Potassium and water channels have been the wiring channels for 2003 Nobel prize. The finding of the intrinsic aqueduct orifices and their vital functions in channel gating shows several years now, water flowing merges with ion activity. The orifices even exist in the newly determined atomic structure of NaK channel (Nature 440, 570-574, 2006), which belongs to another large ion channel family (cyclic nucleotide-gated channels).

**3467-Pos Board B514**

**ChannelTools: A VMD Plugin For Manipulating, Visualizing and Measuring Ion Channel Properties**

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A new set of software tools has been developed for manipulating, visualizing, and quantifying properties of ion channels. ChannelTools is a plugin for the Visual Molecular Dynamics (VMD) program and brings together receptor VMD commands and several independent software routines in one simple graphical user interface. ChannelTools allows quick and easy visualization of ion channels and employs the HOLE program to visualize the channel pore and pore lining surface. An option to apply the atomic co-ordinate standardization previously developed by the authors is implemented yielding a consistent channel orientation, axis, and geometric centre. By employing the ESFERA program, pore volume and surface area can be computed from HOLE program output at the click of a button. Cross-sectional area and radius profile data and plots can also be generated with a single button click. Several different routines for estimating channel conductance are also being developed.

**3468-Pos Board B515**

**Assay Development And Screening For Modulators Of The Human Two-Pore Domain Potassium Channel, TASK-3, Using Automated Electrophysiology**

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The advent of high-throughput electrophysiology utilizing Population Patch Clamp® (PPC) technology has allowed the screening of large compound libraries against ion channels representing novel targets in a variety of disease states. Here we report the design and implementation of an assay enabling the screening of 56,000 compounds against human TASK-3, a member of the two-P potassium channel family. cDNA corresponding to the channel of interest was transfected into HEK-293 cells and a stably-expressing clone selected. Ion channel pharmacology was subsequently validated using Ruthenium Red, Lidocaine, Bupivicaine, Quinidine & pH, with all 5 standard inhibitors giving values within two-fold of reported literature values.

The biophysical properties of TASK-3 prevents the use of conventional methods of leak calculation, however, given the relatively low seal resistance routinely seen when using IonWorks® platforms in a PPC® mode, some form of leak correction must be applied. Currents were recorded at 0mV in order to remove any effect of leak and a final addition of a supramaximal concentration of leak correction must be applied. Currents were recorded at 0mV in order to remove any effect of leak and a final addition of a supramaximal concentration of leak correction must be applied. Currents were recorded at 0mV in order to remove any effect of leak and a final addition of a supramaximal concentration of leak correction must be applied.

**3470-Pos Board B517**

**Action Potential Peak Shape Analysis As A New Tool For Antiarrhythmic Drug Development**

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Cardiac arrhythmia is a critical heart condition characterized by abnormal electrical activity of the heart. There are a wide variety of drugs which are approved for the treatment of arrhythmia; many of them are acting on voltage dependent sodium, potassium and calcium channels. One of the problems concerning determination of the major mechanism of action of arrhythmia drugs is that measurement of their effects on the different ion channels is time-consuming and usually done utilizing different experimental conditions. In order to counter this problem, in this study we applied a novel method, action potential shape analysis, to determine the effect of selected antiarrhythmics on voltage dependent sodium, potassium and calcium channels without performing time-consuming voltage clamp experiments on each ion channel. Our method is based on fitting ion channel parameters to intracellularly or extracellularly recorded action potentials in a realistic model of NG108-15 cells and quantifying drug effects through their action on the shape of the action potentials and consequently on the fitted ion channel parameters. For this study we selected four drugs, quinidine, lidocaine, encainide, and amiodarone, representing Class Ia, Ib, Ic and Class III antiarrhythmics, respectively. Quinidine, encainide and amiodarone blocked both sodium and potassium channels, while lidocaine, at the measured membrane potential, shifted the activation of sodium channels in a depolarizing direction. Amiodarone showed profound calcium channel blocking properties. Our work is a first step towards establishing a new assay system, based on the analysis of the shape of intracellularly and eventually extracellularly recorded action potentials, which can be used for fast quantitative analysis of drug effects on ion channel currents and classification of antiarrhythmics, and also for measurement of possible cardiac side effects of drug candidates.

**3471-Pos Board B518**

**MarkoLAB: A Graphical Interface To Study Stochastic Channel Behavior**

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The most studied feature of an ionic channel is the current flowing through it. This happens when the channel moves into the open state, but most of the time, as revealed by the low open probability values, the channel transitions between closed or inactive states. By focusing only when the channel enters or leaves the open state the most of its activity is being missed. To have a better representation of the total behavior of the channel we constructed a computer program (MarkoLAB) that creates a 3-D plot with all channel’s states. In this graphical interface each state is represented with a column. The height of the column is proportional to the occupancy level. During voltage clamp simulation the transition between states are visualized as changes in the columns’ height. This dynamic plot provides more complete information about the channel behavior and illustrates the stochastic nature of the transitions. Furthermore the macroscopic current is simultaneously shown allowing the user to link the single channel activity with the overall result of the ensemble currents.

This program was developed in LabVIEW language and the stochastic transitions were implemented with a Monte Carlo simulation. This version of the software covers three typical channels under voltage clamp conditions: the L-type calcium channel (InC) and the L-type calcium channel. (InCaL). MarkoLAB is an original tool to gain insight of the channel kinetics and illustrates more clearly concepts as recovery from inactivation or distinguish between voltage-dependent versus calcium-dependent inactivation. This novel representation of channel activity constitutes a powerful aid to demonstrate effect of gene mutations or drugs on the channel function.