

**[Annalisa Bucchi]**  
**CURRICULUM VITAE**

**INFORMAZIONI PERSONALI**

<b>COGNOME</b>	<b>BUCCHI</b>
<b>NOME</b>	<b>ANNALISA</b>

**POSIZIONE**

APRILE 2019-PRESENTE: Professore Associato, Dipartimento di Bioscienze, Università degli Studi di Milano

**EDUCAZIONE**

12/12/2003 -Dottorato di Ricerca in Fisiologia, Università degli Studi di Milano.  
23/02/2000 -Laurea in Scienze Biologiche, Indirizzo Fisiopatologico – Facoltà di Scienze Matematiche, Fisiche e Naturali, Università degli Studi di Milano

**ATTIVITÀ DI RICERCA IN ITALIA**

04-2016/03-2019 Ricercatore a tempo determinato B, Dip. di Bioscienze, Università degli Studi di Milano.  
10-2015/03-2016 Postdoc, Dip. di Bioscienze, Università degli Studi di Milano.  
10-2012/09-2015 Ricercatore a tempo determinato A, Dip. di Bioscienze, Università degli Studi di Milano.  
11-2007/09-2012 Assegnista di Ricerca, Dip. di Scienze Biomolecolari e Biotecnologie/Dip. di Bioscienze, Università degli Studi di Milano.  
01-2007/10-2007 Postdoc, Dip. di Scienze Biomolecolari e Biotecnologie, Università degli Studi di Milano.  
01-2004/09-2004 Postdoc, Dip. Scienze Biomolecolari e Biotecnologie, Università degli Studi di Milano.  
2000-2003 Dottorato di Ricerca in Fisiologia, Dipartimento di Fisiologia e Biochimica Generali, Università degli Studi di Milano.

**ATTIVITÀ DI RICERCA ALL'ESTERO**

11-2012 Invited Research Scientist per 2 settimane presso il laboratorio del Prof. Mark Boyett, Institute of Cardiovascular Sciences, University of Manchester-UK  
12-2009 Invited Postdoc Research Scientist per 1 settimana presso il laboratorio del Prof. Robinson RB, Department of Pharmacology, Columbia University, NY – USA  
10-2004/12-2006 Postdoc Research Scientist, Department of Pharmacology, Columbia University, NY – USA.

**PUBBLICAZIONI SCIENTIFICHE**

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1. Altomare C, **Bucchi A**, Camatini E, Baruscotti M, Viscomi C, Moroni A, DiFrancesco D. (2001). Integrated allosteric model of voltage gating of HCN channels. *Journal of General Physiology*, 117(6):519-32. PMID: 11382803; PMCID:PMC2232403.
2. Viscomi C, Altomare C, **Bucchi A**, Camatini E, Baruscotti M, Moroni A, DiFrancesco D. (2001). C terminus-mediated control of voltage and cAMP gating of hyperpolarization-activated cyclic nucleotide-gated channels. *Journal of Biological Chemistry*, 276 (32):29930-4. PMID: 11397812.
3. **Bucchi A**, Baruscotti M, DiFrancesco D. (2002). Current-dependent block of rabbit sino-atrial node I(f) channels by ivabradine. *Journal of General Physiology*, 120(1):1-13. PMID: 12084770; PMCID: PMC2238187.
4. Qu J, Altomare C, **Bucchi A**, DiFrancesco D, Robinson RB (2002). Functional comparison of HCN isoforms expressed in ventricular and HEK 293 cells. *Pflugers Archiv-European Journal of Physiology*, 444(5):597-601. PMID: 12194012.
5. **Bucchi A**, Baruscotti M, Robinson RB, DiFrancesco D. (2003). I(f)-dependent modulation of pacemaker rate mediated by cAMP in the presence of ryanodine in rabbit sino-atrial node cells. *Journal of Molecular and Cellular Cardiology*, 35(8):905-13. PMID:12878477.
6. Baruscotti M, **Bucchi A**, DiFrancesco D. (2005). Physiology and pharmacology of the cardiac pacemaker ("funny") current. *Pharmacology & Therapeutics*, 107(1):59-79. Review. PMID: 15963351.
7. **Bucchi A**, Tognati A, Milanesi R, Baruscotti M, DiFrancesco D. (2006) Properties of ivabradine-induced block of HCN1 and HCN4 pacemaker channels. *Journal of Physiology*, 572(Pt 2):335-46. PMID: 16484306; PMCID: PMC1779671.
8. Rosen MR, **Bucchi A**, Robinson RB (2006). If modulation: Perspectives in clinical medicine. *European Heart Journal, Supplement*, 8: D3-D8.
9. **Bucchi A**\*, Plotnikov AN\*, Shlapakova I\*, Danilo P Jr, Kryukova Y, Qu J, Lu Z, Liu H, Pan Z, Potapova I, KenKnight B, Girouard S, Cohen IS, Brink PR, Robinson RB, Rosen MR. (2006). Wild-type and mutant HCN channels in a tandem biological-electronic cardiac pacemaker. *Circulation*, 114(10):992-9. PMID: 16923750. \*, uguale contributo.
10. Pian P, **Bucchi A**, Robinson RB, Siegelbaum SA. (2006). Regulation of gating and rundown of HCN hyperpolarization-activated channels by exogenous and endogenous PIP2. *Journal of General Physiology*, 128(5):593-604. PMID: 17074978; PMCID: PMC2151583.
11. **Bucchi A**, Barbuti A, Baruscotti M, DiFrancesco D. (2007). Heart rate reduction via selective 'funny' channel blockers. *Current Opinion in Pharmacology*, 7(2): 208-213. Review. PMID: 17267284.

12. **Bucchi A**, Baruscotti M, Robinson RB, DiFrancesco D. (2007). Modulation of rate by autonomic agonists in SAN cells involves changes in diastolic depolarization and the pacemaker current. *Journal of Molecular and Cellular Cardiology*, 43(1): 39-48. PMID: 17543331.
13. Pian P, **Bucchi A**, Decostanzo A, Robinson RB, Siegelbaum SA. (2007). Modulation of cyclic nucleotide-regulated HCN channels by PIP(2) and receptors coupled to phospholipase C. *Pflugers Archiv- European Journal of Physiology*, 455(1): 125-145. PMID: 17605039.
14. Plotnikov AN\*, **Bucchi A\***, Shlapakova I, Danilo P Jr, Brink PR, Robinson RB, Cohen IS, Rosen MR. (2008). HCN212-channel biological pacemakers manifesting ventricular tachyarrhythmias are responsive to treatment with I(f) blockade. *Heart Rhythm*, 5(2): 282-288. doi: 10.1016/j.hrthm.2007.09.028. PMID: 18242555; PMCID: PMC2254308. \*, uguale contributo.
15. Protas L, Dun W, Jia Z, Lu J, **Bucchi A**, Kumari S, Chen M, Cohen IS, Rosen MR, Entcheva E, Robinson RB.(2009). Expression of skeletal but not cardiac Na<sup>+</sup> channel isoform preserves normal conduction in a depolarized cardiac syncytium. *Cardiovascular Research*, 81(3): 528-535. doi: 10.1093/cvr/cvn290. PMID: 18977767; PMCID: PMC2639131.
16. Zhao X, **Bucchi A**, Oren RV, Kryukova Y, Dun W, Clancy CE, Robinson RB. (2009). In vitro characterization of HCN channel kinetics and frequency dependence in myocytes predicts biological pacemaker functionality. *Journal of Physiology*, 587(Pt7): 1513-1525. doi: 10.1113/jphysiol.2008.163444. PMID: 19171659; PMCID: PMC2678222.
17. Baruscotti M, Barbuti A, **Bucchi A**. (2010). The cardiac pacemaker current. *Journal of Molecular and Cellular Cardiology*, 48(1): 55-64. doi: 10.1016/j.yjmcc.2009.06.019. Review. PMID: 19591835.
18. Baruscotti M, **Bucchi A**, Viscomi C, Mandelli G, Consalez G, Gnecci-Rusconi T, Montano N, Casali KR, Micheloni S, Barbuti A, DiFrancesco D.(2011). Deep bradycardia and heart block caused by inducible cardiac-specific knockout of the pacemaker channel gene *Hcn4*. *Proc Natl Acad Sci U S A*, 108(4): 1705-1710. doi: 10.1073/pnas.1010122108. PMID: 21220308; PMCID: PMC3029742.
19. DiFrancesco JC, Barbuti A, Milanesi R, Coco S, **Bucchi A**, Bottelli G, Ferrarese C, Franceschetti S, Terragni B, Baruscotti M, DiFrancesco D. (2011). Recessive loss-of-function mutation in the pacemaker HCN2 channel causing increased neuronal excitability in a patient with idiopathic generalized epilepsy. *Journal of Neuroscience*, 31(48): 17327-17337. doi: 10.1523/JNEUROSCI.3727-11.2011. PMID: 22131395.
20. **Bucchi A**, Barbuti A, DiFrancesco D, Baruscotti M. (2012). Funny Current and Cardiac Rhythm: Insights from HCN Knockout and Transgenic Mouse Models. *Frontiers in Physiology*, 3:240. doi: 10.3389/fphys.2012.00240. PMID: 22783204; PMCID: PMC3387723.
21. **Bucchi A\***, Baruscotti M\*, Nardini M, Barbuti A, Micheloni S, Bolognesi M, DiFrancesco D. (2013). Identification of the molecular site of ivabradine binding to HCN4 channels. *PLoS One*. 8(1):e53132. doi: 10.1371/journal.pone.0053132. PMID: 23308150; PMCID: PMC3537762. \*, uguale contributo.

22. Scavone A, Capiluppo D, Mazzocchi N, Crespi A, Zoia S, Campostrini G, **Bucchi A**, Milanese R, Baruscotti M, Benedetti S, Antonini S, Messina G, DiFrancesco D, Barbuti A. (2013). Embryonic stem cell-derived CD166+ precursors develop into fully functional sinoatrial-like cells. *Circulation Research*, 113(4):389-98. doi: 10.1161/CIRCRESAHA.113.301283. PMID: 23753573.
23. Lolicato M\*, **Bucchi A\***, Arrigoni C, Zucca S, Nardini M, Schroeder I, Simmons K, Aquila M, DiFrancesco D, Bolognesi M, Schwede F, Kashin D, Fishwick CW, Johnson AP, Thiel G, Moroni A. (2014). Cyclic dinucleotides bind the C-linker of HCN4 to control channel cAMP responsiveness. *Nature Chemical Biology*, 10(6):457-62. doi: 10.1038/nchembio.1521. Erratum in: *Nat Chem Biol.*, 10(8):692. PMID: 24776929. \*, uguale contributo.
24. D'Souza A\*, **Bucchi A\***, Johnsen AB\*, Logantha SJ\*, Monfredi O, Yanni J, Prehar S, Hart G, Cartwright E, Wisloff U, Dobryznski H, DiFrancesco D, Morris GM, Boyett MR (2014). Exercise training reduces resting heart rate via downregulation of the funny channel HCN4. *Nature Communications*, 5:3775. doi: 10.1038/ncomms4775. PMID: 24825544; PMCID: PMC4024745. \*, uguale contributo.
25. Milanese R, **Bucchi A**, Baruscotti M (2015). The genetic basis for inherited forms of sinoatrial dysfunction and atrioventricular node dysfunction. *Journal of Interventional Cardiac Electrophysiology*, 43(2):121-34. doi: 10.1007/s10840-015-9998-z. Review. PMID: 25863800; PMCID: PMC4486151.
26. Ravagli E, **Bucchi A**, Bartolucci C, Paina M, Baruscotti M, DiFrancesco D, Severi S. (2016). Cell-specific Dynamic Clamp analysis of the role of funny I(f) current in cardiac pacemaking. *Progress in Biophysics and Molecular Biology*, 120(1-3):50-66. doi: 10.1016/j.pbiomolbio.2015.12.004. PMID: 26718599.
27. Baruscotti M, Bianco E, **Bucchi A**, DiFrancesco D.(2016). Current understanding of the pathophysiological mechanisms responsible for inappropriate sinus tachycardia: role of the I(f) "funny" current. *Journal of Interventional Cardiac Electrophysiology*, 46(1):19-28. doi: 10.1007/s10840-015-0097-y. Review. PMID: 26781742.
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29. Baruscotti M\*, **Bucchi A\***, Milanese R, Paina M, Barbuti A, Gneccchi-Ruscione T, Bianco E, Vitali-Serdoz L, Cappato R, DiFrancesco D. (2017). A gain-of-function mutation in the cardiac pacemaker HCN4 channel increasing cAMP sensitivity is associated with familial Inappropriate Sinus Tachycardia. *European Heart Journal*, 38(4):280-288. doi: 10.1093/eurheartj/ehv582. PMID: 28182231. \*, uguale contributo.
30. Campostrini G, Bonzanni M, Lissoni A, Bazzini C, Milanese R, Vezzoli E, Francolini M, Baruscotti M, **Bucchi A**, Rivolta I, Fantini M, Severi S, Cappato R, Crotti L, J Schwartz P, DiFrancesco D, Barbuti A. (2017). The expression of the rare caveolin-3 variant T78M alters cardiac ion channels function and membrane excitability. *Cardiovascular Research*, 113(10):1256-1265. doi: 10.1093/cvr/cvx122. PMID: 28898996; PMCID: PMC5852518.

31. Yavari A, Bellahcene M, **Bucchi A**, Sirenko S, Pinter K, Herring N, Jung JJ, Tarasov KV, Sharpe EJ, Wolfien M, Czibik G, Steeples V, Ghaffari S, Nguyen C, Stockenhuber A, Clair JRS, Rimbach C, Okamoto Y, Yang D, Wang M, Ziman BD, Moen JM, Riordon DR, Ramirez C, Paina M, Lee J, Zhang J, Ahmet I, Matt MG, Tarasova YS, Baban D, Sahgal N, Lockstone H, Puliyadi R, de Bono J, Siggs OM, Gomes J, Muskett H, Maguire ML, Beglov Y, Kelly M, Dos Santos PPN, Bright NJ, Woods A, Gehmlich K, Isackson H, Douglas G, Ferguson DJP, Schneider JE, Tinker A, Wolkenhauer O, Channon KM, Cornall RJ, Sternick EB, Paterson DJ, Redwood CS, Carling D, Proenza C, David R, Baruscotti M, DiFrancesco D, Lakatta EG, Watkins H, Ashrafian H. (2017). Mammalian  $\gamma 2$  AMPK regulates intrinsic heart rate. *Nature Communications*, 8(1):1258. doi: 10.1038/s41467-017-01342-5. PMID: 29097735; PMCID: PMC5668267.
32. Saponaro A, Cantini F, Porro A, **Bucchi A**, DiFrancesco D, Maione V, Donadoni C, Introini B, Mesirca P, Mangoni ME, Thiel G, Banci L, Santoro B, Moroni A. (2018). A synthetic peptide that prevents cAMP regulation in mammalian hyperpolarization-activated cyclic nucleotide-gated (HCN) channels. *Elife*, Jun 20;7. pii: e35753. doi: 10.7554/eLife.35753. PMID: 29923826; PMCID: PMC6023613.
33. Bonzanni M, DiFrancesco JC, Milanese R, Campostrini G, Castellotti B, **Bucchi A**, Baruscotti M, Ferrarese C, Franceschetti S, Canafoglia L, Ragona F, Freri E, Labate A, Gambardella A, Costa C, Rivolta I, Gellera C, Granata T, Barbuti A, DiFrancesco D (2018). A novel de novo HCN1 loss-of-function mutation in genetic generalized epilepsy causing increased neuronal excitability. *Neurobiology of Disease*, 118:55-63. doi: 10.1016/j.nbd.2018.06.012. PMID: 29936235.
34. Campostrini G, DiFrancesco JC, Castellotti B, Milanese R, Gnecci-Ruscione T, Bonzanni M, **Bucchi A**, Baruscotti M, Ferrarese C, Franceschetti S, Canafoglia L, Ragona F, Freri E, Labate A, Gambardella A, Costa C, Gellera C, Granata T, Barbuti A, DiFrancesco D. (2018). A Loss-of-Function HCN4 Mutation Associated With Familial Benign Myoclonic Epilepsy in Infancy Causes Increased Neuronal Excitability. *Frontiers in Molecular Neuroscience*, 11:269. doi: 10.3389/fnmol.2018.00269. PMID: 30127718; PMCID: PMC6089338.
35. D'Souza A, Wang Y, Anderson C, Bucchi A, Baruscotti M, Olieslagers S, Mesirca P, Johnsen AB, Mastitskaya S, Ni H, Zhang Y, Black N, Cox C, Wegner S, Bano-Otalora B, Petit C, Gill E, Logantha SJRJ, Dobrzynski H, Ashton N, Hart G, Zhang R, Zhang H, Cartwright EJ, Wisloff U, Mangoni ME, da Costa Martins PA, Piggins HD, DiFrancesco D, Boyett MR. A circadian clock in the sinus node mediates day-night rhythms in Hcn4 and heart rate. *Heart Rhythm*. 2021 May;18(5):801-810. doi: 10.1016/j.hrthm.2020.11.026. Epub 2020 Dec 3. PMID: 33278629; PMCID: PMC8073545.
36. Giannetti F, Benzoni P, Campostrini G, Milanese R, Bucchi A, Baruscotti M, Dell'Era P, Rossini A, Barbuti A. A detailed characterization of the hyperpolarization-activated "funny" current ( $I_f$ ) in human-induced pluripotent stem cell (iPSC)-derived cardiomyocytes with pacemaker activity. *Pflugers Arch*. 2021 Jul;473(7):1009-1021. doi: 10.1007/s00424-021-02571-w. Epub 2021 May 2. PMID: 33934225; PMCID: PMC8245366.
37. Benzoni P, Nava L, Giannetti F, Guerini G, Gualdoni A, Bazzini C, Milanese R, Bucchi A, Baruscotti M, Barbuti A. Dual role of miR-1 in the development and function of sinoatrial cells. *J Mol Cell Cardiol*. 2021 Aug;157:104-112. doi: 10.1016/j.yjmcc.2021.05.001. Epub 2021 May 6. PMID: 33964276.

38. Piantoni C, Carnevali L, Molla D, Barbuti A, DiFrancesco D, Bucchi A, Baruscotti M. Age-Related Changes in Cardiac Autonomic Modulation and Heart Rate Variability in Mice. *Front Neurosci*. 2021 May 17;15:617698. doi: 10.3389/fnins.2021.617698. PMID: 34084126; PMCID: PMC8168539.

39. Boyett MR, Yanni J, Tellez J, Bucchi A, Mesirca P, Cai X, Logantha SJRJ, Wilson C, Anderson C, Ariyaratnam J, Stuart L, Nakao S, Abd Allah E, Jones S, Lancaster M, Stephenson R, Chandler N, Smith M, Bussey C, Monfredi O, Morris G, Billeter R, Mangoni ME, Zhang H, Hart G, D'Souza A. Regulation of sinus node pacemaking and atrioventricular node conduction by HCN channels in health and disease. *Prog Biophys Mol Biol*. 2021 Jun 28:S0079-6107(21)00068-7. doi: 10.1016/j.pbiomolbio.2021.06.008. Epub ahead of print. PMID: 34197836.

40. Benzoni P, Bertoli G, Giannetti F, Piantoni C, Milanese R, Pecchiari M, Barbuti A, Baruscotti M, Bucchi A. The funny current: Even funnier than 40 years ago. Unconventional expression and roles of HCN/f channels all over the body. *Prog Biophys Mol Biol*. 2021 Aug 14:S0079-6107(21)00100-0. doi: 10.1016/j.pbiomolbio.2021.08.007. Epub ahead of print. PMID: 34400215.

## CAPITOLI DI LIBRI

1) Barbuti A, **Bucchi A**, Baruscotti M & DiFrancesco D. (2010). The "funny" pacemaker current" in *Novel Therapeutic Targets for Antiarrhythmic Drugs*. Editor George E. Billman, John Wiley & Sons, Inc. ISBN: 978-047026100-2.

2) Barbuti A., **Bucchi A.**, Milanese R., Bottelli G., Crespi A. & DiFrancesco D. (2011). The "funny" pacemaker current in "Heart Rate and Rhythm-Molecular Basis, Pharmacological Modulation and Clinical Implications". Springer. ISBN 978-3-642-17575-6.

3) **A. Bucchi**, C. Piantoni, A. Barbuti, D. DiFrancesco, M. Baruscotti. "HCN channels and cardiac pacemaking" in *Channelopathies in Heart Disease* (2018). Dierk Thomas e Carol Ann Remme, Springer. ISBN 978-3-319-77811-2; ISBN 978-3-319-77812-9 (eBook).

## PARTECIPAZIONE A CONGRESSI : Più di 25 congressi nazionali ed internazionali INVITED SPEAKER

2004	Institut de Recherches Internationales Servier, Suresnes -F-
2013	Institut de Recherches Internationales Servier, Suresnes -F-
2015	Le Ren Tang Pharmaceutical Factory, Tianjin – Cina.
2016	1st International Conference on Evidence-based Chinese Medicine. 4-5 giugno Tianjin (Cina): "Identification of the mechanism of action of the cardiac rate regulator TongMai YangXin: comparison between <i>in-vitro</i> and <i>in-vivo</i> experiments"
2017	7° Edizione Platform of Laboratories for Advances in Cardiac Experience (PLACE), Roma 22-24 Novembre 2017. "Novel mechanisms of SAN rate modulation".

2018 CECAM Workshop on "Multiscale modelling in electrophysiology: from atoms to organs", Lugano 26-28 Marzo. "Investigating the pacemaker activity of sinoatrial cells with the Dynamic Clamp technique".

### **REVISORE SCIENTIFICO**

Cardiovascular Research, Journal of Physiology, Journal of Pharmacology, British Journal of Pharmacology, Journal of Neuroscience, Journal of Pharmacy and Pharmacology, Plos One, Drugs, Journal of Anatomy, Journal of Histochemistry & Cytochemistry, Drugs, Cellular Physiology and Biochemistry.

-2017 revisore di una richiesta di finanziamento per la French National Research Agency (ANR)

-2018 revisore abstracts sottomessi al congresso EHRA 2019 (European heart Rhythm Association), Lisbona 17-19 Marzo 2019