

Universidade de São Paulo

Biology at University of São Paulo

Prof. Dr. Cristiano L. P. Oliveira

Complex Fluids Group, Department of Experimental Physics Institute of Physics - University of São Paulo Brazil

São Paulo City, State of São Paulo, Brazil



City of São Paulo



Founded: January 25, 1554 Area: 1,523 km2 Elevation: 760 m (2,493.4 ft) Population: 11,316,149 (2011)

São Paulo is the largest city in Brazil, the largest city proper in the southern hemisphere, in the Americas, and the world's sixth largest city by population.

The metropolis has the largest economy by GDP among Latin American and Brazilian cities

The city has lots of cultural options, restaurants and an intense nightlife.

University of São Paulo

- Created in **1934**, the University of São Paulo is one of the most important institutions of higher learning in Brazil.
- Undergraduate program: 240 courses, dedicated to all fields of knowledge, distributed in 42 units of learning and research and offered to more than 57 thousand students.
- Graduate program is composed of **239 programs** (with **308 Masters** degree courses and **299 Ph.D** courses). More than **25 thousand students**.
- 8 Campi: São Paulo, Bauru, São Carlos, Lorena, Piracicaba, Pirassununga, Ribeirão Preto and São Sebastiao
- Ranking of Universities Shanghai University (2010): USP was ranked in 143rd position. The Times (2011) USP placed as number 250. HEE&AC Taiwan (2010), 74th position. Webometrics Ranking of World Universities, 43rd.
- One of the best universities in South America!!!



University of São Paulo

São Paulo Campus

Schoool of Arts, Sciences and Humanities (EACH) School of Communication and Arts (ECA) School of Physical Education and Sports (EEFE) School of Nursing (EE) Polytechnic School (Poli) School of Architecture and Urbanism (FAU) School of Pharmaceutical Sciences (FCF) Law School (FD) School of Economics, Administration and Accounting (FEA) School of Education (FE) School of Philosophy, Literature and Human Sciences (FFLCH) School of Medicine (FM) School of Veterinary Medicine and Animal Husbandry (FMVZ) School of Dentistry (FO) School of Public Health (FSP) Institute of Astronomy, Geophysics and Atmospheric Science (IAG) Institute of Bioscience (IB) Institute of Biomedical Sciences (ICB) Electro-Technical and Energy Institute (IEE) Institute of Advanced Studies (IEA) Institute of Brazilian Studies (IEB) Physics Institute (IF) Geosciences Institute (IGc) Institute of Mathematics and Statistics (IME) São Paulo Institute of Tropical Medicine (IMT) Psychology Institute (IP) Chemistry Institute (IQ) Institute of International Relations (IRI) Oceanographic Institute (IO)

Baurú Campus

Baurú School of Dentistry (FOB)

São Carlos Campus

São Carlos School of Engineering (EESC) Institute of Architecture and Urbanism (IAU) Institute of Mathematical and Computer Sciences (ICMC) São Carlos Institute of Physics (IFSC) São Carlos Institute of Chemistry (IQSC)

Lorena Campus

Lorena School of Engineering (EEL)

Piracicaba Campus

Center of Nuclear Energy in Agriculture (CENA) Higher School of Agriculture "Luiz de Queiroz"

Pirassununga Campus

School of Animal Husbandry and Food Engineering (FZEA)

Ribeirão Preto Campus

Ribeirão Preto School of Physical Education and Sports (EEFERP) Ribeirão Preto School of Nursing (EERP) Ribeirão Preto School of Pharmaceutical Sciences (FCFRP) Ribeirão Preto Law School (FDRP) Ribeirão Preto School of Economics, Administration and Accounting (FEARP) Ribeirão Preto School of Philosophy, Science and Literature (FFCLRP) Ribeirão Preto School of Medicine (FMRP) Ribeirão Preto School of Dentistry (FORP)

USP – Cidade Universitária Armando de Salles Oliveira



Biology at USP

- Difficult to quantify exact numbers : Biology is an object of study on several areas (physics, chemistry, biology, pharmacy, odontology, medicine, etc)
 - Some key groups for protein expression, purification and/or crystallization:
 - Prof. Igor Polykarpov (IFSC)
 - Prof. Glaucius Oliva / Richard Garrat (IFSC)
 - Prof. Roberto Salinas (IQUSP)
 - Prof. Shuck Farah (IQUSP)
 - Prof. Mariz Vainzof (IBUSP)
 - Prof. Antonio Carlos Pereira Martins (FMRP-USP)
 - Among MANY MANY others...
- Multidisciplinary / Interdisciplinary approaches
- Research Support Centers NAP's (181 centers created in the last 3 years)

Research Financing



• USP



• CNPQ



Científico e Tecnológico







Institute of Physics

- Research in Physics started at the department of Physics, started in 1934, with the Foundation of USP
- The institute of Physics was formally created in 1970
- It is composed of 6 departments: Department of Applied Physics, Department of Experimental Physics, Department of General Physics, Department of Nuclear Physics, Department of Materials Physics and Mechanics and Department of Mathematical Physics

Department of Applied Physics

- analysis of materials
- crystallography +
- physics of the air pollution
- plasma physics and fusion research
- thin films of advanced materials
- analysis of materials

Department of Experimental Physics

- experimental quantum optics
- structural and optical properties of complex fluids
- physics teaching
- new digital technologies and distance education
- experimental nuclear physics
- theoretical hadron physics

Department of General Physics

- electron microscopy applied to ceramic materials and biological tissues
- instrumentation for experimental high energy particle physics;
- molecular biophysics
- molecular modeling
- statistical physics
- NMR spectroscopy and imaging

Department of Nuclear Physics

- experimental study of nuclear structures
- experimental study of nuclear reactions
- nuclear astrophysics
- theoretical aspects of nuclear physics
- applied nuclear physics
- dosimetry
- radiation damage
- medical physics

Department of Materials Physics and Mechanics

- ultra-low temperature and high magnetic field effects, superconductivity
- optical, magnetic and electrical spectroscopy and microscopy
- synthesis and growth of semiconductor, magnetic and diluted magnetic materials
- nanomagnetism
- semiconductor, oxide and metallic nanostructures (theory and experiment)
- electronic, optical and magnetic properties of bulk and nanostructured systems (theory and experiment)
- organic and hybrid materials and nanostructures (theory)

Department of Mathematical Physics

- high energy collider physics
- gravitation and cosmology
- neutrino physics
- superstrings
- physics beyond the standard model
- mathematical physics
- quantum field theory
- theory of many body systems
- complex and non-linear systems

SAXS at IFUSP



Among MANY other users

Laboratory SAXS Instrument

Coordinator: CLP Oliveira IF/USP

2st Generation Lab. SAXS



A recent upgrade provided an increase of 40x in flux!!!





- Xenocs Microfocus
 Source and mirrors
 Scatterless Slits.
- •An integrated vacuum
- A 2D-gas detector (VÅNTEC2000)



High flux Low background

Standard: 0.01 to 0.35 1/Å $Flux = 0.4 \times 10^8$ photons per sec

Laboratory SAXS Instrument

Coordinators: AMF Neto, CLP Oliveira GFCx IF/USP 2st Generation Lab. SAXS



Xeuss SAXS Systems

Xenocs Microfocus
Source and mirrors
Scatterless Slits.
Vacuum paths
Pilatus Detector



High flux Low background

Standard: 0.01 to 0.35 1/Å $Flux = 0.4 \times 10^8$ photons per sec

Synchrotron Laboratory

LNLS/Campinas Two SAXS beamlines



Future Brazilian Synchrotron

Sirius/Campinas



Available in 2016....



* UVX is the existing light source at LNLS

Standard SAXS beamlines Coherent SAXS beamlines

More information next Sunday: 14:30 - 15:15: Mateus Cardoso - SAXS at LNLS: UVX and Sirius





Prof. Antonio M. F. Neto Profa. Elisabeth A. de Oliveira Profa. Suhaila M. Shibli Prof. Cristiano L. P. Oliveira





Several IC, MsC, PhD and Postdoc students

GFCx

- All about complex fluids:
 - Polymers
 - Biopolymers
 - Ferrofluids
 - Membranes
 - Surfactants
 - Etc... Soft matter in general

INCT on **Complex Fluids** Instituto de Física da USP

Head: Prof. Antonio M. F. Neto





INCT-FCx in Brazil







51 members



- Physics- 36
- Chemistry -2
- Biology -3
- Mathematics -2
- Medicine -7
- Odontology -1





Activities







Research Interests Prof. Cristiano L. P. Oliveira

- Small Angle Scattering theory
- Methods for modelling scattering data
- Soft matter and Biophysics:
 - Protein-protein interactions and complex formation
 - Protein-surfactant complexes
 - RNA/DNA self assembly structures
- Nanostructured materials / nanoparticles
- Instrumentation Development
- Interdisciplinary / Multidisciplinary projects!

Applications

Hemoglobin-Haptoglobulin

C52/C86

Complexes C250/C281

Haer

αHb

Нр ССР/Нр ССР

C33/C33

C52/C86

C90/C207

C250/C28

LE" ER Nature 489,456–459 (20 September 2012)

Haem

doi:10.1038/nature11369

Structure of the haptoglobin-haemoglobin complex

Christian Brix Folsted Andersen¹, Morten Torvund-Jensen¹, Marianne Jensby Nielsen¹, Cristiano Luis Pinto de Oliveira^{2,3}, Hans-Petter Hersleth⁴, Niels Højmark Andersen⁵, Jan Skov Pedersen³, Gregers Rom Andersen⁶ & Søren Kragh Moestrup¹

Hb-Hp complex

Haemoglobin (Hb): Fundamental oxygen-transporting molecule in blood

Haptoglobin (Hp): protective acute-phase protein, which captures the haemoglobin when it is released into the plasma.

This leads to formation of the haptoglobin-haemoglobin complex, which represents a virtually irreversible non-covalent proteinprotein interaction

Receptor CD163: macrophage scavenger receptor



LETTER *Nature* 489,456–459 (20 September 2012)

doi:10.1038/nature11369

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Hemoglobin-Haptoglobulin Complexes – SAXS investigations



Protein Crystallography Results



SAXS Modeling and comparison with crystallographic structure





Hb-Hp+CD163



Proteasome Gating Control

The proteasome is a multimeric and multicatalytic intracellular protease responsible for the degradation of proteins involved in cell cycle control, various signaling processes, antigen presentation, and control of protein synthesis.





ORIGINAL RESEARCH COMMUNICATION

ANTIOXIDANTS & REDOX SIGNALING Volume 16, Number 11, 2012 © Mary Ann Liebert, Inc. DOI: 10.1089/ars.2011.4210

Redox Control of 20S Proteasome Gating

Gustavo M. Silva,^{1,2} Luis E.S. Netto,² Vanessa Simões,¹ Luiz F.A. Santos,³ Fabio C. Gozzo,³ Marcos A.A. Demasi,⁴ Cristiano L.P. Oliveira,⁵ Renata N. Bicev,⁵ Clécio F. Klitzke,⁶ Mari C. Sogayar,⁴ and Marilene Demasi¹



Review Article

Redox regulation of the proteasome *via* S-glutathionylation $\stackrel{\ensuremath{\sc regulation}}{}$



Marilene Demasi ^{a,*}, Luis E.S. Netto ^b, Gustavo M. Silva ^{a,b,1}, Adrian Hand ^a, Cristiano L.P. de Oliveira ^c, Renata N. Bicev ^c, Fabio Gozzo ^d, Mario H. Barros ^e, Janaina M.M. Leme ^{a,b}, Erina Ohara ^a
Proteassome Gating TEM studies

Native conditions Plain Buffer

Plain Buffer + DTT



Solution Studies





Model for native protein







Model for Protein + DTT







Stable self assembly DNA structures

Self Assembly in Nature

Aggregation/Fibrillation



Winners of the Race to Learn DNA's Structure – Watson and Crick, 50's









ARTICLE

pubs.acs.org/JPCC

Simulative Analysis of a Truncated Octahedral DNA Nanocage Family Indicates the Single-Stranded Thymidine Linkers as the Major Player for the Conformational Variability

Francesco Oteri,[†] Mattia Falconi,[†] Giovanni Chillemi,[‡] Felicie F. Andersen,[§] Cristiano L.P. Oliveira,^{Ⅱ,#} Jan S. Pedersen,^Ⅱ Birgitta R. Knudsen,[§] and Alessandro Desideri^{*,†,⊥}

VOL. 4 • NO. 3 • 1367-1376 • 2010

Structure of Nanoscale Truncated Octahedral DNA Cages: Variation of Single-Stranded Linker Regions and Influence on Assembly Yields

Cristiano Luis Pinto Oliveira,^{†,#} Sissel Juul,^{‡,#} Hanne Lærke Jørgensen,[‡] Bjarne Knudsen,[§] David Tordrup,[‡] Francesco Oteri,[∥] Mattia Falconi,^{∥⊥} Jørn Koch,[¶] Alessandro Desideri,^{∥⊥} Jan Skov Pedersen,[†] <u>Felicie Fau</u>con Andersen,^{‡,*} and Birgitta Ruth Knudsen^{‡,*}

VOL. 3 • NO. 7 • 1813-1822 • 2009

Deciphering the Structural Properties That Confer Stability to a DNA Nanocage

Mattia Falconi,^{†,‡} Francesco Oteri,[†] Giovanni Chillemi,[§] Felicie F. Andersen,^{||} David Tordrup,^{||} Cristiano L. P. Oliveira,¹¹ Jan S. Pedersen,¹¹ Birgitta R. Knudsen,^{||} and Alessandro Desideri^{+,+,*}

Published online 20 December 2007

Nucleic Acids Research, 2008, Vol. 36, No. 4 1113–1119 doi:10.1093/nar/gkm1124

Assembly and structural analysis of a covalently closed nano-scale DNA cage

Felicie F. Andersen¹, Bjarne Knudsen², Cristiano Luis Pinto Oliveira³, Rikke F. Frøhlich¹, Dinna Krüger¹, Jörg Bungert⁴, Mavis Agbandje-McKenna⁴, Robert McKenna⁴, Sissel Juul¹, Christopher Veigaard¹, Jørn Koch⁵, John L. Rubinstein⁶, Bernt Guldbrandtsen⁷, Marianne S. Hede¹, Göran Karlsson⁸, Anni H. Andersen¹, Jan Skov Pedersen³ and Birgitta R. Knudsen^{1,*}

Joint Project

Prof. Cristiano L. P. Oliveira

PhD Student Cassio Alves – IFUSP MsC Student Renata Bicev – IFUSP

Prof. Carla Columbano - IQUSP Prof. Alessandro Desideri – Univ. Roma / Italy Prof. Birgitta Knudsen – Univ. Aarhus / Denmark Prof. Jan S. Pedersen – Univ. Aarhus / Denmark

Assembly / Simulation of new geometries Automatic Sequence / Structure Generator Combination of SAXS / TEM / MD / Molecular Biology



Modeling Method

scattering¹

research papers

58

59

60

61

62

63

64

65

66

Modelling of nanoscale particles by small-angle

^aInstitute of Physics, University of São Paulo, Rua do Matão, 187, São Paulo, São Paulo, 05314-970, Brazil, and ^bDepartment of Chemistry, University of Aarhus, Gustav Wieds Vej 14, Aarhus, DK-8000 C, Denmark. Correspondence e-mail: crislpo@if.usp.br

in press

J. Appl. Cryst. (2014). 47 [doi:10.1107/S1600576713028549]

Thumbnail image for contents page

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Received 17 May 2013

Crystallography

ISSN 1600-5767

Journal of

Applied

Accepted 17 October 2013





SAXS Modeling













Alves et al, in press

SAXS Simulation







Alves et al, in press

sugar side chain 🔩

Membrane Structure

Journal of Applied Crystallography

cholesterol J. Appl. Cryst. (2012). 45, 1278–1286 J. Oroteins

© 2007 B

Gaussian deconvolution: a useful method for a form-free modeling of scattering data from mono- and multilayered planar systems

Cristiano L. P. Oliveira, Barbara B. Gerbelli, Emerson R. T. Silva, Frédéric Nallet, Laurence Navailles, Elisabeth A. Oliveira and Jan Skov Pedersen

Model Membranes



Model Membranes



http://www.encapsula.com/products_01.html http://www.scf-online.com/english/25_e/25_e_pr/galenic_25_e_pr.htm http://www.the-simple-homeschool.com/cell-transport.html http://stat.phys.spbu.ru/Personal/Shch/7.html

Vesicles / Lipossomes





Unilamelar

Multi-lamelar



New Modeling Method



- Full curve fitting by the simultaneous modeling of hte form factor and structure factor
- Direct modeling of the electron density profile with a high level of detail

Model stabilized by the point of inflection method

research papers

Journal of Applied Crystallography ISSN 0021-8898

Received 25 June 2012 Accepted 6 October 2012 JAC (2012), 45, 1278-1286

Gaussian deconvolution: a useful method for a form-free modeling of scattering data from monoand multilayered planar systems

Cristiano L. P. Oliveira,* Barbara B. Gerbelli, Emerson R. T. Silva, Frédéric Nallet, Laurence Navailles, Elisabeth A. Oliveira and Jan Skov Pedersen

research papers

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Article pubs.acs.org/Langmuir

(2012), Langmuir 28(31): 11535-11545

Correlation of the Physicochemical and Structural Properties of pDNA/Cationic Liposome Complexes with Their *in Vitro* Transfection

Tiago A. Balbino,[†] Antônio A. M. Gasperini,[‡] Cristiano L. P. Oliveira,[§] Adriano R. Azzoni,^{||} Leide P. Cavalcanti,[‡] and Lucimara G. de La Torre^{*,†}

Chemical Engineering Journal 226 (2013) 423-433



Contents lists available at SciVerse ScienceDirect Chemical Engineering Journal

journal homepage: www.elsevier.com/locate/cej

Chemical Engineering Journal

Continuous flow production of cationic liposomes at high lipid concentration in microfluidic devices for gene delivery applications

CrossMark

Tiago A. Balbino^a, Nayla T. Aoki^a, Antonio A.M. Gasperini^b, Cristiano L.P. Oliveira^c, Adriano R. Azzoni^d, Leide P. Cavalcanti^b, Lucimara G. de la Torre^{a,*}



Article

pubs.acs.org/Langmuir

Langmuir 2013, 29, 13717-13722

Steric-Induced Effects on Stabilizing a Lamellar Structure

Barbara B. Gerbelli,[†] Rafael L. Rubim,[†] Emerson R. Silva,^{†,§} Frédéric Nallet,[‡] Laurence Navailles,[‡] Cristiano L. P. Oliveira,[†] and Elisabeth A. de Oliveira^{*,†}

Gaussian Deconvolution: Applications

<u>Hydration Effects on Soya Lectina – NANOSTAR IFUSP</u>





0.2

n

04

0.6

Phase Fraction

0.8

Collaboration with Profa. Lucimara de la Torre - UNICAMP



Contents lists available at SciVerse ScienceDirect

Chemical Engineering Journal

journal homepage: www.elsevier.com/locate/cej

Continuous flow production of cationic liposomes at high lipid concentration in microfluidic devices for gene delivery applications



Chemical

Engineering Journal

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Collaboration with Profa. Lucimara de la Torre - UNICAMP



pubs.acs.org/Langmuir

Article

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Lipoproteins

Motivation

Low-Density Lipoproteins

Main carrier of cholesterol, playing a critical role in the human cholesterol metabolism

LDL

HDL





World Health Organization

Risk factor to cardiovascular diseases (atherosclerosis)

•Abnormal blood lipids

High total cholesterol, LDL-cholesterol and triglyceride levels, and low levels of HDL cholesterol increase risk of coronary heart disease and ischaemic stroke.





The life style Visceral obesity



Univ

Complex Fluids Group University of São Paulo, Brazil



Fig. 1 - Constituição da lipoproteína de alta densidade (HDL). FL= fosfolípides; apo = apoproteína; CL= colesterol; CE = colesterol esterificado; TG = triglicérides.





Complex Fluids Group University of São Paulo, Brazil





Chylomicrons (×60,000)



VLDL (×180,000)



LDL ($\times 180,000$)



HDL ($\times 180,\!000)$



The oxidation of the LDL

"Normal" state





Disease state



oxidized LDL - oxLDL or moLDL

oxLDL induces the formation of aggregates



Complex Fluids Group University of São Paulo, Brazil



How to diferenciate/quantify the "good" LDL and the "bad" LDL?

Z Scan technique!



The Z-Scan Technique



Complex Fluids Group University of São Paulo, Brazil

Typical Z-Scan results



LDL / HDL

Structural characterization in SAXS solution

LDL studies by SAXS



Time-course studies by synchrotron X-ray solution scattering of the structure of human low-density lipoprotein during Cu²⁺-induced oxidation in relation to changes in lipid composition

David F. MEYER*, Adam S. NEALIS*, Colin H. MACPHEE+, Pieter H. E. GROOT+, Keith E. SUCKLING+, K. Richard BRUCKDORFER*



Final Remarks

- University of São Paulo is one of the most important universities in South America
- Studies in Molecular biology has an important whole in the university research
- Although some groups already use SAS on solution studies there is a huge space for the growth of this technique and its correlation with other experiments
- The use of Laboratory SAXS equipments provides nice data and a good way of planning experiments
- The current and future Brazilian Synchrotrons together with a future SANS line will strength even more the SAS technique. Therefore the training of students and scientists <u>is crucial</u>!

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- Italy
 - Prof. Alessandro Desideri, University of Rome, Italy
 - Prof. Mattia Falconi, Italy
- Brazil
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 - Profa. Márcia Fantini, IFUSP
 - Prof. Marilene Demasi, IB
 - PhD Student Cassio Alves
 - MsC Student Renata Bicev

Among MANY others









Instituto de Física

Universidade de São Paulo
Thank you !