driven software engineering for molecular simulations", Pisa, Italy, May 2024.

43. CECAM Flagship Workshop – "Computational chemistry across scales and disciplines: celebrating the 60th birthday of Ursula Röthlisberger", Lausanne, Switzerland, October 2024.

44. The 4th Keylab international Conference "Experimental and Computational Approaches in Molecular Medicine (ECAMM-2024)", Hanoi, Vietnam, October 2024.

45. "Innovative high-performance computing approaches for molecular neuromedicine", NOVEMBER 5th–7th, 2024, Forschungszentrum Jülich, Germany.

46. Recent Advances in Computational Biophysics: Methods and Applications, February 2025, Forschungszentrum Jülich, Germany.

INVITED LECTURES

IN CONFERENCES/WORKSHOPS

1992

1. Workshop on Advanced Calculations in Chemistry, Montelivretti, Italy.

1993

2. SISSA Discussion Day, SISSA, Trieste, Italy.

1994

3. September: European Bioinorganic Conference (EUROBIC II), Florence, Italy.

1995

4. June: ICTP International School of Computational Material Science, Trieste, Italy.
5. September: Italian National Congress of Crystallography, Taormina, Italy.

1996

6. August: European Bioinorganic Conference EUROBIC III, Noordwijkerhout, The Netherlands.

1997

7. March: NATO Advanced Workshop – Molecular Modeling and Dynamics of Biological Molecules Containing Metal Ions, S. Miniato, Italy.

1998

8. May: CECAM Workshop on Combined Quantum Mechanical-Classical Hybrid Methods for the Simulation of Chemical Reactions, Lyon, France.

9. June: CECAM Workshop on Computational Exploration of Energy Landscapes in Protein Dynamics, Turin, Italy.
10. August: European Bioinorganic Conference (EUROBIC IV), Sevilla, Spain.

1999

11. January: Car-Parrinello Molecular Dynamics Conference, Schloss Ringberg, Munich, Germany.
12. March: XVIII Congress of Theoretical Physics, Fai Della Paganella, Italy.
13. July: CECAM workshop on Molecular Dynamics Simulations of Lipid Membranes and Membrane Associated Proteins, Lyon, France.
14 August: ICTP Workshop on Calculation of Material Properties Using Total Energy and Force Methods and ab initio Molecular Dynamics, Trieste, Italy.
15. September: Fifth European SGI/Cray MPP Workshop, Bologna, Italy.

2000

16. March: International Conference on Research Trends in Science and Technology, Beirut, Lebanon.
17. March: 15 Years of Car-Parrinello in Physics and Chemistry, Minneapolis, USA.
18. August: Psi-k 2000 Conference, Schwabisch Gmund, Germany.
19. August: Statistical Mechanics of Complex Systems Conference, Bled, Slovenia.
20. October: CECAM workshop on Molecular modeling methods for the development of NMR in structural biology, Lyon, France.

2001

21. January Car-Parrinello Molecular Dynamics Meeting, Schloss Ringberg, Germany.
22. March: 2001 International Conference on Computational Nanoscience, Helton Head Island, SC, USA.
23. April: American Chemical Society Meeting, S. Diego, CA, USA.
24. June: CECAM workshop on New methods for combining Born-Oppenheimer ab initio calculations and empirical force fields in large scale simulation studies, Lyon, France.
25. June: Thirteenth Annual Workshop on Recent Developments in Electronic Structure Algorithms, Princeton, NJ, USA.
26. June: International Workshop on Protein Folding, Structure and Design, ICTP Workshop, Trieste, Italy.
27. September: 9th Swiss Workshop of Methodology in Receptor Research, Zurich, Switzerland.
28. October: ICGEB meeting on The Biology of the Post-Genomic Era, Trieste, Italy.

29. November: Workshop on Modeling Quantum Chemistry, Molecular dynamics and Spectroscopy, Leiden, The Netherlands.

2002

30. January: School on Biophysics: Water in Biomolecules, Venice, Italy.
31. March: US-Italy Workshop on Frontiers in Materials Research, Nanoscience and Nanotechnology Washington, DC, USA.
32. June: Italian Chemical Society Meeting, Verona, Italy.
33. July: Quantum Bioinorganic Chemistry Conference, Lund, Sweden.
34. August: WATOC Conference, Lugano, Switzerland.
35. September: EURESCO Conference on Computational Biophysics: Integrating Theoretical Physics and Biology, San Feliu, Spain.
36. December: COFIN meeting: Inorganic structural biology in the post-genomic era: methodologies and targeting, Florence, Italy.

2003

37. January: ICTP XI International Workshop on Computational Physics and Material Science: Total Energy and Force Methods, Trieste, Italy.
38. July: Second Joint French – Swiss Meeting on Medicinal Chemistry, Beaune, France.
39. September: Biocrystallography course: from gene to drug, Trieste, Italy.
40. September: Workshop on Ab initio Electrons Excitations Theory: Towards Systems of Biological Interest, San Sebastian, Spain.
41. November: Argentine Chemical Society: Meeting of the Organic Chemistry Section, Rosario, Argentina.
42. December: Italian Chemical Society: Meeting on the Computational Chemistry Division, Siena, Italy.

2004

43. March: EURESCO Conference on molecules of biological interest in the gas phase, Exeter, UK.
44. June: Workshop on Mathematical Virology, Oxford, UK.
45. June: Workshop on Soft Matter Physics, Dubrovnik, Croatia.
46. July: EMBO School of Biophysics, Verona, Italy.

2005

47. March International Conference on Research Trends in Science and Technology, Beirut, Lebanon.
48. March ACS National Meeting, San Diego, CA, USA.
49. April Workshop on Biophysics, Oxford, UK.
50. May: Workshop on Beta-Lacamases, Leonessa, Italy.
51. June: Workshop on Drug Design, Siena, Italy.
52. July: ERICE School CSCM 2005, Erice, Italy.

53. August: Telluride Workshop on Protein Dynamics, Telluride, CO, USA.
54. August: ACS National Meeting, Washington, USA.
55. August: Nancy EUROCHEM conference, Nancy, France.
56. September: Biomolecular Simulations 2005 Meeting, Bordeaux, France.
57. September: CPMD Meeting, Ascona, Switzerland.
58. November: Biological Dynamics: from Molecules to Cell, Amsterdam, The Netherlands.
59. December: Pacifichem, Honolulu, Hawai, USA.

2006

60. March: CINECA Meeting, Bologna, Italy.
61. June: ICTP Conference on Drug development for the third world, Trieste, Italy.
62. June: Trieste Conference on van der Waals Interactions, Trieste, Italy.
63. July: Varenna School on Protein Folding and Design, Varenna, Italy.
64. August CCP 2006: Conference on Computational Physics, Gyeongju, Korea.
65. October: CECAM workshop on Recent Advance in Modeling DNA, Lyon, France.
66. November: Argentinean National Biophysics Conference, Rosario, Argentina.
67. November: NMR Meeting of the Argentinean Biophysics Society, Rosario, Argentina.
68. November: EURESCO CONFERENCE on Inorganic Chemistry: Metal-Nucleic Acid interactions, Athens, Greece.

2007

69. January: 'Winter School on Physical Organic Chemistry', Bressanone, Italy.
70. April: Ab initio modeling of Biomolecules: Towards Computational Spectroscopy, Rome, Italy.
71. May: International Drug Discovery Science and Technology (IDDST) Conference, Shangai, China.
72. August: Conference on Mathematical Virology, Edimburgh, UK.
73. September: CCP 2007: Conference on Computational Physics, Bruxelles, Belgium.
74. September: CECAM workshop Ionic Transport: from Nanopores to Biological Channels, Lyon, France.
75. September: International Conference of Computational Methods in Sciences and Engineering, Corfu, Greece.
76. September: 2nd Opatija Meeting On Computational Solutions in the Life Sciences, Opatija, Croatia.
77. November: 5th Anniversary Congress of International Drug Discovery Science and Technology, Xi'an, China.

2008

78. April: MGMS Spring Meeting: Bio-inorganic Chemistry, Cardiff, UK.
79. June: Drug Design and Discovery for Developing Countries, Trieste, Italy.
80. June: Pushing the Boundaries of Biomolecular Simulations", Ascona, Switzerland.
81. July: 1st World Summit on Antivirals, Kunming, China.
82. September: 6th Congress on Electronic Structure: Principles and Applications – ESPA 2008, Palma de Mallorca, Spain.
83. October: 6th International Drug Discovery, Science and Technology (IDDST 2008), Beijing, China.
84. December: Ab Initio Modelling in Applied Biosciences: Structure, Dynamics and Function, Uppsala, Sweden.
85. December: 'Winter Modeling 2008, Pisa, Italy.

2009

86. January: 'Biomolecular Simulation Meeting 2009', York, UK.
87. June: '2nd Conference on Drug Development for the Third World: from Computational Molecular Biology to Experimental Approaches', Trieste, Italy.
88. July: 'Conference on Antivirals', Beijing, China.
89. August: 'SEADIM Conference', Habana and Varadero, Cuba.

2010

90. February-March: Workshop on Computational Modelling and Simulation of Biological Systems, Unidad de Gestión Cientifica, Institut Pasteur Montevideo, Uruguay.
91. April: TYC Workshop on Biological Interfaces, King's College London, England.
92. June: Multiscale modeling for engineering applications: from atoms to macroscopic systems, University of Turin, Italy.
93. July: Role of first principle calculations for mechanistic systems biology, Fritz-Haber-Institut der Max-Planck-Gesellschaft, Berlin, Germany.
94. August: 3rd Mathematical Virology Workshop Ambleside, The University of York, Cumbria, England.
95. September: PSI_K Conference 2010, Henry Ford Building, Berlin, Germany.
96. September: Universität Leipzig, Wilhelm-Ostwald-Institut für Physikalische und Theoretische Chemie, Leipzig, Germany.
97. October: BIT's 8th Annual Congress of 2010 International Drug Discovery Science and Technology, Beijing, China.
98. October: BIT's 1st Annual World Congress of NanoMedicine-2010, Beijing, China.

99. November, EESI Workshop, Amsterdam, Netherlands.
100. November: BioScience 2010 – Workshop on expanding the frontiers of biomolecular science, Forschungszentrum Jülich, Germany.
101. December: Lincei Meeting 2010 – Accademia Nazionale Dei Lincei, Rome, Italy.
102. December: HPC-Anwenderforum, Dresden, Germany.
103. December: Exascale Meeting, Barcelona, Spain.

2011

104. March: Workshop on Large-Scale Computer Simulation, German Research School for Simulation Sciences, Aachen / Jülich, Germany.
105. March: IPAM Long Program – Navigating Chemical Compound Space for Materials and Bio Design (CCS2011), Los Angeles, USA.
106. April: The European Future Technologies Conference and Exhibition, Budapest, Hungary.
107. May: Mainz Materials Simulation Days 2011, Mainz, Germany.
108. June: IBIOMETION Padova, Italy.
109. June: TheoBio2011 – 5th Theoretical Biophysics International Symposium, Madeira, Portugal.
110. July: Bioinorganic Chemistry School, University of Siena, Italy.
111. July: Workshop on Structural Bioinformatics and Computational Biophysics, SISSA – University of Trieste, Italy.
112. July: SEADIM – 8th Seminars of Advanced Studies on Molecular Design and Bioinformatics, University of Havana, Cuba.
113. July: CBSC Workshop: From Computational Biophysics to Systems Biology 2011, FZ / JSC Jülich, Germany.
114. September: CECAM Workshop: Combining experimental and computational techniques to study protein behavior, Lugano, Switzerland.
115. October: CECAM Conference: Innovative Approaches to Computational Drug Discovery. Lausanne, Switzerland.
116. October: 1st CAS-HGF Workshop on Supercomputing Beijing, China.
117. October: FET-HBP Pharma Application Workshop at EPFL, Lausanne, Switzerland.
118. December: FET-HBP Pharma Application Workshop at EPFL, Lausanne, Switzerland.

2012

119. January: Fourth International Conference on the Development of Biomedical Engineering (BME4), Ho Chi Minh City, Vietnam.
120. March: Jülich Winter School 2012, Forschungszentrum Jülich, Germany.

121. May: Leermakers Symposium, Wesleyan University Middletown, CT, USA.
122. May: CECAM 2012 Workshop on Alzheimer's disease, Paris, France.
123. May/June: Intel Leadership Conference on HPC for Life Science, Brussels, Belgium.
124. June: CECAM Workshop "DNA sequencing and detection with nanoprobes", Pisa, Italy.
125. July: X Girona Seminar on Theoretical and Computational Chemistry for the Modeling of Biochemical Systems: From Theory to Applications, Girona, Spain.
126. September: Workshop FZ Jülich / AlQuds University 2012, Forschungszentrum Jülich, Germany.
127. October: MMM 2012 – Multiscale Materials Modeling Conference, Biopolis, Singapore.

2013

128. February: Car-Parrinello Special Symposium at the King and Prince Resort on historic St. Simons Island, Georgia, USA.
129. May: XXXII National Meeting on Condensed Matter, Sao Paolo, Brazil.
130. The first International Workshop on Theoretical and Computational Physics (IWTCP-1): Condensed Matter, Softer Matter and Material Physics, Danang, Vietnam.
131. September: Ψk-CECAM Research Conference on Multi-Scale Modeling from First Principles, Platja d´Aro, Spain.
132. September: BDEBATE-BSC-IRB "Towards In Silico Humans" Barcelona, Spain.
133. September: XCIX Congresso Nazionale, Trieste, Italy.
134. October: CECAM Workshop – Frontiers of computational biomolecular spectroscopy and mass spectrometry, Forschungszentrum Jülich, Germany.
135. November: Biomed Conference on "Frontiers in dynamics simulations of biological molecules", Barcelona, Spain.
136. January: 6th SISSA/ELETTRA Prion Research Workshop, SISSA University of Trieste, Italy.
137. January: MolSim-2013, University of Amsterdam, Holland.
138. March: National University of Vietnam, Ho Chi Minh, Vietnam.
139. March: SISSA, University of Trieste, Italy.
140. May: Workshop on Macromolecular Structure and Dynamics, Uppsala University, Uppsala, Sweden.

2014

141. January: VI International Conference BIFI2014, Zaragoza, Spain.

142. January: Symposium (CompSE) – Reduced-Order Models in Computational Science and Engineering, Aachen, Germany.
143. April: Bertini's memorial conference, Structure and Dynamics of Biological Macromolecules, Rome, Italy.
144. April: Computer Simulations of Biological Systems, Theran, Iran.
145. May: Prion: Epigenetics and neurogenerative diseases, Trieste, Italy.
146. May: 1st Annual Meeting of the iBrain Graduate School, Düsseldorf, Germany.
147. May: Prostab, International Conference on Protein Stabilisation, Stresa, Italy.
148. May: Symposium on Current Topics in Molecular Biophysics, Sao Paulo, Brazil.
149. May: 43th SBBq, Foz de Iguazu, Brasil.
150. June: Prace SSC Meeting, Athens, Greece.
151. June: 5th International conference on the development of Biomedical Engineering, Ho Chi Minh City, Vietnam.
152. July: Modeling and Design of Molecular Materials 2014, Kudowa-Zdrój, Poland.
153. October: Virus and Cells – Computational Challenges and Approaches, Heidelberg, Germany.
154. December: CMMST VRE, Amsterdam, Nederlands.
155. December: CECAM, Dublin, Ireland.

2015

156. January: International Conference on Computational Physics (ICCP9), University of Singapore.
157. February: Workshop in honour of Wanda Andreoni, EPFL, Lausanne, Switzerland.
158. February: Modeling of Chemical and Biological Reactivity (MCBR4), Heidelberg, Germany.
159. March: Workshop "Nanopores: Experiments and mathematical modelling", Darmstadt, Germany.
160. September: "Italian Physics Society Conference", Palermo, Italy.

2016

161. February: "Minerva Mühlheim Conference", Mühlheim, Germany.
162. April: "Max Planck Institute-Rosario: Inauguration day conference", Rosario, Argentina.
163. May: Structural and Functional Annotation of Bioinorganic Systems, SISSA, Trieste, Italy.
164. June: Workshop "Biomolecular Simulations across Scales", University of Shanghai, Shanghai, China.

165. July: Advanced molecular simulation and experimental biophysical approaches for drug design, HCM City, Vietnam.
166. July: Advanced molecular simulation and experimental biophysical approaches for drug design within the 6th International Conference on the Development of Biomedical Engineering in Vietnam, VNU University, Hanoi, Vietnam.
167. July: Shanghai Workshop on Frontiers in Molecular Biophysics, University of Shanghai, Shanghai, China.
168. August: ACS Philadelphia National Meeting, Philadelphia, USA.
169. October: Erice Free Energy Landscapes, E. Majorana Center, Erice, Italy. Invited talk on Investigating neuronal G-protein coupled receptors by molecular simulation.
170. November: New insights and advances in neuroscience and oncology, Max Planck Institute, Rosario, Argentina.

2017

171. February: DAAD Gatemesse, New Dehli, India.
172. February: DAAD Gatemesse, Hyderabad, India.
173. April: Deutsche Biotechnologietage, Hannover, Germany.
174. May: CECAM workshop, Paris, France.
175. June: TheoBio, San Sebastian, Spain.
176. July: International Conference "Mathematical Modeling and Computational Physics, 2017" (MMCP2017), Joint Institute for Nuclear Research, Dubna, Russia.
177. July: International Conference on Biological Inorganic Chemistry, Florianopolis, Brazil.
178. September: National Convention on Inorganic chemistry, Paestum, Italy.
179. October: Viruses and Cells – Computational Challenges and Approaches, Heidelberg, Germany.

2018

180. March: CECAM: Multiscale modelling in electrophysiology, Università della Svizzera Italiana, Lugano, Switzerland.
181. May: Exploring and Quantifying Rough Free Energy Landscapes, Erice, Italy.
182. June: Protein Electrostatics meeting, Belgrade, Serbia.
183. July: Ion in Solution, Telluride, CO, USA.
184. July: CECAM workshop Frontiers and challenges of computing metals for biochemical, medical and technological applications, Paris, France.
185. July: Theoretical Chemistry and Computational Modelling, Pisa, Italy.
186. September: CECAM workshop, Charged Species in Bulk and at Interfaces: Mobility and Motility of Macromolecular Systems, Vienna, Austria.

187. November: New insights and advances in neuroscience and oncology, Max Planck Institute, Rosario, Argentina.

2019

188. December: Understanding Nature from Computation, Shanghai, China.
189. February: CECAM workshop, Lausanne, Switzerland.
190. March: Workshop “Molecular Dynamics Today”, Bologna, Italy.
191. May: 12th Wartburg Symposium on Flavor Chemistry & Biology, Wartburg, Germany.
192. July: BrainComp, Cetraro, Italy.
193. September: Conference in Portugal “Synuclein Meeting 2019”.
194. September: Congress University Siena.
195. September: Congress Genoa.
196. October: CECAM workshop, Israel.
197. November: German workshop on structural predictions of membrane proteins (DYNION), Jülich.

2020

198. February: HBP Summit Athens, Greece.

2021

199. September: EBRAINS National Node Germany at the Bernstein Conference.

2022

200. July: RTG2450 / GRK2450 Workshop “Multiscale modelling in materials science, chemistry, and biology”, KIT, Karlsruhe, Germany.
201. July: Barcelona MMSML Workshop Methods in Molecular Simulations and Machine Learning, Barcelona, Spain.
202. July: CECAM Workshop “Multiscale Molecular Dynamics with MiMiC", École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland.
203. September: CECAM Workshop “20 years of Metadynamics", École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland.
204. September: CECAM Workshop “Understanding function of G-Protein Coupled Receptors by atomistic and multiscale simulations”, Università della Svizzera italiana, Lugano, Switzerland.
205. September: 23rd European Symposium on Quantitative Structure-Activity Relationship, Heidelberg University and Heidelberg Institute for Theoretical Studies, Heidelberg, Germany.

2023

206. March: 35th Molecular Modelling Workshop 2023 in Erlangen, Germany.
207. April: Joint CECAM-CSF (ETH Zurich) Conference “Multiscale

Simulations of DNA from Electrons to Nucleosomes", Ascona, Switzerland.

208. July: Telluride Ion Channel Workshop, Colorado, USA.
209. August: BPS Conference "Protons Reactions: From Basic Science to Biomedical Applications", Tahoe, California, USA.
210. September: Workshop "Reducing complexity of nonequilibrium systems", Freiburg, Germany.

2024

211. August: ACS meeting, Symposium honoring Prof. Merz, Tahoe, California, USA.
212. September: CECAM workshop "Understanding the function of G-Protein Coupled Receptors by atomistic and multiscale simulations", Lugano, CH.
213. September: CECAM Workshop understanding peripheral protein membrane interactions membrane recognition dynamics function and therapeutic opportunities, Lausanne, CH.
214. September: CECAM workshop "Pushing the Frontiers of MD simulations" in Lausanne, CH.
215. October: ECAMM 2024 workshop, University of Hanoi, Vietnam.

IN UNIVERSITIES AND RESEARCH INSTITUTES

1995

1. August: Pharmacy Department, ETH, Zurich, Switzerland.

1996

2. September: The Beckman Institute of the University of Illinois, Urbana-Champaign, IL, USA.
3. November: C4 Workshop – Use of Fast Computers in Molecular Chemistry – ETH, Zurich, Switzerland.

1997

4. February: Chemistry Department, Dortmund University, Germany.
5. October: Biophysics Department, ETH, Zurich.

1998

6. January: Joint ICTP/SISSA Condensed Matter Seminar, Trieste, Italy.
7. July: Institute of Structural Biology Jean-Pierre Ebel', Grenoble, France.
8. October: National Institute of Chemistry, Ljubljana, Slovenia.
9. October: Department of Chemistry, University of Zagreb, Croatia.

1999

10. January: Chemistry Department, Trieste University, Trieste. Italy.
11. July: The Beckman Institute of the University of Illinois, Urbana-Champaign, IL, USA.

12. July: Department of Theoretical Biophysics, Los Alamos National Labs, Los Alamos (NM), USA.
13. July: Chemistry Department, University of Princeton, Princeton (NJ), USA.
14. September: Biophysics Department, University of Rosario, Argentina.
15. September: Chemistry Department, University of Buenos Aires; Argentina.
16. December: Chemistry Department, University of Siena, Italy.

2000

17. March: Physics Department, UCSD, San Diego, CA, USA.
18. March: Chemistry Department, UC Irvine, CA, USA.
19. March: The Beckman Institute of the University of Illinois, Urbana-Champaign, IL (USA).
20. April: Physics Department, University of Padua, Italy.
21. June: National Institute of Chemistry, Ljubljana, Slovenia.
22. July: Fritz-Haber Institute, Berlin, Germany.
22. September: Pharmacy Department, University of Madison, WC, USA.
23. October: Department of Biology, University of Osnabrueck, Germany.
24. December: Department of Physics, University of Florence, Italy.

2001

25. March: Department of Biophysics, Wesleyan University, Middletown, CT, USA.
26. March: Chemistry Department, Univ. of Pennsylvania, Philadelphia, USA.
27. July: Department of Physics, University of Modena, Italy.
28. October: Chemistry Department, University of Lund, Sweden.

2002

29. March: Glaxo Research Center, Verona, Italy.
30. September: Department of Pharmacy, University Pompeu Fabra, Barcelona, Spain.

2003

31. March: Venetian Institute of Molecular Medicine, Padua, Italy.
32. May: Department of Physics, University of Modena, Italy.
33. June: C4 Workshop -Use of Fast Computers in Molecular Chemistry – ETH, Zurich, Switzerland.
34. November: Department of Biophysics, University of Rosario, Argentina.

2004

35. March: Department of Physics, University of Modena, Italy.
36. March: Department of Chemistry, University of Palermo, Italy.
37. April: Italian Research Council, Pisa, Italy.

2005

38. March: Department of Chemistry, University of Cambridge, UK.

39. April: Department of Chemistry, University of Ljubljana, Slovenia.
40. June: University of Linz, Austria.

2006

41. December: Department of Chemistry, University of Sussex, UK.

2007

42. February: Department of Physics, University of Ho-Chi-Minh-City, Vietnam.

2008

42. February: Swinburne University, Melbourne, Australia.
43. September: Scuola Normale Superiore di Pisa, Pisa, Italy.

2009

45. October: University of Bari, Italy
46. November: University of Santa Barbara, CA, USA.

2010

47. December: University of Siena, Siena, Italy.

2011

48. February: Leibniz Institute of Molecular Pharmacology, Berlin, Germany.
49. May: University Hospital Aachen, Germany.
50. August: University College Dublin, Ireland.
51. September: University of Southampton, England.
52. October: Johannes Kepler University, Linz, Austria.
53. October: Beijing University of Technology, Beijing, China.
54. December: Biophysical Society Argentina, Buenos Aires, Argentina.

2012

55. February: SISSA, University of Trieste, Italy.
56. June: University of Perugia, Italy.
57. September: Institut de Biologie Physico-Chimique (IBPC), Paris, France.
58. October: Jena University Hospital, Germany.
59. November: Institute of Organic Chemistry and Biochemistry AS CR, Prague, Czech Republic.

2013

60. January: Master in Coffee Economics and Science – Ernesto Illy Foundation 2013, Trieste, Italy.
62. Psi-k School in Ab initio Molecular Dynamics for Biomolecules in S. Stefano di Sessanio, University of L'Aquila, Italy.
63. November: University of Catania, Italy.
64. December: Heidelberger Institut für Theoretische Studien (HITS), Heidelberg, Germany.
65. December: C. u. O. Vogt-Institut für Hirnforschung. Universitätsklinikum Düsseldorf, Germany.

2014

66. April: Deutsches Institut für Ernährungsforschung (DIFE), Berlin, Germany.
67. October: University of Parma, Italy.
68. December: Max Planck Institute for Polymer Research, Mainz, Germany.

2015

69. April: The Hebrew University, Jerusalem, Israel.

2016

70. May: Università Bicocca, Milan, Italy.

2017

71. April: University of Cagliari, First Workshop on Hybrid Methods in Molecular Simulation, Italy.
72. December: Center for Research and Advanced Studies, Mexico City, Mexico.

2018

73. May: University of Erlangen, Physics Department, Germany.
74. June: FZJ-Hebrew University Day, Jerusalem, Israel.
75. October: Computer Simulation in the Physical & Life Sciences, Rom, Italy.

2019

76. July: Uppsala University, Sweden.
77. September: University of Porto, Portugal.

2020

78. June: International Centre for Theoretical Physics, Trieste, Italy (webseminar).
79. November: PROTON (training event on molecular dynamics simulations) (webseminar).

2021

80. August: Istituto Italiano di Tecnologia (IIT), Genova, Italy.

2022

81. April: Departmental Colloquium: 20th Annual Hans & Marlies Zimmer International Scholar Program, Department of Chemistry, University of Cincinnati, USA.
82. December: Medicinal Chemistry Seminars 2022, University of Modena and Reggio Emilia, Italy.

2023

83. January: HBP BRAVE Meeting, Dipartimento di Scienza e Tecnologia del Farmaco Università degli Studi di Torino, Italy

2024

84. August: Cinestav, Mexico City, Mexico.
85. December: CNRS Paris, France.
86. December: CNRS Nancy, France.
87. December: CNRS Strasburg, France.
88. December: CNRS Marseille, France.

EXTERNAL EXAMINER EXPERIENCE

External examiner for the PhD thesis of:

(i) E. Sigfridsson, Department of Chemistry, Lund University, Sweden (2002).
(ii) Davide Provasi, Department of Physics, University of Milano, Italy (2002).
(iii) Lars Olsen, Department of Mathematics and Physics, The Royal Veterinary and Agricultural University, Frederiksberg, Denmark (2003).
(iv) J. Raber, Uppsala, Sweden (2007).
(v) Sophie Schwaiger, Karolinska University, Stockholm, Sweden (2012).
(vi) X. Xu, virtual Master thesis defence at École Polytechnique Fédérale de Lausanne (EPFL), (2021).
(vii) Maria Letizia Merlini, virtual PhD thesis defence at École Polytechnique Fédérale de Lausanne (EPFL), (2022).
(viii) Haydar Taylan Turan, virtual PhD thesis defence at University Basel, Switzerland, (2022).
(ix) Giudo Frisari, virtual PhD thesis defence at École Polytechnique Fédérale de Lausanne (EPFL), (2022).

External examiner for the Master thesis of:

Grace Mayuni, University of Cape Town, South Africa (2022).

HIRING COMMITTEE EXPERIENCE

External member for hiring a W3 professor in theoretical biophysics at the University of Linz (Austria), 2008.
External member of commission for hiring a W2 professor in experimental biophysics at RWTH, University of Aachen (Germany), 2012.
External member in the evaluation committee for a permanent associate professor position in theoretical molecular and bio-molecular physics at the Department of Physics and Astronomy, University of Aarhus, Denmark, 2015.
External member of commission for hiring W3 Computational Life Science at RWTH Aachen University, 2020.
External member of commission for hiring a W2 professor in "Bildgebung in der Medizinphysik", Jülicher Model, Bergische Universität Wuppertal, FZJ, 2021
External member of commission for Junior Research Fellows, Pisa, Italy, 2022

STUDENTS

(Co-)supervised PhD students:

Frank Alber (1996–1998); Lorenzo de Santis (1997–1999); Leonardo Guidoni (1998–2000); Stefano Piana (1998–2000); Sergio Pantano (1999–2001); Maria Lore Sulpizi (1999–2001); Giovanni Settanni (1999–2001); Valeria Costa (1999–2002); Marco Punta (1999–2002); Matteo dal Peraro (2000–2004); Katrin Spiegel (2000–2004); Michele Cascella (2000–2004); Alejandro Giorgetti (2000–2004); Pietro Vidossich (2001–2006); Marco Berrera (2002–2006); Marilisa Neri (2003–2007); Giacomo Fiorin (2003–2006); Vincenzo Carnevale (2003–2007); Kamil Khafizof (2003–2008); Fernando Herrera (2004–2008); Attilio Vargiu (2003–2008); Agata Kranic (2004–2008); Fabio Simona (2004–2008); Vanessa Leone (2005–2009); Rolando Hong (2005–2009); Roberto Marchese (2006–2010); Giulia Rossetti (2006–2010); Salvatore Bongarzone (2006–2010); Gianpaolo Chiriano (2006–2010); Valeria Losasso (2006–2012); Chao Zhang (2009–2012); Ha Hung Chuong Nguyen (2009–2013); Quy Vo Cam (2009–2013); Trung Hai Nguyen (2009–2013); Trang Do (2009–2013); Xiaojing Cong (2007–2013); Domenica Dibenedetto (2010–2014); Jinyu Li (2011–2015); Massimo Sandal (2012–2016); Matic Pavlin (2013–2016); Ruyin Cao (2013–2017); Anna Bochicchio (2013–2017); Viacheslav Bolnykh (2015–2019); Wenping Lyu (2015–2019); Thomas Tarenzi (2015–2019); Luca Pesce (2015–2019); Fabrizio Fierro (2015–2019); Luca Maggi (2016–2020); Jakob Schneider (2016–2020); Ksenia Korshunova (2016–2021); Somayeh Asgharpour (2019–2022); Oscar Palomino-Hernandez (2018–2022); Ke Zuo (2019–2023); Divya Sitani (2017–2024);Florian Schackert (2019–2023); Bharath Raghavan (2020–2024). Several of my PhD students are now professors in prestigious universities and research institutions worldwide, including EPFL, University of South California, University of Oslo, University of Uppsala, RWTH Aachen University, NIH.

Currently (co-)supervising the PhD students:

Nitin Malapally (2021), Linh Hoang Gia (2022), Hoa Thi Nguyen (2022), Marta Devodier (2023), Sachin Shivakumar (2023), Song Xie (2023), Lukas Müllender (2023), Song Xie (2024).

Supervised the master students:

Frank Alber (1996); Matteo dal Peraro (2000); Pietro Vidossich (2002); Paola Lupieri (2006); Michela Candotti (2007); Felix Ihno Stamm (2021); Anton Dorn (2022), Eva Bertalan (2022), Vishal Sudha Baghavath Eswaran (2022).

TEACHING

Course at RWTH Aachen University, Aachen, Germany from WS 2023/24, Computer simulation and machine learning for molecular medicine, (60 hours, Mandatory Course, about 30 students).

Course at RWTH Aachen University, Aachen, Germany, from 2010 till 2023: From Molecular to Continuum Physics (70 hours, Mandatory Course, about 30 students).

PUBLICATIONS

1. Conflitti P, Lyman E, Sansom MSP, Hildebrand PW, Gutiérrez-de-Terán H, Carloni P, Ansell TB, Yuan S, Barth P, Robinson AS, Tate CG, Gloriam D, Grzesiek S, Eddy MT, Prosser S, Limongelli V. Functional dynamics of G protein-coupled receptors reveal new routes for drug discovery. Nat Rev Drug Discov. 2025 Jan 2. doi: 10.1038/s41573-024-01083-3.
2. Xie, S. ; Zuo, K. ; De Rubeis, S. ; Ruggerone, P. ; Carloni, P. Molecular basis of the CYFIP2 and NCKAP1 autism-linked variants in the WAVE regulatory complex. Protein science 34(1), e5238 (2025) [10.1002/pro.5238].
3. Paiva P, Ippoliti E, Carloni P, Fernandes PA, Ramos MJ Atomistic adsorption of PETase onto large-scale PET 3D-models that mimic reality. Phys Chem Chem Phys. 2025 Jan 22;27(4):2139-2150. doi: 10.1039/d4cp03488k.
4. Carloni P, Sanbonmatsu K. Exascale simulations and beyond. Curr Opin Struct Biol. 2024 Dec;89:102939. doi: 10.1016/j.sbi.2024.102939. Epub 2024 Oct 5.
5. Müllender L, Rizzi A, Parrinello M, Carloni P, Mandelli D. Effective data-driven collective variables for free energy calculations from metadynamics of paths PNAS Nexus. 2024 Apr 12;3(4):pgae159. doi: 10.1093/pnasnexus/pgae159.
6. Xie, S. ; Zuo, K. ; De Rubeis, S. ; Ruggerone, P. ; Carloni, P. Molecular basis of the CYFIP2 and NCKAP1 autism-linked variants in the WAVE regulatory complex. DOI: 10.26434/chemrxiv-2024-x3sn8.
7. de Bruyn, E. (First author) ; Dorn, A. E. (First author) ; Rossetti, G. ; Fernandez, C. ; Outeiro, T. F. ; Schulz, J. B. ; Carloni, P. (Last author) Impact of Phosphorylation on the Physiological Form of Human alpha-Synuclein in Aqueous Solution. DOI: 10.1021/acs.jcim.4c01172.
8. Dmitrieva, N. ; Gholami, S. ; Alleva, C. ; Carloni, P. ; Alfonso-Prieto, M.; Fahlke, C. Transport mechanism of DgoT, a bacterial homolog of SLC17 organic anion transporters. DOI: 10.1038/s44318-024-00279-y.
9. Diaz-Pier, S. ; Carloni, P. Impact of quantum and neuromorphic computing on biomolecular simulations: Current status and perspectives. DOI: 10.1016/j.sbi.2024.102817.
10. Antalík, A. ; Levy, A. ; Kvedaravičiūtė, S. ; Johnson, S. K. ; Carrasco-Busturia, D. ; Raghavan, B. ; Mouvet, F. ; Acocella, A. ; Das, S. ; Gavini, V. ; Mandelli, D. ; Ippoliti, E. ; Meloni, S. ; Carloni, P. ; Rothlisberger, U. ; Olsen, J. M. H. MiMiC: A high-performance framework for multiscale molecular dynamics simulations. DOI: 10.1063/5.0211053.

11. Malapally, N. (First author) ; Bolnykh, V. ; Suarez, E. ; Carloni, P. ; Lippert, T. ; Mandelli, D. 3D DFT by block tensor-matrix multiplication via a modified Cannon's algorithm: Implementation and scaling on distributed-memory clusters with fat tree networks. DOI: 10.1016/j.jpdc.2024.104945.
12. Dmitrieva, N. ; Gholami, S. ; Alleva, C. ; Carloni, P. ; Alfonso-Prieto, M. ; Fahlke, C. M. Transport mechanisms of DgoT—a bacterial homolog of organic anion transporters. DOI: 10.1016/j.bpj.2023.11.811.
13. Fahlke, C. (Editor) ; Asgharpour, S. ; Chi, L. A. ; Spehr, M. ; Carloni, P. ; Alfonso-Prieto, M. Fluoride Transport and Inhibition Across CLC Transporters. DOI: 10.1007/164_2022_593.
14. L Müllender, A Rizzi, M Parrinello, P Carloni, D Mandelli, Effective data-driven collective variables for free energy calculations from metadynamics of paths, PNAS Nexus, page 159, Oxford University Press (online), 2024.
15. TL Beck, P Carloni, DN Asthagiri. All-Atom Biomolecular Simulation in the Exascale Era, Journal of Chemical Theory and Computation, 20(5):1777-1782, 2024.
16. J. Schimunek, P. Seidl, ..., P. Carloni, ..., A. Varnek|, G. Klambauer, T.M. Hermans, A community effort in SARS-CoV-2 drug discovery, Molecular Informatics 43 (1), e202300262, 2024.
17. L Mazzei, A Paul, M Cianci, M Devodier, D Mandelli, P Carloni, S Ciurli, Kinetic and structural details of urease inactivation by thiuram disulphides, Journal of Inorganic Biochemistry 250, 112398, 2024.
18. S Albani, E Costanzi, GL Hoang, M Kuzikov, M Frings, N Ansari, N Demitri, ..., P Carloni, ..., G Rossetti, Unexpected Single-Ligand Occupancy and Negative Cooperativity in the SARS-CoV-2 Main Protease, Journal of Chemical Information and Modeling, 2024, 64(3):892-904.
19. Paulikat M, Piccini G, Ippoliti E, Rossetti G, Arnesano F, Carloni P. Physical Chemistry of Chloroquine Permeation through the Cell Membrane with Atomistic Detail. J Chem Inf Model. 2023; 63(22):7124-7132.
20. Rizzi A, Carloni P, Parrinello M. Free energies at QM accuracy from force fields via multimap targeted estimation. Proc Natl Acad Sci U S A. 2023; 120(46):e2304308120.
21. Joseph BP, Weber V, Knüpfer L, Giorgetti A, Alfonso-Prieto M, Krauß S, Carloni P, Rossetti G. Low Molecular Weight Inhibitors Targeting the RNA-Binding Protein HuR. Int J Mol Sci. 2023; 24(17):13127.
22. Zhang J, Song D, Schackert FK, Li J, Xiang S, Tian C, Gong W, Carloni P, Alfonso-Prieto M, Shi C. Fluoride permeation mechanism of the Fluc channel in liposomes revealed by solid-state NMR. Sci Adv. 2023; 9(34):eadg9709.
23. Goßen J, Ribeiro RP, Bier D, Neumaier B, Carloni P, Giorgetti A, Rossetti G. AI-based identification of therapeutic agents targeting GPCRs: introducing

ligand type classifiers and systems biology. Chem Sci. 2023; 14(32):8651-8661.
24. Raghavan B, Paulikat M, Ahmad K, Callea L, Rizzi A, Ippoliti E, Mandelli D, Bonati L, De Vivo M, Carloni P. Drug Design in the Exascale Era: A Perspective from Massively Parallel QM/MM Simulations. J Chem Inf Model. 2023; 63(12):3647-3658.
25. Zuo K, Kranjc A, Capelli R, Rossetti G, Nechushtai R, Carloni P. Metadynamics simulations of ligands binding to protein surfaces: a novel tool for rational drug design. Phys Chem Chem Phys. 2023; 25(20):13819-13824.
26. Mueller NPF, Carloni P, Alfonso-Prieto M. Molecular determinants of acrylamide neurotoxicity through covalent docking. Front Pharmacol. 2023; 14:1125871.
27. Raghavan B, Schackert FK, Levy A, Johnson SK, Ippoliti E, Mandelli D, Olsen JMH, Rothlisberger U, Carloni P. MiMiCPy: An Efficient Toolkit for MiMiC-Based QM/MM Simulations. J Chem Inf Model. 2023; 63(5):1406-1412.
28. Schackert FK, Biedermann J, Abdolvand S, Minniberger S, Song C, Plested AJR, Carloni P, Sun H. Mechanism of Calcium Permeation in a Glutamate Receptor Ion Channel. J Chem Inf Model. 2023; 63(4):1293-1300.
29. Oliva F, Musiani F, Giorgetti A, De Rubeis S, Sorokina O, Armstrong DJ, Carloni P, Ruggerone P. Modelling eNvironment for Isoforms (MoNvIso): A general platform to predict structural determinants of protein isoforms in genetic diseases. Front Chem. 2023; 10:1059593.
30. Zuo K, Capelli R, Rossetti G, Nechushtai R, Carloni P. Predictions of the Poses and Affinity of a Ligand over the Entire Surface of a NEET Protein: The Case of Human MitoNEET. J Chem Inf Model. 2023; 63(2):643-654.
31. B Neumaier, R Cologni, M Holschbach, D Bier, P Carloni, 18F-Labelled inhibitors for targeting of IDH1 mutant gliomas, Nuclear Medicine and Biology 126, 108637, 2023.
32. N Dmitrieva, C Alleva, MA Prieto, P Carloni, CM Fahlke, Exploring the transport cycle of DgoT, a bacterial homolog of human vesicular glutamate transporters, Biophysical Journal 122 (3), 231a, 2023.
33. Paulikat M, Vitone D, Schackert FK, Schuth N, Barbanente A, Piccini G, Ippoliti E, Rossetti G, Clark AH, Nachtegaal M, Haumann M, Dau H, Carloni P, Geremia S, De Zorzi R, Quintanar L, Arnesano F. Molecular Dynamics and Structural Studies of Zinc Chloroquine Complexes. J Chem Inf Model. 2023; 63(1):161-172.
34. Paulikat M, Aranda J, Ippoliti E, Orozco M, Carloni P, Proton Transfers to DNA in Native Electrospray Ionization Mass Spectrometry: A Quantum Mechanics/Molecular Mechanics Study, J. Phys. Chem. Lett. 2022.
35. Marjault HB, Yang-Sung S, Zuo K, Carloni P, Mittler R, Nechushtai R. Structure-Based Screening Reveals a Ligand That Stabilizes the [2Fe-2S] Clusters of Human mitoNEET and Reduces Ovarian Cancer Cell Proliferation, The Journal of Physical Chemistry B, 2022.

36. Asgharpour S, Chi LA, Spehr M, Carloni P, Alfonso-Prieto M. Fluoride Transport and Inhibition Across CLC Transporters. Handb Exp Pharmacol. 2022.
37. Buratti FA, Boeffinger N, Garro HA, Flores JS, Hita FJ, Gonçalves PDC, Copello FDR, Lizarraga L, Rossetti G, Carloni P, Zweckstetter M, Outeiro TF, Eimer S, Griesinger C, Fernández CO. Aromaticity at position 39 in α-synuclein: A modulator of amyloid fibril assembly and membrane-bound conformations. Protein Sci. 2022; 31(7):e4360.
38. Colini Baldeschi A, Zattoni M, Vanni S, Nikolic L, Ferracin C, La Sala G, Summa M, Bertorelli R, Bertozzi SM, Giachin G, Carloni P, Bolognesi ML, De Vivo M, Legname G. Innovative Non-PrP-Targeted Drug Strategy Designed to Enhance Prion Clearance. J Med Chem. 2022; 65(13):8998-9010.
39. van Keulen SC, Martin J, Colizzi F, Frezza E, Trpevski D, Diaz NC, Vidossich P, Rothlisberger U, Hellgren Kotaleski J, Wade RC, Carloni P, Multiscale molecular simulations to investigate adenylyl cyclase-based signaling in the brain, WIREs, 2022.
40. Ahmad K, Rizzi A, Capelli R, Mandelli D, Lyu W, Carloni P. Enhanced-Sampling Simulations for the Estimation of Ligand Binding Kinetics: Current Status and Perspective. Front Mol Biosci. 2022; 9:899805.
41. Palomino-Hernandez O, Santambrogio C, Rossetti G, Fernandez C, Grandori R, Carloni P. Molecular Dynamics-Assisted Interpretation of Experimentally Determined Intrinsically Disordered Protein Conformational Components: The Case of Human α-Synuclein. J Phys Chem B. 2022; 126(20):3632-3639.
42. Marjault HB, Karmi O, Zuo K, Michaeli D, Eisenberg-Domovich Y, Rossetti G, de Chassey B, Vonderscher J, Cabantchik I, Carloni P, Mittler R, Livnah O, Meldrum E, Nechushtai R. An anti-diabetic drug targets NEET (CISD) proteins through destabilization of their [2Fe-2S] clusters. Commun Biol. 2022; 5(1):437.
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45. Gia Hoang L, Goßen J, Capelli R, Nguyen TT, Sun Z, Zuo K, Schulz JB, Rossetti G, Carloni P. Multiple Poses and Thermodynamics of Ligands Targeting Protein Surfaces: The Case of Furosemide Binding to mitoNEET in Aqueous Solution. Front Cell Dev Biol. 2022; 10:886568.

46. Meyer M, Jurek B, Alfonso-Prieto M, Ribeiro R, Milenkovic VM, Winter J, Hoffmann P, Wetzel CH, Giorgetti A, Carloni P, Neumann ID. Structure-function relationships of the disease-linked A218T oxytocin receptor variant. Mol Psychiatry. 2022; 27(2):907-917.
47. Zhao Q, Capelli R, Carloni P, Lüscher B, Li J, Rossetti G. Enhanced Sampling Approach to the Induced-Fit Docking Problem in Protein-Ligand Binding: The Case of Mono-ADP-Ribosylation Hydrolase Inhibitors. J Chem Theory Comput. 2021; 17(12):7899-7911.
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50. Zuo K, Marjault HB, Bren KL, Rossetti G, Nechushtai R, Carloni P. The two redox states of the human NEET proteins' [2Fe-2S] clusters. J Biol Inorg Chem. 2021; 26(7):763-774.
51. Ansari N, Rizzi V, Carloni P, Parrinello M. Water-Triggered, Irreversible Conformational Change of SARS-CoV-2 Main Protease on Passing from the Solid State to Aqueous Solution. J Am Chem Soc. 2021; 143(33):12930-12934.
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53. Gossen J, Albani S, Hanke A, Joseph BP, Bergh C, Kuzikov M, Costanzi E, Manelfi C, Storici P, Gribbon P, Beccari AR, Talarico C, Spyrakis F, Lindahl E, Zaliani A, Carloni P, Wade RC, Musiani F, Kokh DB, Rossetti G. A Blueprint for High Affinity SARS-CoV-2 Mpro Inhibitors from Activity-Based Compound Library Screening Guided by Analysis of Protein Dynamics. ACS Pharmacol Transl Sci. 2021; 4(3):1079-1095.
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Molecular Basis of CLC Antiporter Inhibition by Fluoride

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ABSTRACT: CLC channels and transporters conduct or transport various kinds of anions, with the exception of fluoride, which acts as an effective inhibitor. Here, we performed sub-nanosecond DFT-based QM/MM simulations of the *E. coli* anion/proton exchanger ClC-ec1 and observed that fluoride binds incoming protons within the selectivity filter, with excess protons shared with the gating glutamate E148. Depending on E148 conformation, the competition for the proton can involve either a direct F^-/E148 interaction or the modulation of water molecules bridging the two anions. The direct interaction locks E148 in a conformation that does not allow for proton transport, and thus inhibits protein function.

The CLC family encompasses anion channels and anion/proton exchangers across the three kingdoms of life[1−6] and fulfills various cell functions. Human CLC channels and transporters contribute to the regulation of cellular excitability, epithelial ion transport, or Cl^- and pH homeostasis in intracellular organelles.[7−9] Mutations in genes encoding these proteins cause a variety of diseases, including muscle overexcitability, deafness, epilepsy, intellectual disability, nephrolithiasis, and osteopetrosis.[10,11] The significant physiological importance as well as the intriguing coexistence of voltage-gated anion channels and anion/proton transporters in one gene family makes the CLC family a highly interesting topic for studying the chemical basis of transmembrane ion transport.

The Cl^-/H^+ antiporter ClC-ec1 was the first member of the CLC family that was studied by X-ray crystallography.[12,13] The protein mediates the transmembrane exchange of Cl^- for H^+ with a 2:1 stoichiometry.[14] Anion/proton exchange occurs in a permeation pathway limited by two glutamates, one pointing toward the intracellular side (E203, the so-called proton glutamate)[12,15] and the other toward the extracellular side (E148, the so-called gating glutamate).[12,14,16,17] Protons from the cytosol bind the carboxyl group of E203 and subsequently reach E148 via a water wire[18−21] between these two residues. After protonation, E148 rotates outward and thus exposes itself to the external side of the channel (from a *down* to an *up* conformation), to release the proton to the extracellular side and to open a permeation pathway that allows for chloride transit.[12,22,23] CLC anion channels and transporters allow for the transport of various anions, with significant permeability not only for Cl^- but also for larger and polyatomic anions, such as Br^-, I^-, NO_3^-, and SCN^-.[24−26]

Transport of F^- anion, which is smaller than Cl^-,[29] has not been extensively studied across the CLC proteins. Intriguingly, it is negligibly permeant through CLC-1 and CLC-2,[25,30] and it inhibits anion/proton exchange in ClC-ec1.[25,31−33]

Indeed, flux assays and current measurements show that reconstituted transporters do not transport F^-. Fluoride efflux from CLC-ec1-containing liposomes is indistinguishable from protein-free liposomes,[33] while other anions can pass the protein-containing liposomes even without exchange with H^+.[27] Neutralization of the gating glutamate by mutation to Ala permits high F^- conductance and effective F^- equilibrium binding.[33] In contrast, mutants that only disrupt the anion pathway's inner gate (Y445A) or impair H^+ binding from the cytoplasmic side (E203Q) are still highly selective for Cl^- over F^-.[33,34] Hence, F^- inhibition is likely to be caused by specific F^-−H^+ interactions at the central binding site, rather than by a strong Cl^-/ F^- selectivity of the anion conduction pathway.

X-ray studies on E148Q ClC-ec1 show that Q148 (in *down* conformation) directly interacts with the F^- within a hydrogen bond distance.[33] A neutral E148 in *down* conformation could keep F^- blocked in the protein binding site through a strong hydrogen bond interaction, whereas protonation of E148 triggers the *down/up* transition and hence proton release to the extracellular side with chloride as the main anion and in the absence of fluoride.[18,22]

Here, we investigate the molecular basis of fluoride inhibition on the ClC-ec1 transport cycle by multiscale molecular simulations. Our model system consists of the CLC-ec1 X-ray structure,[12] embedded in a POPC[35,36] bilayer in the presence of counterions (Figure 1), in which F^- replaces the Cl^- in the central binding site in both the subunits. Our project takes advantage of a recently developed, massively parallel DFT-based QM/MM interface between the CPMD

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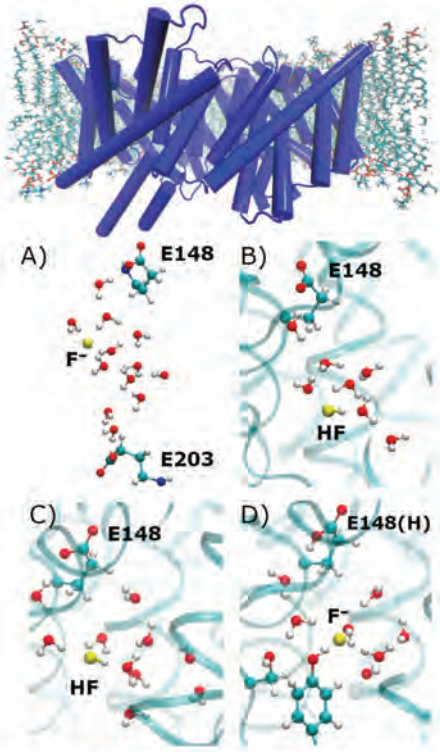

Figure 1. QM/MM MD simulations at the B3LYP/CHARMM level of theory for different initial proton locations. (Top panel) *E. coli* ClC antiporter (ClC-ec1) in a lipid bilayer. Water and counterions are not shown for clarity. (Bottom panel A) Snapshot from our classical MD simulation. Here 12 water molecules form a hydrogen bond network connecting E203, E148, and F^- (yellow sphere). The excess proton is added to different water molecules in five simulations. Only three are shown here. (B–D) QM/MM configurations after 0.5 ps. The proton, after hopping through a chain of water molecules, has already formed either H–F (B, C) or protonated E148 species (D). The starting configurations, as well as the other two trajectories, are depicted in Figure S3A–E. The QM region includes F^-, E148, R147, hydronium, the water molecules connecting them, and (in D) also Y445 and S107.

and GROMACS codes[37,38] that was run on the computational facilities at the Juelich Supercomputing Center. Overall, this has allowed us to model 16 ps of DFT-based QM/MM molecular dynamics (MD) and 455 ps of well-tempered metadynamics (MTD[39]) free energy calculations[37,38] (at the B3LYP[40,41] and BLYP levels of theory, respectively). Since the crystallographic structure lacks water molecules inside the channel, we obtained the average solvation around the anion within the transporter core through 300 ns of classical MD simulations using the CHARMM force field.[42]

The central region is hydrated with up to 12 water molecules, forming a continuous water chain connecting E203 and E148 (Figures 1A and S1). The E148 side chain (in its deprotonated state) does not change conformation during the simulation time (Figure S2).

On average, two water molecules lie in between E148 and F^- and four solvent molecules coordinate the fluoride in its binding site, where Y445 and S107 side chains complete the coordination around the anion with either direct or water-mediated H-bonds (Figures S1 and S2).

As mentioned above, the proton transfer (PT) from E203 to E148 is a crucial step in ClC-ec1 proton transport.[19,22]

We performed five independent QM/MM MD simulations, in which one proton is added in different positions of the water network connecting F^-, E203, and E148 (Figure 1A). In all circumstances, PT processes via the water wire occur already within less than 1 ps, either to E148 or to F^-, leading to the formation of HF. The resulting acids (protonated E148 and HF) do not dissociate afterward (Figure S3A–E). No significant conformational changes of E148 occurred over the remaining simulation time. The formation of a stable HF molecule is fully consistent with the well-known halogens' acid–base properties: HF dissociation in water is rather unfavorable ($\Delta G = 4.3$ kcal/mol), while this is not the case for other binary acids including HCl ($\Delta G = -9.5$ kcal/mol[23]). However, in the case of the Cl^- ion, the PT process toward the E148 could include a transient state in which the proton binds the chloride for a short time,[43] while a direct interference of the F^- with the excess proton has only been hypothesized so far.[44]

Next, we investigate whether E203 may affect these PT pathways. By including E203 and its hydration sphere in the QM region, our QM/MM simulations mostly reproduced the same results as above. Yet, in one QM/MM simulation, the proton does migrate to E203 (Figure S4E). We thus conclude that, in the presence of fluoride, E203 only serves as part of the proton pathways toward the two negatively charged groups, while playing no role for fluoride inhibition as proton acceptor, as established by the experiments.[33]

To estimate the relative stability of the two states characterized by the proton bound to either the F^- anion or E148, we investigated the free energy landscape associated with the PT between the two anions with two intervening water molecules (Figure 2A) via QM/MM MTD simulations. The free energy, as a function of chosen collective variables (the fluoride– and E148–proton distances), shows two minima at d(H–F) = 1.0 Å, d(H–E148) = 1.7 Å and d(H–F) = 1.6 Å, d(H–E148) = 1.0 Å, corresponding to the two protonation states (Figure 2A). The minima are similar in free energy (~1 kcal/mol), and they are separated by a free energy barrier of a few kcal/mol[45] (Figure S5). In this conformation, the proton goes back and forth, through two water molecules, from F^- to E148 in a kind of competition/sharing mechanism. The position of the E148 side chain may change depending on its protonation state.[18,22] In particular, the calculations so far relied on the E148 crystallographic conformation, in which the carboxylic side chain is exposed to the external side of the permeation pathway (*up*). In contrast, E148 in its *down* conformation is exposed to the inner part of the channel, where it can interact with the anion. We therefore investigated the *down/up* conformational change by calculating the associated free energy as a function of E148's N–Cα–Cβ–Cγ (χ_1) torsional angle, which dictates the transition (Figure 2C and D). In both cases the anion is present in the binding

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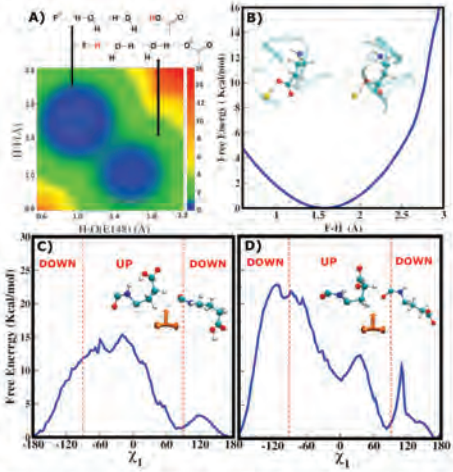

Figure 2. Free energy profiles (in kcal/mol) emerging from QM/MM MTD simulations at the BLYP/CHARMM level of theory. (A) Free energy associated with the PT process between fluoride and E148 modulated by two water molecules. The schematic representation of the two free energy minima is displayed on the top of the figure. Here, E148 is in the *up* conformation. (B) Free energy profile associated with the direct PT process between F^- and E148 in the *down* conformation. The minimum is reached at H−F and H−O(E148) (Figure S8D) distances of 1.5 and 1.0 Å, respectively. No barrier separates the state in which the proton is bound to the fluoride (H−F 1.0 Å). (C, D) Free energy as a function of E148's χ_1 dihedral angle for E148 protonated (C) and deprotonated (D). The relative positions of the E148 carboxyl group above or below the backbone unit define the *up or down* conformations. The transition from one conformation to the other is indicated by dashed red lines.

site as F^- and HF when E148 is protonated and deprotonated, respectively.

In the presence of F^- anion, the *down* conformation is far more favored than the *up* one regardless of the protonation state, in agreement with previous calculations.[23,46] In addition, *up* is a local minimum only if E148 is deprotonated (Figure 2C and D). Upon protonation, the *up* → *down* transition is actually a barrierless process. There is no longer a minimum near the *up* conformation region.

Once exposed to the internal side of the channel, E148 can form a direct hydrogen bond with F^-. To investigate the nature of this interaction, we performed an MTD-based free energy calculation using the H−F distance as a collective variable. It turns out that the proton is fully shared by fluoride and E148, as shown by the presence of a single minimum in the H−F free energy (Figure 2B). This may be consistent with the similarities of the pK_a value of Glu (4.2)[47] and HF (3.2).[29] While this direct interaction was invoked already as the key structural determinant for the inhibition mechanism,[33] our findings point to a much more complex scenario than a simple H-bond interaction: the H−F distance ranges between 1 Å (HF−E148) and 2 Å (F−HE148, Figure 2B).

Bringing the proton from its complex with E148 and F^- to the bulk requires the *down* → *up* transition of the protonated E148. The estimated free energy barrier of this transition (~15 kcal/mol, Figure 2C) is much higher than the corresponding one for chloride (5 kcal/mol).[22] The inverse (*up* → *down*) process is basically barrierless (Figure 2C), leading to the rather stable[48] F−H-E148 triad structure (Figure 2B).

These considerations lead us to suggest the following mechanism of inhibitions: protons coming from the extracellular side will migrate spontaneously to the protein cavity and will be trapped there by E148 (in a *down* conformation) and F^- (Figure 2B). This explanation is consistent with the available experimental data on CLC-ec1, from the formation of a fluoride-Gln H-bond in the E148Q mutant to the fact that the E148A variant allows for F^- transport.[33]

In conclusion, we here identify the high affinity of both F^- and E148 for protons as the basis of the transport inhibition of the CLC anion/proton exchangers from *E. coli*. Our hypothesis predicts impaired fluoride inhibition of CLC channels that lack a glutamate at this position, like the renal CLC-K,[49] and restored block in mutant channels with reinserted glutamate.[50] The comparative analysis of fluoride inhibition in multiple CLC channels and transporters, some of which differ in binding affinity and selectivity of binding sites within the anion transport pathway,[51] may identify additional determinants of fluoride block across this important anion channel/transporter family.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.9b13588.

Computational details for the system setup, classical MD, QM/MM, and QM/MM MTD simulations; hydration and structural analysis of the MD simulations; snapshots of the QM/MM dynamics illustrating the proton pathways; convergence of the FE profiles; population analysis (PDF)

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Notes

The authors declare no competing financial interest.

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