

Curriculum Vitae of Antonino Natalello

PRESENT POSITION

Since September 2018: Associate professor of APPLIED PHYSICS at the Department of Biotechnology and Biosciences, University of Milano-Bicocca, Milan, Italy.

A. Natalello obtained the National Scientific Qualification (Abilitazione Scientifica Nazionale) for Full Professor of Applied Physics on December 2017.

EDUCATION

- 2002: Laurea (Master Degree) in Industrial Biotechnology (110/110 cum laude), University of Milano-Bicocca, Milan, Italy.
- 2006: PhD in Industrial Biotechnology, University of Milano-Bicocca, Italy. Title of the Thesis "Protein stability and aggregation studied by biophysical methods" (Supervisor: Prof. S. M. Doglia).
- February 2005-Jun 2005: visiting scientist/PhD student at the Institute of Organic Chemistry of the Johannes Kepler University (Linz, Austria) performing research activities on mass spectrometry for protein studies.

PREVIOUS POSITIONS

- Since September 2018: Associate Professor of APPLIED PHYSICS at the Department of Biotechnology and Biosciences, University of Milano-Bicocca, Milan, Italy.
- 2015-2018: Temporary Assistant Professor (RTD b - art. 24, comma 3, lettera b, legge 240/2010) of APPLIED PHYSICS at the Biophysics laboratory of the Department of Biotechnology and Biosciences, University of Milano-Bicocca, Milan, Italy
- 2013-2015: postdoctoral fellow, Department of Physics, University of Milano-Bicocca, Milan, Italy.
- 2008-2012: postdoctoral fellow, Department of Biotechnology and Biosciences, University of Milano-Bicocca, Milan, Italy.
- 2007: research fellow from "Regione Lombardia", Department of Biotechnology and Biosciences, University of Milano-Bicocca.

TEACHING ACTIVITIES

- 2002-2014 Tutor in teaching laboratories for general and organic chemistry (First level degrees in Biotechnology and Biology).
- Since 2015, Biophysics /Spectroscopy for biotechnology (First level degree in Biotechnology)
- Since 2019, General Physics (First level degree in Biotechnology)

GRANTS

- February 2023-present: FONDAZIONE CARIPLO Project n. 2022-0529 "RITESSERE. Silk Sericin materials from textile industry by-products".
Role in the project of A. Natalello: PI of the research unit of the University of Milano-Bicocca. 36 months. (PI of the Politecnico di Milano, Prof. S. Vesentini)
- February 2021-present: FONDAZIONE CARIPLO Project n. 2020-0838 "From local dairy waste to SUGAR blocks for the synthesis of bioPoLymerS (SURPLaS)".
PI: Prof.ssa S. Brocca.
Role in the project of A. Natalello: responsible for the bioanalytical activities by optical spectroscopies. 30 months.
- November 2019-present: FONDAZIONE CARIPLO Project n. 2018-0458 "Osteocalcin in bone metabolism and aging: molecular mechanisms and biomarkers of the bone-energy crosstalk".
PI: Prof.ssa L. Cipolla.
Role in the project of A. Natalello: responsible for the conformational characterizations of the proteins under investigations (by optical spectroscopies) and of their biomolecular interactions (by Isothermal Titration Calorimetry and Surface Plasmon Spectroscopy). 36 months.
- 2017-FFABR: Finanziamento annuale individuale delle attività base di ricerca (MIUR).
- 2014-2016: FONDAZIONE CARIPLO Project n.2013.0964 "Structure-function relation of amyloid: understanding the molecular bases of protein misfolding diseases to design new treatments".
Role in the project of A. Natalello: PI of the research unit of the University of Milano-Bicocca. 36 months. (PI of the Policlinico San Matteo, Pavia. Prof. G. Merlini)
- 2010-2012: Grant ASTIL of the Lombardy Region for the project "Diesel-Biotech: Produzione di biodiesel per via biotecnologica" Italian Regional Government.
PI: Prof.ssa Lotti.
Role in the project of A. Natalello: involved in the bioanalytical activities by optical spectroscopies. 18 months.
- 2009-2010: PRIN 2007. Project n. 2007XY59ZJ_004 "A multidisciplinary approach to the study of in vivo and vitro aggregation of polyglutamine-containing proteins. Role of molecular and environmental factors".
PI: Prof. P. Tortora.

Role in the project of A. Natalello: involved in the conformational characterizations of the proteins under investigations (by optical spectroscopies). 24 months

- 2007: "Regione Lombardia", Bando "ingegno". Project title: "Protein aggregation in biomedicine and biotechnology".

Role in the project of A. Natalello: PI. 12 months.

MEMBERSHIP OF SCIENTIFIC SOCIETIES

- SIF - Società Italiana di Fisica
- SIBPA - Società Italiana di Biofisica Pura e Applicata

OTHER TITLES

- November 2014. National Scientific Qualification (Abilitazione Scientifica Nazionale) for Associate Professor of Experimental Physics of Matter (sector 02/B1).
- Jun 2014. National Scientific Qualification for Associate Professor of Biochemistry (Sector 05/E1).
- Since 2015, PI of the Biospectroscopy group at the department of Biotechnology and Bioscience of the University of Milano-Bicocca.
- Since 2015, Scientific responsible for Spectroscopic analyses (FTIR and CD) for third parties of the department of Biotechnology and Bioscience of the University of Milano-Bicocca.
- Since 2019, Scientific committee member of the "molecular Biorecognition" departmental platform (department of Biotechnology and Bioscience of the University of Milano-Bicocca)
- Since 2020, Editorial Board Member of "International Journal of Molecular Sciences"; IF 2022= 6.2
- Since 2021, Departmental representative for students with disabilities and specific learning disorders (DSA).
- Invited ad hoc reviewer for several Journals, among them: PLoS ONE, J. Am. Chem. Soc., Biochemistry, ChemComm, Eur. Biophys. J., Biomaterials, Microb. Cell Fact., BioTechniques, Energy & Fuels, Biomolecules, BioMed Research International, Biotechnology for Biofuels, FEBS Journal, Molecular Pharmaceutics, Biophys. Chem., Sci. Rep., BBA-Proteins and Proteomics, Int. J. Mol. Sci..

RESEARCH INTERESTS

-Protein stability, aggregation, interactions. Major research topics: protein stability; amyloid aggregation; structure-function relation; aggregation of recombinant proteins; protein-protein and protein-ligand interactions; nano- and bio-materials.

-Bioanalytical applications of spectroscopic methods. Major research topics: FTIR (micro)spectroscopy of complex biological systems; in situ studies of biological processes; spectroscopic markers.

These topics are investigated by several biophysical approaches, among them: infrared spectroscopy and microspectroscopy (FTIR and microFTIR), fluorescence and circular dichroism (CD) spectroscopies, "Native" mass spectrometry, Isothermal Titration Calorimetry (ITC), and Surface Plasmon Resonance (SPR) spectroscopy. In particular, we have investigated several aspects of protein aggregation processes also considering their biomedical and biotechnological implications, as the in vivo formation of inclusion bodies in bacterial cells and the investigation of amyloid formation in vitro and in situ. Great experience has been acquired in this field thanks to the analysis of several proteins and peptides in vitro and in complex biological systems (such as intact cells and human tissues). In the framework of the Cariplo Foundation granted project "Structure-function relation of amyloid", we developed an isotope edited FTIR approach to investigate the role of mutations and of a molecular chaperone on the misfolding and co-aggregation of human β -2 microglobulin variants. This approach allowed studying simultaneously the conformational properties of the isotopically labelled (^{13}C) and unlabelled protein (^{12}C) variants (at the same time) when co-present in the same sample. In particular, the sequence of events occurring during the co-polymerization of the D76N variant and wild type β -2 microglobulin and the effect of the chaperon crystallin in the aggregation process were characterized (Natalello et al. 2016 J. Biol. Chem. 291, 9678-9689, in collaboration with Prof. V. Bellotti, University of Pavia).

The role of glutamine (Q) side chains in the two aggregation stages of the poly-Q protein Ataxin-3 was also studied by biophysical approaches. In particular, by H/D exchange experiments we showed for the first time that an IR marker band can be ascribed to glutamine side-chain hydrogen bonding (Natalello et al. 2011, PLoS One. 6:e18789). This IR marker band was employed in several subsequent publications to monitor the formation of mature poly-Q aggregates in vitro and in ex vivo protein samples (in collaboration with Prof. M.E. Regonesi, UniMiB).

In situ studies of amyloid deposits and the comparison of ex vivo and in vitro fibrils have been also performed in different systems, including pathogenic immunoglobulin light chains derived from patients (see "Ami et al. 2016 Sci Rep. 6:29096" and "Ami et al. 2019 Anal. Chem. 91, 2894-2900").

In particular, FTIR spectroscopy is a label-free and non-invasive approach that we apply not only to isolated biomolecules but also to intact cells and tissues. In our studies, we combine IR spectroscopy with multivariate analysis to obtain a "spectroscopic fingerprinting" of the sample under investigation, which

represents a snapshot of the composition and structure of its main biomolecules. For instance, we applied this approach to fat aspirates from patients affected by systemic amyloidosis (Ami et al. 2019 Anal. Chem. 91, 2894–2900) and to tears from patients affected by amyotrophic lateral sclerosis (Ami et al. 2021 Anal. Chem. 93, 51, 16995–17002). In both systems, we found that our approach differentiates the samples from the diseased individuals from control specimens with high sensitivity and specificity. It is worth noting that the wavenumbers most important for discrimination allowed us to disclose spectroscopic markers related to the pathological molecular mechanisms.

PAST AND PRESENT COLLABORATIONS

These studies were performed in the framework of collaborations with Italian and foreign researchers, among them:

- Prof.ssa M. Lotti, Prof.ssa S. Brocca, Prof.ssa R. Grandori, Prof.ssa Regonesi, Prof. F. Peri, and Prof. P. Tortora (University of Milano-Bicocca, Italy);
- Dr. F. Lavatelli (University of Pavia, Italy);
- Prof.ssa D. Picone (Department of Chemical Sciences, University of Naples 'Federico II', Napoli, Italy)
- Prof. V. Bellotti, Prof.ssa S. Giorgetti (University College London (UK) and University of Pavia (Italy));
- Prof. M. Bolognesi, Prof. S. Ricagno (University of Milan, Italy);
- Prof.ssa A. Relini (University of Genoa, Italy);
- Prof. G. Legname (Scuola Internazionale Superiore di Studi Avanzati, SISSA, Trieste, Italy);
- Dr. M. Salmona (IRCCS-Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy);
- Prof. G. Merlini (Policlinico San Matteo, Pavia);
- Prof. M. Stefani, Prof.ssa M. Bucciattini (University of Florence);
- Prof. P. Goloubinoff (University of Lausanne, Switzerland);
- Prof. E. García-Fruitós (Universitat Autònoma de Barcelona, Spain);
- Prof. J-L Reymond (University of Berne, Switzerland).

PUBLICATIONS

- 108 publications on peer-reviewed, international journals;
- total citations (March 2023): >4000 in Google Scholar; >3200 in Scopus;
- h-index (March 2023): h=39 (Google Scholar); h=33 (Scopus).
- 9 chapters on international books;
- > 60 participations to national and international congresses.

Google Scholar: <https://scholar.google.com/citations?hl=it&user=CQkk38UAAAAJ>

ORCID: <https://orcid.org/0000-0002-1489-272X>

SELECTED PUBLICATIONS (*Corresponding Authors)

- Ami, D., Franco, A.R., Artusa, V., Mereghetti, P., Peri, F., **Natalello*, A.** A Global Picture of Molecular Changes Associated to LPS Treatment in THP-1 Derived Human Macrophages by Fourier Transform Infrared Microspectroscopy (2022) International Journal of Molecular Sciences, 23 (21), art. no. 13447
- Mangiagalli, M., Ami, D., de Divitiis, M., Brocca, S., Catelani, T., **Natalello*, A.**, Lotti*, M. Short-chain alcohols inactivate an immobilized industrial lipase through two different mechanisms (2022) Biotechnology Journal, 17 (6), art. no. 2100712
- Ami*, D., Mereghetti, P., **Natalello*, A.** Contribution of Infrared Spectroscopy to the Understanding of Amyloid Protein Aggregation in Complex Systems (2022) Frontiers in Molecular Biosciences, 9, art. no. 822852
- Ami, D., Duse, A., Mereghetti, P., Cozza, F., Ambrosio, F., Ponzini, E., Grandori, R., Lunetta, C., Tavazzi, S., Pezzoli*, F., **Natalello*, A.** Tear-Based Vibrational Spectroscopy Applied to Amyotrophic Lateral Sclerosis (2021) Analytical Chemistry, 93 (51), pp. 16995-17002.
- Ami, D., Sciandrone, B., Mereghetti, P., Falvo, J., Catelani, T., Visentin, C., Tortora, P., Ventura, S., **Natalello*, A.**, Regonesi*, M.E. Pathological atx3 expression induces cell perturbations in e. Coli as revealed by biochemical and biophysical investigations (2021) International Journal of Molecular Sciences, 22 (2), art. no. 943, pp. 1-21.
- Sala, B.M., Le Marchand, T., Pintacuda, G., Camilloni*, C., **Natalello*, A.**, Ricagno*, S. Conformational Stability and Dynamics in Crystals Recapitulate Protein Behavior in Solution (2020) Biophysical Journal, 119 (5), pp. 978-988.
- Villa, A.M., Doglia, S.M., De Gioia, L., Bertini*, L., **Natalello*, A.** Anomalous Intrinsic Fluorescence of HCl and NaOH Aqueous Solutions (2019) Journal of Physical Chemistry Letters, 10 (22), pp. 7230-7236.
- Ami, D., Mereghetti, P., Foli, A., Tasaki, M., Milani, P., Nuvolone, M., Palladini, G., Merlini, G., Lavatelli, F., **Natalello*, A.** ATR-FTIR spectroscopy supported by multivariate analysis for the characterization of adipose tissue aspirates from patients affected by systemic amyloidosis (2019) Analytical Chemistry, 91 (4), pp. 2894-2900.

- Orsini*, F., Ami, D., Lascialfari, A., **Natalello*, A.** Inhibition of lysozyme fibrillogenesis by hydroxytyrosol and dopamine: An Atomic Force Microscopy study (2018) *International Journal of Biological Macromolecules*, 111, pp. 1100-1105.
- Tedeschi, G., Mangiagalli, M., Chmielewska, S., Lotti, M., **Natalello*, A.**, Brocca*, S. Aggregation properties of a disordered protein are tunable by pH and depend on its net charge per residue (2017) *Biochimica et Biophysica Acta - General Subjects*, 1861 (11), pp. 2543-2550.
- **Natalello, A.**, Santambrogio, C., Grandori*, R. Are Charge-State Distributions a Reliable Tool Describing Molecular Ensembles of Intrinsically Disordered Proteins by Native MS? (2017) *Journal of the American Society for Mass Spectrometry*, 28 (1), pp. 21-28.
- Konijnenberg, A., Ranica, S., Narkiewicz, J., Legname, G., Grandori, R., Sobott*, F., **Natalello*, A.** Opposite Structural Effects of Epigallocatechin-3-gallate and Dopamine Binding to α -Synuclein (2016) *Analytical Chemistry*, 88 (17), pp. 8468-8475.
- Ami*, D., Lavatelli, F., Rognoni, P., Palladini, G., Raimondi, S., Giorgetti, S., Monti, L., Doglia, S.M., **Natalello, A.**, Merlini*, G. In situ characterization of protein aggregates in human tissues affected by light chain amyloidosis: a FTIR microspectroscopy study (2016) *Scientific Reports*, 6, art. no. 29096.
- **Natalello, A.**, Mangione, P.P., Giorgetti, S., Porcari, R., Marchese, L., Zorzoli, I., Relini, A., Ami, D., Faravelli, G., Valli, M., Stoppini, M., Doglia, S.M., Bellotti, V., Raimondi*, S. Co-fibrillogenesis of wild-type and D76N β 2-microglobulin: The crucial role of fibrillar seeds (2016) *Journal of Biological Chemistry*, 291 (18), pp. 9678-9689.
- **Natalello, A.**, Mattoo, R.U.H., Priya, S., Sharma, S.K., Goloubinoff*, P., Doglia*, S.M. Biophysical characterization of two different stable misfolded monomeric polypeptides that are chaperone-amenable substrates (2013) *Journal of Molecular Biology*, 425 (7), pp. 1158-1171.

Milan, 02 March 2023