



**Riccardo Fesce**

 UNIVERSITY OF INSUBRIA



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## Contact data

### Associate Professor

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## Biography

Born 1953, married, three sons.  
Medical Doctor (Milano, 1979)  
Specialized in Medical Pharmacology (Milano, 1985)

1983-85 - Research Associate, Department of Biophysics, the Rockefeller University, New York, NY. He developed original procedures to adapt stochastic approaches of noise, fluctuation and spectral analysis to electrophysiological recordings from excitable cells, and applied them to study synaptic transmission at the neuromuscular junction.

1985-2001 Research Associate, C.N.R. (National Research Council), Cytopharmacology Centre, Milano. He was in charge of the research line "Synaptic transmission". He used electron microscopy, freeze-fracture, electrophysiology and mathematical-kinetic modelling to study through a multidisciplinary approach the dynamics of quantal neurotransmitter release at the neuromuscular junction, the sympathetic ganglionic synapse, and the vestibular cytoneural junction. He developed and applied mathematical, pharmaco-dynamic and bio-statistical models to study cytoskeletal dynamics, intracellular calcium-ion distribution, receptor cross-talk, to simulate reverse-PCR-based gene fingerprinting and to develop a full multiple-conductance model of ortho-sympathetic neurone bioelectrical properties.

Head of Operative Unit of several national research projects:  
"Aging" (1990-92), Italian Space Agency (ASI, 1990-92),  
"Biotechnology" (1997-2000)

1993 Head of the "Theoretical Biology" Centre, DIBIT, San Raffaele Scientific Institute, Milano.

2001 Associate Professor, Physiology – University of Insubria, Varese. He has continued his studies on synaptic function and investigated the functional properties of neuronal GABA neurotransporter (GAT-1) to build a molecular kinetic model of the transport cycle.

Foundingmember of the "Neuroscience Center", University of Insubria, Busto Arsizio (VA)

## Qualifications and awards

Reviewer for international Scientific Journals: Journal of General Physiology, Journal of Cell Biology, European Journal Neuroscience, Brain Research.

1995-1997 Deputy Editor for European Journal of Neuroscience

Expert/reviewer for:

- "Human Frontier Science Program" research grants and fellowships (1996, 1998, 1999)
- Italian Research Ministry (MURST) funding programs (1998, 1999, 2001)
- Internal Funding Program, Parma University (1999)
- E.U. V Framework Programme, "Quality of Life and Management of Living Resources", Generic action "Neurosciences" (1999)
- Basic Research programmes (FIRB, 2001)

## Research interests

### 1. Synaptic transmission and sensory signal processing .

Traditionally interested in synaptic transmission, he has studied several aspects of quantal transmitter release at the neuromuscular junction [1-3, 6-7, 10-11, 18-19], and developed original procedures to this purpose.

In collaboration with Oscar Sacchi, Ferrara - Italy, he has developed a mathematical model of the bioelectrical properties of the sympathetic neurone at the rat superior cervical ganglion (SCG) [15]. Using this model, the properties of signal processing have been investigated at the ganglionic synapse, in response to presynaptic activation, and the bioelectrical behaviour of the neurone below spike threshold [16, 20, 26, 29].

In collaboration with M.L. Rossi, Ferrara - Italy, he has characterised the properties of transmitter release at the cyto-neural junction of the frog labyrinth [4, 12, 22].

### 2. Neuro-transporters.

In collaboration with Antonio Peres and his group in Varese he has studied the kinetics of GAT-1 neurotransporter, heterologously expressed in xenopus oocytes, and set up a kinetic model of the charge and substrate translocation cycle in this system [25]

### 3. Modelling biochemical and cellular systems

In collaboration with colleagues at DIBIT, San Raffaele Scientific Institute, Milano, he has studied the dynamics of intracellular calcium-ion distribution [5, 21, 22, 30], modelled actin cytoskeleton rearrangement [8, 9], receptor cross-talk in transductional paths [13, 14], and applied kinetic and mathematical modelling techniques to solve aspects of PCR-based genetic fingerprinting [17], urokinase receptor oligomerisation [24], protein quality control in the ER [27], allosteric modulation of multiple binding sites in human albumin [28].

### 4. Current research lines

Main current interests are (1) cellular and networks aspects of cannabinoid and opiate modulation of synaptic transmission, in central neurones, either cultured or in situ, and (2) under-threshold bioelectrical signal elaboration and processing at the ganglionic sympathetic

## Teaching experience and appointments

neurone.

1980-2000 – Collaborations and teaching appointments in Pharmacology from 1980 to 2000 at the University of Milano-Italy, Faculty of Medicine and Surgery – Specialization courses in Medical Pharmacology, Cardiology, Nephrology.

1990-2000 – Teaching appointments in Physiology, “synapse Neurobiology” at the University of Ferrara, Faculty of Sciences.

1999 – Teaching appointments in Physiology at the San Raffaele, Vita-Salute University, Faculty of Medicine, Milano, Italy

2001 – Associate Professor at the University of Insubria (Varese, Italy). Teaching appointments in Cellular Physiology, System Physiology, Neurophysiology.

## Representative publications

1) R. Fesce, J.R. Segal and W.P. Hurlbut. Fluctuation analysis of nonideal shot noise. Application to the neuromuscular junction. *J. Gen. Physiol.*, 88: 25-57, 1986.

2) R. Fesce, B. Ceccarelli, J.R. Segal and W.P. Hurlbut. Effects of black widow spider venom and calcium on quantal secretion at the frog neuromuscular junction. *J. Gen. Physiol.*, 88: 59-81, 1986.

3) B. Ceccarelli, R. Fesce, F. Grohovaz and C. Haimann. The effect of potassium on exocytosis of transmitter at the frog neuromuscular junction. *J. Physiol. (London)*, 401: 163-183, 1988.

4) M.L. Rossi, C. Bonifazzi, M. Martini e R. Fesce. Static and dynamic properties of synaptic transmission at the cytoneural junction of frog labyrinth posterior canal. *J. Gen. Physiol.* 94: 303-327, 1989.

5) A. Malgaroli, R. Fesce and J. Meldolesi. Spontaneous  $[Ca^{2+}]_i$  fluctuations in rat chromaffin cells do not require inositol 1,4,5-trisphosphate elevations but are generated by a caffeine- and ryanodine-sensitive intracellular  $Ca^{2+}$  store. *J. Biol. Chem.* 265: 3005-3008, 1990.

6) W.P.Hurlbut, N. Iezzi, R. Fesce and B. Ceccarelli. Correlation between quantal secretion and vesicle loss at the frog neuro-muscular junction. *J. Physiol.*, 425: 501-526, 1990.

7) R. Fesce. Stochastic approaches to the study of synaptic function. *Progr. Neurobiol.*, 35: 85-133, 1990.

8) F. Valtorta, P. Greengard, R. Fesce, E. Chiergatti and F. Benfenati. Effects of the neuronal phosphoprotein synapsin I on actin polymerization. I. Evidence for a phosphorylation-dependent nucleating effect. *J. Biol. Chem.*, 267:11281-11288, 1992.

9) R. Fesce, F. Benfenati, P. Greengard and F. Valtorta. Effects of the neuronal phosphoprotein synapsin I on actin polymerization. II. Analytical interpretation of kinetic curves. *J. Biol. Chem.*, 267:11289-11299, 1992.

- 10) F. Torri-tarelli, M. Bossi, R. Fesce, P. Greengard and F. Valtorta. Synapsin I partially dissociates from synaptic vesicles during exocytosis induced by electrical stimulation. *Neuron*, 9:1143-1153, 1992.
- 11) R. Fesce, F. Grohovaz, F. Valtorta and J. Meldolesi. Neurotransmitter Release: fusion or 'kiss and run'?. *Trends In Cell Biol.*, 4:1-4, 1994.
- 12) M.L. Rossi, M. Martini, B. Pelucchi and R. Fesce. The quantal nature of synaptic transmission at the cytoneural junction of the frog labyrinth. *J. Physiol. (London)*, 478:17-35, 1994.
- 13) M.G. Cattaneo, R. Fesce and L.M. Vicentini. Mitogenic effect of serotonin in human small cell lung carcinoma cells via both 5-HT1A and 5-HT1D receptors. *Eur. J. Pharmacol.* 291:209-211, 1995.
- 14) L.M. Vicentini, M.G. Cattaneo and R. Fesce. Evidence for receptor subtype cross-talk in the mitogenic action of serotonin on human small-cell lung carcinoma cells. *Eur. J. Pharmacol.* 318: 497-504, 1996.
- 15) O. Sacchi, O. Belluzzi, R. Canella and R. Fesce. A model of signal processing at a mammalian sympathetic neurone. *J. Neurosci. Meth.* 80: 171-180, 1998.
- 16) O. Sacchi, M.L. Rossi, R. Canella and R. Fesce. Synaptic current at the rat ganglionic synapse and its interactions with the neuronal voltage-dependent currents. *J. Neurophysiol.* 79: 727-742, 1998.
- 17) G.G. Consalez, A. Cabibbo, A. Corradi, C. Alli, M. Sardella, R. Sitia and R. Fesce. A computer-driven approach to PCR-based differential screening, alternative to differential display. *Bioinformatics* 15 (2): 93-105, 1999.
- 18) R. Fesce. The kinetics of nerve-evoked quantal secretion. *Phil. Trans. R. Soc. London B.* 354: 319-329, 1999.
- 19) R. Fesce and J. Meldolesi Peeping at the vesicle kiss. *Nature Cell Biology* 1: E3-4, 1999.
- 20) O. Sacchi, M. L. Rossi, R. Canella, and R. Fesce. Participation of a Chloride Conductance in the Subthreshold Behavior of the Rat Sympathetic Neuron. *J. Neurophysiol.* 82: 1662-1675, 1999.
- 21) F. Bertuzzi, A.M. Davalli, R. Nano, C. Socci, F. Codazzi, R. Fesce, V. DiCarlo, G. Pozza and F. Grohovaz. Mechanisms of coordination of Ca<sup>2+</sup> signals in pancreatic islet cells. *Diabetes* 48: 1971-1978, 1999.
- 22) G. Rispoli, M. Martini, M.L. Rossi, G. Rubbini & R. Fesce. Ca<sup>2+</sup>-dependent kinetics of hair cell Ca<sup>2+</sup> currents resolved with the use of cesium BAPTA. *Neuroreport* 11: 2769-2774, 2000.
- 23) F. Valtorta, J. Meldolesi & R. Fesce. Synaptic vesicles: is kissing a matter of competence? *Trends Cell Biol.* 11:324-8, 2001.

- 24) N. Sidenius, A. Andolfo, R. Fesce & F. Blasi. Urokinase regulates vitronectin binding by controlling urokinase receptor oligomerization. *J Biol Chem.* 277:27982-90, 2002.
- 25) R. Fesce, S. Giovannardi, F. Binda, E. Bossi & A. Peres. The relation between charge movement and transport-associated currents in the rat GABA cotransporter rGAT1. *J Physiol.* 545:739-50, 2002.
- 26) O. Sacchi, M.L. Rossi, R. Canella & R. Fesce. A voltage- and activity-dependent chloride conductance controls the resting status of the intact rat sympathetic neuron. *J Neurophysiol.* 90:712-22, 2003.
- 27) G. Bertoli, T. Simmen, T. Anelli, S.N. Molteni, R. Fesce & R. Sitia. Two conserved cysteine triads in human Ero1{alpha} cooperate for efficient disulfide bond formation in the endoplasmic reticulum. *J Biol Chem.* 279:30047-30052, 2004.
- 28) G. Fanali, R. Fesce, C. Agrati, P. Ascenzi & M. Fasano. Allosteric modulation of myristate and Mn(III)heme binding to human serum albumin. Optical and NMR spectroscopy characterization. *FEBS J.* 2005 Sep;272(18):4672-83.
- 29) O. Sacchi, M.L. Rossi, R. Canella, R. Fesce. Biophysical properties of the silent and activated rat sympathetic neuron following denervation. *Neuroscience.* 2005;135(1):31-45.
- 30) M. Micheletti, A. Brioschi, R. Fesce & F. Grohovaz. A novel pattern of fast calcium oscillations points to calcium and electrical activity cross-talk in rat chromaffin cells. *Cell Mol Life Sci.* 2005 Jan;62(1):95-104.

### Clinical interests

Has collaborated on clinical research in hepatology (De Carlis et al. *Transpl Int.* 9:S414-7, 1996; De Carlis et al., *Transplant Proc.* 31:397-400, 1999), and Diabetology (21, above).