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## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

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NAME Carazo, Jose Maria		POSITION TITLE Full Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) carazog			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of Granada, Spain	Ms.C	1981	Physics
University Autonoma, Madrid, Spain	Ph.D	1984	Structural Biology

### A. Personal statement.

I have a sustained experience in the field of Three-dimensional Electron Microscopy (3DEM), especially in the methods development area. My laboratory has opened whole new areas in the field, naming just as example the recent successful family of Maximum Likelihood algorithms (developed in Madrid from 2007 to 2011), the very much used EMDataBank (started from the European Union Bioimage project that I coordinated from 1996 to 1999), or the new mathematics on SOM neural networks. All our software is compiled and distributed as a software suite named XMIPP, which has been downloaded by more than 2500 registered users in the last years.

In the context of the construction of the Spanish Synchrotron ALBA, I defended the construction of a new beam line for Soft X-ray Tomography of cells, complementing approaches initiated at the Berlin and Berkeley synchrotrons. This beam line is a reality since 2012, offering access to an instrument unique of its kind. Irrespective of the photon source and of the beam line design, there are fundamental issues regarding the image-forming interaction of photons with biological matter at these wave lengths, issues that clearly demand specific image processing developments.

I believe in multidisciplinary approaches to science as a way of finding truly new discoveries at the interface of different disciplines, I also believe in "team work" and focused multidisciplinary collaborations

I would like to add that as a recognition to both my contributions to the EM field and also to my way of forming successful teams around me, and in the context of an international competition in Europe, we have been selected as the Instruct Center for Image Processing in Structural Biology, which is part of the Strategic European Research Infrastructure INSTRUMENT, starting in 2011. This central role certainly will help us in assuring the dissemination of our "fresh" developments in a global manner.

### B. Positions and Honors.

#### Positions and Employment

1981-1984	Pre-doctoral fellow, IBM Research Center, Madrid, Spain
1985-1986	Post-doctoral fellow, Centro de Biología Molecular Severo Ochoa, Madrid, Spain
1987-1988	Research Affiliate II, New York State Department of Health
1989-	Head of the Biocomputing Unit, National Center of Biotechnology, Madrid, Spain
1990-2000	Tenure Scientist, National, Center of Biotechnology, Madrid, Spain
2001-2002	Senior Research Scientist, National Center of Biotechnology, Madrid, Spain
1998-2001	Deputy Director for Research, National Center of Biotechnology, Madrid,
2002-2003	Deputy Director for Research Planning and Monitoring, Science and Technology Ministry
1995-2003	Adj. Professor of Computer Science, Autonoma University, Madrid, Spain
2003-2004	Senior Research Scientist National Center of Biotechnology, Madrid, Spain
2005 -	Full Professor, National Center of Biotechnology, Madrid, Spain
2015 – 2017	European Synchrotron Radiation Facility, Science Advisory Committee (SAC)

- 2015 Australian Centre of Excellence for Advanced Molecular Imaging, International Scientific Advisory Committee (ISAC)
- 2015 Netherlands Centre for Electron Nanoscopy (NeCEN), Chair of the Application Review Committee
- 2016 Member of the Outstanding User Program of the National Center for Protein Science, Shanghai

#### **Other Experience and Professional Memberships**

- 1997-2001 President of the Spanish Microscopy Society.
- 2005- Senior member of the IEEE Computer Society
- 2003-2014 Principal Founder of the spin-off Integromics, developing software in the Bioinformatics area and sold to Perkin Elmer on July 2014

#### **Honors**

- 1984 PhD Excellence Award by the Spanish Academy of Science.
- 1986 Okazato Research Award, by JEOL.
- 1998 Rhone-Poulenc Excellence Award by the French Academy of Science
- 2008 Frost & Sullivan Most Innovative European Bioinformatics Company of the year to our spin-off company Integromics

### **C. Selected recent peer-reviewed publications (last 10 years only –since 2005-, 29 publications selected from a total of 203)**

1. C.O.S.Sorzano, R.Marabini, G.T.Herman and J.M.Carazo. Multiobjective algorithm optimization using multivariate statistics in three-dimensional electron microscopy reconstructions. *Pattern Recognition*, 2005: 38:2587-2601.
2. Y. Gómez-Llorente, R.J. Fletcher, X.S. Chen, J.M. Carazo and C. San Martín. Polymorphism and double hexamer structure in the archaeal minichromosome maintenance (MCM) helicase from *Methanobacterium thermoautotrophicum*. *Journal of Biological Chemistry*, 2005: 280:40909-40915.
3. S.H.W. Scheres, M. Valle, R. Nuñez, C.O.S. Sorzano, R. Marabini, G.T. Herman and J.M. Carazo. Maximum-likelihood multi-reference refinement for electron microscopy images, *Journal of Molecular Biology*, 2005: 348:139-149.
4. M. Valle, X.S. Chen, L.E. Donate, E. Fanning and J.M. Carazo. Structural basis for the cooperative assembly of large T antigen on the origin of replication. *Journal of Molecular Biology*, 2006: 357:1295-1305.
5. R. Núñez-Ramírez, M. Velten, G. Rivas, P. Polard, J.M. Carazo and L.E. Donate. Loading a ring: structure of the *Bacillus subtilis* DnaB protein, a co-leader of the replicative helicase. *Journal of Molecular Biology*, 2007: 367:764-769. .
6. H. Tidow, R. Melero, E. Mylonas, S.M. Freund, J.G. Grossmann, J.M. Carazo, D.I. Svergun, M. Valle and A.R. Fersht. Quaternary structures of tumor suppressor p53 and a specific p53 DNA complex. *Proceedings of the National Academy of Sciences*, 2007: 104:12324-12329. PMID: PMC1941468.
7. S.H.W. Scheres, H. Gao, M. Valle, G.T. Herman, P.P.B. Eggermont, J. Frank and J.M. Carazo. Disentangling conformational states of macromolecules in 3D-EM through likelihood optimization, *Nature Methods*, 2007: 4:27-29.
8. S.H. Scheres, R. Núñez-Ramírez, C.O.S. Sorzano, J.M. Carazo and R. Marabini. Image processing for electron microscopy single-particle analysis using XMIPP. *Nature Protocols*, 2008: 3:977-990. PMID: PMC2778070.
9. C.O.S.Sorzano, J.A. Velázquez-Muriel, R.Marabini, G.T.Herman and J.M.Carazo. Volumetric restrictions in single particle 3DEM reconstructions. *Pattern Recognition*, 2008: 41: 616-626. PMID: PMC2812911
10. S. Nickell, F. Beck, S.H.W. Scheres, A. Korinek, F. Förster, K. Lasker, O. Mihalache, N. Sun, I. Nagy, A. Sali, J.M. Plitzko, J.M. Carazo, M. Mann and W. Baumeister. Insights into the molecular architecture of the 26S proteasome. *Proceedings of the National Academy of Sciences*, 2009: 106:11943-11947. PMID: PMC2715492.
11. S.H.W. Scheres, R.M. Melero, M. Valle & J.M. Carazo. Averaging of electron subtomograms and random conical tilt reconstructions through likelihood optimization. *Structure*, 2009: 17, 1563-1572

12. Cuesta I, Núñez-Ramírez R, Scheres SH, Gai D, Chen XS, Fanning E, Carazo JM. Conformational rearrangements of SV40 large T antigen during early replication events. *J Mol Biol.* 2010; 397:1276-86..PMCID: PMC2862297
13. Melero R, Rajagopalan S, Lázaro M, Joerger AC, Brandt T, Veprintsev DB, Lasso G, Gil D, Scheres SH, Carazo JM, Fersht AR, Valle M Electron microscopy studies on the quaternary structure of p53 reveal different binding modes for p53 tetramers in complex with DNA. *Proc Natl Acad Sci U S A.* 2011; 108(2):557-62. PMID: 21178074.
14. Oton J, Sorzano CO, Pereiro E, Cuenca-Alba J, Navarro R, Carazo JM, Marabini R. Image formation in cellular X-ray microscopy. *J Struct Biol.*2012; 178(1): 29-37. PMID:22343468
15. [Vargas J](#), [Otón J](#), [Marabini R](#), [Jonc S](#), [de la Rosa-Trevín JM](#), [Carazo JM](#), [Sorzano CO](#). FASTDEF: Fast defocus and astigmatism estimation for high-throughput transmission electron microscopy. *JSB.* 2013; e 181(2): 136–148 PMID: 23261401
16. Vargas J, Abrishami V, Marabini R, de la Rosa-Trevín JM, Zaldivar A, Carazo JM, Sorzano CO. Particle quality assessment and sorting for automatic and semiautomatic particle-picking techniques.*J Struct Biol.* 2013 Sep;183(3):342-53. doi: 10.1016/j.jsb.2013.07.015. PMID: 23933392
17. Abrishami V, Zaldivar-Peraza A, de la Rosa-Trevín JM, Vargas J, Otón J, Marabini R, Shkolnisky Y, Carazo JM, Sorzano CO. A pattern matching approach to the automatic selection of particles from low-contrast electron micrographs. *Bioinformatics.* 2013 Oct 1;29(19):2460-8. doi: 10.1093/bioinformatics/btt429. PMID: 23958728
18. de la Rosa-Trevín JM, Otón J, Marabini R, Zaldivar A, Vargas J, Carazo JM, Sorzano CO.Xmipp 3.0: An improved software suite for image processing in Electron Microscopy. *J Struct Biol.* 2013 Sep 25. doi:pii: S1047-8477(13)00256-6. 10.1016/j. PMID: 24075951
19. Otón J, Sorzano CO, Marabini R, Pereiro E, Carazo JM. Measurement of the modulation transfer function of an X-ray microscope based on multiple Fourier orders analysis of a Siemens star. *Opt Express.* 2015 Apr 20;23(8):9567-72. doi: 10.1364/OE.23.009567. PMID: 25968993
20. Marabini R, Carragher B, Chen S, Chen J, Cheng A, Downing KH, Frank J, Grassucci RA, Bernard Heymann J, Jiang W, Jonc S, Liao HY, Ludtke SJ, Patwari S, Piotrowski AL, Quintana A, Sorzano CO, Stahlberg H, Vargas J, Voss NR, Chiu W, Carazo JM. CTF Challenge: Result summary. *J Struct Biol.* 2015 Jun;190(3):348-59. doi: 10.1016/j.jsb.2015.04.003. PMID: 25913484
21. Segura J, Sorzano CO, Cuenca-Alba J, Aloy P, Carazo JM. Using neighborhood cohesiveness to infer interactions between protein domains. *Bioinformatics.* 2015 Apr 2. pii: btv188. PMID: 25838464
22. Abrishami V, Vargas J, Li X, Cheng Y, Marabini R, Sorzano CO, Carazo JM. Alignment of direct detection device micrographs using a robust Optical Flow approach. *J Struct Biol.* 2015 Mar;189(3):163-76. doi: 10.1016/j.jsb.2015.02.001. PMID: 25681631
23. Sorzano CO, Vargas J, de la Rosa-Trevín JM, Otón J, Álvarez-Cabrera AL, Abrishami V, Sesmero E, Marabini R, Carazo JM.A statistical approach to the initial volume problem in Single Particle Analysis by Electron Microscopy. *J Struct Biol.* 2015 Mar;189(3):213-9. doi: 10.1016/j.jsb.2015.01.009.
24. C.O.S. Sorzano, J. Vargas, J. Otón, V. Abrishami, J.M. de la Rosa-Trevín, S. del Riego, A. Fernández-Alderete, C. Martínez-Rey, R. Marabini, J.M. Carazo. Fast and accurate conversion of atomic models into electron density maps. *AIMS Biophysics.* 2(1): 8-20. 2015
25. J.M. Carazo, C.O.S. Sorzano, J. Otón, R. Marabini, J. Vargas. Three-dimensional reconstruction methods in Single Particle Analysis from transmission electron microscopy data.. *Archives of Biochemistry and Biophysics.* 581: 39–48. 2015
26. V. Abrishami, J.R. Bilbao-Castro, J. Vargas, R. Marabini, J.M. Carazo, C.O.S. Sorzano. A fast iterative convolution-based weighting approach for direct Fourier three-dimensional reconstruction. *Ultramicroscopy.* 157: 79 - 87. 2015
27. C.O.S. Sorzano, M. Alcorlo, J.M. de la Rosa-Trevín, R. Melero, I. Foche, A. Zaldivar-Peraza, L. del Cano, J. Vargas, V. Abrishami, J. Otón, R. Marabini, J.M. Carazo. Cryo-EM and the elucidation of new macromolecular structures: Random Conical Tilt revised. *Sci. Rep.*. 5:14290. 2015 DOI: 10.1038/srep14290
28. Condezo GN, Marabini R, Ayora S, Carazo JM, Alba R, Chillón M, San Martín C.Structures of Adenovirus Incomplete Particles Clarify Capsid Architecture and Show Maturation Changes of Packaging Protein L1 52/55k.*J Virol.*89(18):9653-64. 2015.doi: 10.1128/JVI.01453-15
29. J. Vargas, J. Otón, R. Marabini, J.M. Carazo, C.O.S. Sorzano. Particle alignment reliability in single particle electron cryomicroscopy: a general approach. *Nature Scientific Reports( In press)*

## **D. Research Support**

### **Ongoing Research Support**

UE (653706): H2020-INFRAIA-2014-2015 European Union iNEXT: Infrastructure for NMR, EM and X-ray crystallography for translational research Role: PI	01/09/2015 – 31/08/2019
UE (654142): H2020-EINFRA-2014-2 European Union EGI-Engage: Engaging the EGI Community towards an Open Science Commons Role: PI	01/03/2015 – 31/08/2017
UE (675858): H2020- EINFRA-2015-1 European Union West life: World-wide E-infrastructure for structural biology Role: PI	01/11/2015 – 31/10/2018
UE (654248): H2020- INFRADEV-1-2014-1 European Union CORBEL: Coordinated Research Infrastructures Building Enduring Life-science services Role: PI	01/09/2015 – 31/08/2018
UE(676559): H2020-INFRADEV-3-2015 European Union ELIXIR-EXCELERATE: Fast-track ELIXIR implementation and drive early user exploitation across the life-sciences. Role: PI	01/09/2015 – 31/08/2019
UE (CAP-INFRA/1376) European Union BioStruct: Transnational access and enhancement of integrated Biological Structure determination and synchrotron X-ray facilities. Role: PI	01/09/2011 – 31/08/2015
CAM S2010/BMD-2305 Community of Madrid PROFUN-II: Hacia la proteómica funcional del centrosoma Role: Coordinator of six research groups & PI	01/01/2011 - 30/04/2016
AIC-A-2011-0638 MICINN Comienzo de la fase operativa del Instruct Image Processing Center Role: PI	01/12/2011- 01/12/2016
PT13/0001/0009. ISCIII Plataforma de recursos biomoleculares y bioinformáticos, PRB2 Role. PI	01/01/2014 – 31/12/2017
BIO2013-44647-R MINECO Procesamiento tridimensional de imagen robusto y automatizado en biología estructural Role: PI	01/01/2014 – 31/12/2016

## **Completed Research Support (since 2010)**

Image Processing in Biological 3D Electron Microscopy

Funding entity NIH 2R01 HL070472-05 Herman (PI)

Timing of the project:

09/01/2005 - 08/31/2010

Role: Co-PI

Centrosome – 3D (CSD2006-00023)

Funding entity Spanish Ministry of Education and Sciences (MEC)

Timing of the project:

11/01/2006 - 11/05/2012

Role: PI

Hacia la proteomica funcional: una aproximación conjunta desde la proteomica, la bioinformática y la biología estructural (S-GEN-0166-2006)

Funding entity: Community of Madrid

Timing of the project:

01/01/2007 – 12/31/2011

Research leader: J.M.Carazo (PI) (Coordinator of six research groups)

Análisis de grandes cantidades de imágenes de microscopia electrónica tridimensional: Desarrollo de métodos y aplicación al análisis del replisoma.

Funding entity: BIO2007 - 67150 Spanish Ministry of Education and Sciences (MEC)

Timing of the project:

10/01/2007 – 10/01/2010

Research leader: J.M.Carazo (PI)

Tomografía de Rayos X: Una herramienta de integración entre biología molecular y celular.

Funding entity: Spanish High Research Council (CSIC) PIF08-020-2:

Timing of the project:

09/01/2008 - 08/31/2011

Role: Coordinator (Coordinator of three research groups)

Resolve chronic inflammation and achieve healthy ageing by understanding non-regenerative repair.

Funding entity UE (CE: FP7-202047)

Resolve chronic inflammation and achieve healthy ageing by understanding non-regenerative repair.

Timing of the project:

04/01/2008 - 09/30/2013

Role: PI

Associated center for image processing in microscopy for structural biology

Funding entity MICINN: ACI2009-10220

Timing of the project:

01/01/2010 - 12/15/2012

Role: PI

Puesta en marcha del Centro Asociado INSTRUMENT en procesamiento de imágenes en Microscopía

Funding entity MICINN ACI2010-1088:

Timing of the project:

01/01/2011 - 03/31/2013

Role: PI

Hacia una Microscopía electrónica tridimensional de alto rendimiento.

MICINN. BIO2010-16566

Timing of the project:

01/01/2011 - 06/30/2014 Role: PI