

Curriculum Vitae
of
LAURA ANDOLFI

PERSONAL INFORMATION

Date of Birth 12th of Agost 1971

Place of birth Montefiascone (Viterbo)

Work address: IOM-CNR, SS14 km 163.5 I-34149 Trieste (Italy)

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EDUCATION

- 2000- 2004** **PhD course in Mathematics and Natural Science.** Leiden University (The Netherlands) Thesis “*Scanning Probe Microscopy and electron transfer properties of engineered plastocyanin adsorbed on gold substrate*”. Defence 4/03/2004.
- 1990- 1997** **Master Degree in Biology** University of Tuscia Viterbo (Italy). Thesis “*Analysis of site-specific induction of cytogenetic damage by using Site-specific induction analysis of cytogenetic damage through the diplochromosome system of endoreduplicated cells*”. Defence 20/11/1997- 110/110 cum laude.

PRESENT POSITION

- Since August 2020** **Research staff member** at Istituto Officina dei Materiali del Consiglio Nazionale delle Ricerche (IOM-CNR) di Trieste (Italy)
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PROFESSIONAL EXPERIENCEs

January 2014 – July 2020 Senior Post-Doc at Istituto Officina dei Materiali del Consiglio Nazionale delle Ricerche (IOM-CNR) di Trieste (Italy).

October 2011- December 2013 Project collaboration contract at Center of Molecular Biomedicine (CBM) - AREA Science Park, Basovizza Trieste (Italy).

December 2010 – September 2011 Research Fellowship at Dipartimento Universitario Clinico di Biomedicina Trieste University (Italy).

July 2005 – June 2009 Contract for researcher and teaching within the ministerial program “Il Rientro dei Cervelli” (D.M. 20 March 2003 Ministry of University Education and Research) at University of Tuscia Viterbo (Italy).

July 2003 – June 2005 Post-doc fellowship at Dipartimento di Scienze Ambientali, Centro di Biofisica e Nanoscienze, at University of Tuscia Viterbo (Italy).

August – September 2002 Short Term Project (COST D21) at Inorganic Chemistry Laboratory, Oxford University (UK) project title “Electrochemistry of copper proteins adsorbed on gold electrodes”.

March – September 1998 Research contract at Laboratorio di Genetica Molecolare Citogenetica e Mutagenesi at University of Tuscia Viterbo (Italy).

RESEARCH ACTIVITIES

My research interest is focused on the application of scanning probe microscopy (SPM) to the investigation of various biological processes from micro to nanoscale.

- **Mechanobiology:** Study of the mechanical properties (e.g. elasticity, viscosity, viscoelasticity) of somatic cells and gametes by single cell force spectroscopy based on atomic force microscopy (AFM). Biological events activated by different mechanical stimulus in physiological and pathological cell conditions (Mechanotransduction processes).
 - **Cell Morphology:** Use of AFM and SNOM microscopy for a high-resolution analysis of the morphology of various cell types of biomedical interest.
 - **Single molecule:** Analysis at the single molecule level of the morphology and functional properties of hybrid systems consisting of redox-active proteins immobilized on electrodes using AFM and Scanning tunneling microscopy (STM) for application in biosensing.
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TECHNICAL COMPETENCES

Scanning Probe Microscopy (SPM) Atomic Force Spectroscopy/Microscopy (AFM/AFS). Modalità di AFM “imaging” (tapping, contact and conductive) in various conditions (air, fluid, controlled atmosphere, and electrochemical control). Scanning Near-Field Optical Microscopy (SNOM) in air. Scanning Tunnelling Microscopy/Spectroscopy (STM/STS).

Single Cell Force Spectroscopy cell adhesion measurements on different types of substrates functionalized with extracellular matrix and nanostructured proteins; Indentation measurements (nano-indentation and compression) of single cells or cellular spheroids.

Cell Biology Growth and maintenance of cell cultures; immuno-cytochemistry methodologies.

Biochemistry Expression of proteins in bacterial cells, extraction of proteins from bacteria and purification techniques (Ion Exchange and FPLC Gel Filtration. SDS-PAGE and IEF).

Molecular Biology PCR for nucleotide amplification / Agarose gel; nucleotide digestion by restriction enzymes.

Optical Spectroscopy/microscopy UV/Vis and Fluorescence of proteins in solution, cellular samples and fixed tissues

SUPERVISION and TEACHING ACTIVITY

Co-supervisor of 8 master thesis at University of Trieste (Italy).

Supervisor of a PhD student in Nanotechnology Course 37th cycle at University of Trieste (Italy), Thesis “Nano-Mechanical Systems for the understanding of cellular Mechano-Response at the Nanoscale”

Co-supervisor of 3 PhD students at the School of Nanotechnology at University of Trieste

Supervision of a Post-doc Fellow at CNR-IOM: Martina Conti on the project “Development and fabrication of substrates or cantilevers to be integrated into devices to apply a controllable mechanical stimulus to the cultured cell to analyze: (i) how the mechanical stimulus influences the distribution of Piezo mechanosensitive channels in the cell; (ii) the response of Piezo mechanosensitive channels to a specific mechanical stimulus, combining these substrates with fluorescence microscopy for calcium imaging.”

Supervision of *Pre-Doc* Fellow at CNR-IOM: Rabia Aziz on the project "Artificial intelligence strategies for development and the control of mechanical indentation systems for applications in mechanobiology"

Atomic Force Microscopy Seminar for the "Winter School of Microscopy" for the Doctoral School of Agricultural Sciences and Biotechnology of the University of Udine (22 February 2019).

Laboratory course on force spectroscopy with atomic force microscope of cells in culture at the IOM-CNR (Trieste) for the 4th, 5th and 6th edition of Neurobiology Summer School organized by the International School of Advanced Studies (SISSA).

Teaching assignments in Biophysics 2005/2006 and 2007/2008 at the University of Tuscia Viterbo; Laboratory tutoring for the Biophysics course for Biological Sciences and Environmental Sciences master's degree students.

DISSEMINATION ACTIVIY

Coordination and organization of dissemination activities of CNR-IOM presented at Trieste Next 21 and Sharper Night - European Researches Night 2021.

REVIEWER ACTIVITY

- Reviewer of international journals: BioNanoScience; RCS Advances; Jove; Nature publishing group; Food and Function; Multifunctional Materials; Journal of the Mechanical Behavior of Biomedical Materials; Applied Science; Frontiers; Acta Biomaterialia.
 - External Reviewer for the doctoral dissertation at SISSA Phd programme in Neurobiology "Complexity and Versatility of Calcium Signaling and Dynamics" (Yunzhen Li) (defended on October, 20th, 2021).
 - Reviewer for ARC 2016, Research funding Program - "Concerted Research Actions" 2017 - 2021 University of Mons (Belgium).
 - Reviewer for Young Researcher proposal post-doctoral (PD) projects of the National Research, Development and Innovation Office (NKFIH) (Hungary) (2015);
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PARTICIPATION in NATIONAL AND INTERNATIONAL RESEARCH PROJECTS

- 2022 – (1 year project) **coordinator of CNR Unit** collaborator for Ricerca Corrente 2022 IRCCS Burlo Garofolo Trieste "SPRINT Study from vitrification to lyophilization protocols: Sperm PReservation Improvement strategies besides paNdemic Times".
- 2019 – 2022 **researcher involved** in the EU-H2020 Interreg ITA-SLO project NanoRegion
- 2017 –2021 **senior research fellow** in the Friuli Venezia Giulia Region project, "Regional Law 17/2004: Contributions for clinical, translational, basic, epidemiological and organizational research", project "BioMec -" Application of technologies biomechanics to integrate traditional methods in the hospital context "
- 2015- 2017 **senior research fellow** within the Finalized Research-Ministry of Health project (RF-2011-02351812). Application of ultrastructural analysis of cells in the field of assisted reproductive technologies. Project coordinator Prof. Giuseppe Ricci.
- 2011- 2012 **project collaboration contract** in the European Project - 7th framework program FP7 (SMD FP7-NMP 2800-SMALL-2 proposal no. CP-FP 229375-2). Single Molecule Detection (SMD) Project coordinator Prof. Enzo di Fabrizio.

- 2012- 2013 **project collaboration contract** in the European Project - 7th framework program FP7 (FOCUS - FP7-ICT-2009-6 contract no. 270483). Single Molecule Activation and Computing-(FOCUS) Project coordinator Prof Vincent Torre.
 - 2010- 2011 **senior research fellow** within the project financed by the Autonomous Region of Friuli Venezia Giulia with L.R. 26/2005 art.23 (D.P. Reg. N.120 / Pres. Of 04-05-2007). Development of Scanning Probe Microscopy as a New Technology in the Biomedical Field. Project coordinator Prof. Marina Zwyer.
 - 2005 - 2009 **Scientific Coordinator** of the project funded by the Ministry of Education of the University and Research within the Ministerial Decree of 20 March 2003 "Il Rientro dei Cervelli". Study of complexes formed by active redox immobilized on metal electrodes: nanotechnological applications.
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PATENT

1 International Patent application: Device, Apparatus and System for use in Photonics, Nanotechnology, Microscopy and Biology. publication number: WO2015/082635-A1.; Authors: V. Torre, M. Mazzolini, M. Lazzarino, L. Andolfi.

LIST of PUBLICATIONS on PEER REVIEWED JOURNALS

The scientific research activity is documented on 48 publications on international peer-review journals, including 18 as the first or last author, and 2 book chapters.

h-index 19 (Scopus), 22 (Scholar)

47. **Andolfi, L.**, Meschini, R., Filippi, S., Bedolla D.E., Piccirilli F., Lepore, M., Delfino, I. X-rays induced alterations in mechanical and biochemical properties of isolated SH-SY5Y nuclei. *Biochimica et Biophysica Acta - General Subjects* (2023) 1867: 130291
46. Battistella, A., **Andolfi, L.**, Stebel, M., Ciubotaru, C., Lazzarino, M. Investigation on the change of spermatozoa flagellar beating forces before and after capacitation. *Biomaterials Advances*, (2023) 145: 213242. (*corresponding author*)
45. Conti, M., **Andolfi, L.**, Betz-Güttner, E., Zilio, S.D., Lazzarino, M. Half-wet nanomechanical sensors for cellular dynamics investigations. *Biomaterials Advances* (2023) 144: 213222
44. Conti, M., Bolzan, I., Dal Zilio, S., Parisse P, **Andolfi, L.**, Lazzarino, M. Water–Air Interface to Mimic In Vitro Tumoral Cell Migration in Complex Micro-Environments. *Biosensors*, (2022) 12: 822. (*corresponding author*)
43. Battistella, A., **Andolfi, L.**, Zanetti, M., Dal Zilio S., Stebel M., Ricci, G., Lazzarino, M. Atomic force spectroscopy-based essay to evaluate oocyte postovulatory aging. *Bioengineering and Translational Medicine*, (2022) 7: e10294
42. M Zanetti, **L Andolfi**, MRG Taylor, L Mestroni, M Lazzarino. AFM macro-probes to investigate whole 3D cardiac spheroids *Micro and Nano Engineering* (2022) 15, 100134.
41. B. Bortot, M. Apollonio, G. Baj, **L. Andolfi**, L. Zupin, S. Crovella, M. di Giosia, A. Cantelli, R. Sapopetti, L. Ulfo, A. Petrosino, G. Di Lorenzo, F. Romano, G. Ricci, M. Mongiat, A. Danielli, M. Calvaresi, S. Biffi. Advanced photodynamic therapy with an engineered M13 phage targeting EGFR: Mitochondrial localization and autophagy induction in ovarian cancer cell lines. *Free Radical Biology and Medicine* (2022) 179, 242.

40. **L. Andolfi**, A. Battistella, M. Zanetti, M.Lazzarino, L. Pascolo, F. Romano, G. Ricci. Scanning Probe Microscopies: Imaging and Biomechanics in Reproductive Medicine Research International Journal of Molecular Sciences (2021) 22, 3823. (*corresponding author*).
39. B. Troian, R. Boscolo, G. Ricci, M. Lazzarino, G. Zito, S. Prato, **L. Andolfi**. The Ultra-structural analysis of Anomalous Human Spermatozoa by Aperture Scanning Near-Field Optical Microscopy. Journal of Biophotonics (2020) 13, e2418 (*corresponding author*).
38. L. Puzzi, D. Borin, P. Gurha, R. Lombardi, V. Martinelli, M. Weiss, **L. Andolfi**, M. Lazzarino, L. Mestroni, A. J. Marian, O. Sbaizero Knock Down of Plakophilin 2 Dysregulates Adhesion Pathway through Upregulation of miR200b and Alters the Mechanical Properties in Cardiac Cells. Cells (2019) 8, 1639.
37. E. Giolo, M. Martinelli, S. Luppi, F. Romano, G. Ricci, M. Lazzarino, **L. Andolfi**. Study of the mechanical properties of fresh and cryopreserved individual human oocyte. European Biophysics Journal (2019) 48(6):585-592 (*corresponding author*)
36. **L. Andolfi**, S.L.M. Greco, D. Tierno, R. Chignola, M. Martinelli, E. Giolo, S. Luppi, I. Delfino, M. Zanetti, A. Battistella, G. Baldini, G. Ricci, M. Lazzarino. A novel AFM macro-probe to study the biomechanical properties of large cells and 3D cell spheroids. Acta Biomaterialia (2019) 94:505-513 (*corresponding author*)
35. **L. Andolfi**, A. Murello, D. Cassese, J Ban, S. Dal Zilio, M. Lazzarino. High aspect ratio silicon nanowires control fibroblast adhesion and cytoskeleton organization. Nanotechnology (2017) 28: 155102 (*corresponding author*)
34. S. Biffi, **L. Andolfi**, C. Caltagirone, A. Falchi, C. Garrovo, V. Lippolis, A. Lorenzon, P. Macor, V. Meli, M. Monduzzi, M. Obiols-Rabasa, L. Petrizza, L. Prodi, A. Rosa, J. Schmidt, Y. Talmon, S. Murgia. Cubosomes for in vivo fluorescence lifetime imaging. Nanotechnology (2017) 28: 055102
33. S. J. Morley, Y. Qi, L. Iovino, **L. Andolfi**, D. Guo, N. Kalebic, L. Castaldi, C. Tischer, C. Portulano, G. Bolasco, K. Shirlekar, C. M. Fusco, A. Asaro, F. Fermani, M. Sundukova, U. Matti, L. Reymond, A. De Ninno, L. Businaro, K. Johnsson, M. Lazzarino, J. Ries, Y. Schwab, J. Hu, Paul A. Heppenstall. Acetylated tubulin is essential for touch sensation in mice. E-Life (2016) 5:e20813.
32. **L. Andolfi**, E. Masiero, E. Giolo, M. Martinelli, S. Luppi, S. dal Zilio, I. Delfino, R. Bortul, M. Zweyer, G. Ricci, M. Lazzarino. Investigating the mechanical properties of zona pellucida of whole human oocytes by atomic force spectroscopy. Integrative Biology (2016) 8, 886-893. (*corresponding author*)
31. L. Petrizza, E. Rampazzo, L. Prodi, S. Biffi, C. Garrovo, **L. Andolfi**, P. Giubbetto, G. Zauli, I. Nicolov, G. Kurdi, P. Secchiero. Multimodal NIR-Emitting PluS Silica Nanoparticles with Fluorescent, Photoacoustic and Photothermal Capabilities. International Journal of Nanomedicine (2016) 11: 4865–4874
30. Y. Qi, **L. Andolfi**, F. Frattini, F. Mayer, M. Lazzarino, J. Hu. Membrane stiffening by STOML3 facilitates mechanosensation in sensory neurons. Nature Communications 6 (2015) 8512.
29. G. Ricci, **L. Andolfi**, G. Zabucchi, S. Luppi, R. Boscolo, M. Martinelli, M. Zweyer, E. Trevisan. Ultrastructural morphology of sperm from human globozoospermia BioMed Research International (2015) Article ID 798754, 8 pages.
28. M. Mazzolini, G. Facchetti, **L. Andolfi**, R. Proietti Zaccaria, S. Tuccio, J. Treu, C. Altafini, E. Di Fabrizio, M. Lazzarino, G. Rapp and V. Torre. The phototransduction machinery in the rod outer

segment has a strong efficacy gradient. Proceeding of the National Academy of Science 112 (2015) E2715–E2724.

27. **L. Andolfi**, E. Trevisan, B. Troian, S. Prato, R. Boscolo, E. Giolo, S. Luppi, M. Martinelli, G. Ricci and M. Zwayer. The application of Scanning Near Field Optical Imaging to the study of Human Sperm Morphology. *Journal of Nanobiotechnology* 13 (2015) 2 .
26. **L. Andolfi**, E. Bourkoula, E. Migliorini, A. Palma, A. Pucer, M. Skrap, G. Scoles, A. P. Beltrami, D. Cesselli, M. Lazzarino. Investigation of Adhesion and Mechanical Properties of Human Glioma Cells by Single Cell Force Spectroscopy and Atomic Force Microscopy. *PLoS ONE* 9 (2014) e112582. (*corresponding author*)
25. F. Bisio, R. Proietti Zaccaria, R. Moroni, G. Maidecchi, A. Alabastri, G. Gonella, A. Giglia, **L. Andolfi** , S. Nannarone, L. Mattera, M. Canepa. Pushing the High-Energy Limit of Plasmonics. *ACS Nano* 8 (2014) 9239-9247.
24. S. Biffi, L. Petrizza, E. Rampazzo, R. Voltan, M. Sgarzi, C. Garrovo, L. Prodi, **L. Andolfi**, C. Agnoletto, G. Zauli and P. Secchiero. Multiple dye-doped NIR-emitting silica nanoparticles for both flow cytometry and in vivo imaging. *RSC Advances* 4 (2014) 18278-18285.
23. E. Migliorini, J. Ban, G. Grenci, **L. Andolfi**, A. Pozzato, M. Tormen, V. Torre, M. Lazzarino. Nanomechanics controls neuronal precursors adhesion and differentiation. *Biotechnology and Bioengineering* 110 (2013) 2301–2310.
22. **L. Andolfi**, E. Trevisan, M. Zwayer, S. Prato, B. Troian, F. Vita, V. Borelli, M. R. Soranzo, M. Melato, and G. Zabucchi The crocidolite fibres interaction with human mesothelial cells as investigated by combining electron microscopy, atomic force and scanning near-field optical microscopy. *Journal of Microscopy* 249 (2013) 173–183.
21. A.R. Bizzarri, S. Di Agostino, **L. Andolfi**, S. Cannistraro “A Combined Atomic Force Microscopy Imaging and Docking Study to Investigate the Complex Between p53 DNA Binding Domain and Azurin” *Journal of Molecular Recognition*, 22 (2009) 506-515.
20. V.E.V. Ferrero, **L. Andolfi**, G. Di Nardo, S.J. Sadeghi, A. Fantuzzi, S. Cannistraro, G. Gilardi “Protein and electrode engineering for the covalent immobilisation of P450 BMP on gold” *Analytical Chemistry* 80 (2008) 8438-8446.
19. A.R. Bizzarri, **L. Andolfi**, M. Taranta, S. Cannistraro “Optical and electronic coupling of the redox copper Azurin ITO-coated quartz substrate” *Biosensors and Bioelectronics* 24 (2008) 204-209.
18. I. Delfino, B. Bonanni, **L. Andolfi**, C. Baldacchini, A.R. Bizzarri, S. Cannistraro “Yeast cytochrome c integrated with electronic elements: a nanoscopic and spectroscopic study down to single molecule level” *Journal of Physics: Condensed Matter* 19 (2007) 1-18.
17. Bonanni, B.; **Andolfi, L.**; Bizzarri, A. R.; Cannistraro, S. “Functional Metalloproteins Integrated with Conductive Substrates: Detecting Single Molecules and Sensing Individual Recognition Events”. *Journal of Physical Chemistry B Feature Article* 111 (2007) 5062-5075.
16. **L. Andolfi**, P. Caroppi, A. R. Bizzarri, M. C. Piro, F. Sinibaldi, T. Ferri, F. Politelli, S. Cannistraro, R. Santucci “Nanoscopic and redox characterization of engineered horse cytochrome c chemisorbed on a bare gold electrode” *The Protein Journal* 26 (2007) 271-279.
15. **L. Andolfi**, A. R. Bizzarri, S. Cannistraro “Electron Tunneling in a Metal-Protein-Metal Junction investigated by Scanning Tunneling and Conductive Atomic Force Spectroscopies” *Applied Physics Letters* 89 (2006) 183125-183127.
14. **L. Andolfi**, A. R. Bizzarri, S. Cannistraro “Assembling of Redox Proteins on Au(111) Surfaces: a Scanning Probe Microscopy Investigation for Application in Bio-Nanodevices” *Thin Solid Films* (2006) 515 (2006) 212-219.

13. I. Delfino, K. Sato, M.D. Harrison, **L. Andolfi**, A. R. Bizzarri, C. Dennison, S. Cannistraro "Optical Spectroscopic Investigations of the Alkaline Transition in Umecyanin from Horseradish Roots" *Biochemistry* 44 (2005) 16090-16097.
12. **L. Andolfi**, S. Cannistraro "Conductive Atomic Force Microscopy Study of Plastocyanin Molecules Adsorbed on Gold Electrode" *Surface Science* 598 (2005) 68-77.
11. A.R. Bizzarri, **L. Andolfi**, M. Stchakovsky, S. Cannistraro "AFM, STM and Ellipsometry Characterization of a Monolayer of Azurin Molecules Self-Assembled on a Gold Surface in Air" AZoNano.com – Online Journal of Nanotechnology (2005).
10. R. Guzzi, **L. Andolfi**, S. Cannistraro, M.Ph. Verbeet, G.W. Canters, L. Sportelli "Thermal stability of wild type and disulfide bridge containing mutant of poplar plastocyanin" *Biophysical Chemistry* 112 (2004) 35-43.
9. D. Alliata, **L. Andolfi**, S. Cannistraro "Tip to substrate distances during STM imaging of biomolecules" *Ultramicroscopy* 101 (2004) 231-240.
8. **L. Andolfi**, D. Bruce, S. Cannistraro, G.W. Canters, J.J. Davis, H.A.O. Hill, J. Crozier, C. W. Wrathmell. "The electrochemical characteristics of blue copper protein monolayers on gold". *Journal of Electroanalytical Chemistry* 565 (2004) 21-28.
7. **L. Andolfi**, G.W. Canters, M. Ph. Verbeet, S. Cannistraro "Scanning tunneling spectroscopy investigation of self-assembled plastocyanin mutants onto gold substrates under controlled environment" *Biophysical Chemistry* 107 (2004) 107-116.
6. **L. Andolfi**, B. Bonanni, G.W. Canters, M. Ph. Verbeet, S. Cannistraro "Scanning Probe Microscopy characterisation of gold-chemisorbed poplar plastocyanin mutants" *Surface Science* 530 (2003) 181-194.
5. **L. Andolfi**, S. Cannistraro, G.W. Canters, P. Facci, A.G. Ficca, I.M.C. van Amsterdam, M.Ph. Verbeet, "A Poplar Plastocyanin mutant suitable for adsorption onto gold surface via disulphide bridge" *Archives of Biochemistry and Biophysics* 399 (2002) 81-88.
4. P. Facci, D. Alliata, **L. Andolfi**, B. Schnyder, R. Kotz. "Formation and characterization of protein monolayers, on oxygen-exposing surface by multiple-step self-chemisorption". *Surface Science* 504 (2002) 282-292.
3. R. Rinaldi, A. Biasco, G. Maluccio, R. Cingolani, D. Alliata, **L. Andolfi**, P. Facci, F. De Rienzo, R. di Felice, E. Molinari. "Solid-state molecular rectifier based on self-organized metalloproteins" *Advanced Materials* 14 (2002) 1453-1457.
2. M. Milani, **L. Andolfi**, M. Ph. Verbeet, S. Cannistraro, M. Bolognesi. "The 1.6 Angstrom Resolution structure of a mutant Plastocyanin bearing a 21-25 engineered disulfide bridge" *Acta Crystallographica D57* (2001) 1735-1738.
1. G. Casini, L. Trasarti, **L. Andolfi**, P. Bagnoli. "Morphologic maturation of tachykinin peptide-expressing cells in the postnatal rabbit retina" *Developmental Brain Research* 99 (1997) 131-141.

BOOK CHAPTERS

2. **L. Andolfi** and M Lazzarino. Investigating Adhesion Proteins by Single Cell Force Spectroscopy. In *Novel Approaches for Single Molecule Activation and Detection*, Editors: Fabio Benfenati, Enzo Di Fabrizio, Vincent Torre, pp 149-168, Springer - Berlin 2014. (*corresponding author*)
1. B. Bonanni, D. Alliata, **L. Andolfi**, A.R. Bizzarri, S. Cannistraro. Redox metalloproteins on metal surface as hybrid system for bio-nanodevices: an extensive characterization at the single molecule

level. in Surface Science Research Development Ed. C.P. Norris, Nova Science Publishers, Inc., (Invited paper) Chapter 1 (2004) pp 1-73.