IRCN

First Joint Meeting of the **Argentine Society for Neurosciences** (SAN)

and the **Argentine Workshop in Neurosciences** (TAN)

Huerta Grande, September 4-6, 2009

IRCN Organizing Committee

M. Julia Cambiasso
Laboratorio de Neurofisiología. Instituto M y M Ferreyra, Córdoba.
M. Fernanda Ceriani
Laboratorio de Genética del Comportamiento, Instituto Leloir, Buenos Aires.
Eleonora Katz
Laboratorio de Neurobiología, INGEBI-CONICET y FCEN, UBA, Buenos Aires.
Gabriel Mindlin
Departamento de Física, FCEN-UBA, Buenos Aires
Nora Rotstein
Laboratorio de Neurobiología del Desarrollo. INIBIBB, Bahía Blanca.
Milena Winograd
Laboratorio de Neurociencia Integrativa, FCEN-UBA, Buenos Aires.
Agustín Anastasía
Centro de Biología Celular y Molecular, FCEFyN, Universidad Nacional de Córdoba.

Course Organizing Committee

Pedro Bekinschtein
Instituto de Biología Celular y Neurociencias, Facultad de Medicina, UBA
Mariano Sigman
Depto de Física, FCEN, UBA
Noelia Weisstaub
Instituto de Biología Celular y Neurociencias "E. de Robertis", Facultad de Medicina, UBA

Logistic Organization

Silvina Ceriani

Poster Number (196) Session 1

KINETIC SCHEME FOR ACTIVATION AND DESENSITIZATION OF HOMOMERIC 5-HT3A RECEPTOR.

Corradi Jeremías [1], **Gumilar Fernanda**[1], **Bouzat Cecilia**[1]
[1]Instituto de Investigaciones Bioquímicas de Bahía Blanca
jcorradi@criba.edu.ar

The 5-HT3A receptor is a member of the Cys-loop family of ligand-gated ion channels. To perform kinetic analysis, we introduced the mutations R432Q/R436D/R440A in the 5-HT3A subunit to obtain a high-conductance form (5-HT3A-HC), in which single-channel currents can be detected. At all 5-HT concentrations (0.1 µM) channel activity appears as openings of ~4.7 pA (-70 mV) in quick succession forming bursts, which coalesce into clusters. By combining single-channel and macroscopic data we generated a kinetic model that perfectly describes activation, deactivation and desensitization. The model shows that full activation arises from receptors with three molecules of agonist bound. It also reveals an earlier conformational change of the fully-liganded receptor that occurs while the channel is still closed. From this pre-open closed state the receptor enters into an open-closed cycle involving three open states, which conforms the cluster whose duration parallels the time constant of desensitization. This suggests that at a synapse the lifetime of the elementary response of 5-HT3A receptors is determined mainly by desensitization. Since the desensitized state is a stable state, the inter-response latency is expected to be prolonged. A similar model but lacking the pre-open closed state can describe the data only if the opening rates are fixed to account for the slow activation rate. Thus, our kinetic model provides a foundation for studying structure-function relationships as well as molecular mechanisms of drug action in 5-HT3 receptors.