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Abstract for an Invited Paper
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Principles Governing Metal Ion Selectivity in Ion Channel Proteins

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Our research interests are to

1. (i) unravel the principles governing biological processes and use them to identify novel drug targets and guide drug design, and

2. (ii) develop new methods for studying macromolecular interactions.

This talk will provide an overview of our work in these two areas and an example of how our studies have helped to unravel the principles underlying the conversion of Ca^{2+}-selective to Na^{+}-selective channels. Ion selectivity of four-domain voltage-gated Ca^{2+}(Ca_v) and sodium (Na_v) channels, which is controlled by the selectivity filter (SF, the narrowest region of an open pore), is crucial for electrical signaling. Over billions of years of evolution, mutation of the Glu from domain II/III in the **EEEE**/**DEEA** SF of Ca^{2+}-selective Ca_v channels to Lys made these channels Na^{+}-selective. This talk will delineate the physical principles why Lys is sufficient for Na^{+}/Ca^{2+}selectivity and why the **DEKA** SF is more Na^{+}-selective than the **DKEA** one.

References:
[1] Competition among metal ions for protein binding sites: Determinants of metal ion selectivity in proteins. Todor Dudev & Carmay Lim, *Chemical Reviews* (**2013**) http://dx.doi.org/10.1021/cr4004665
[2] Effect of Metal Hydration on the Selectivity of Mg^{2+} vs. Ca^{2+} in Magnesium Ion Channels. Todor Dudev & Carmay Lim *J. Am. Chem. Soc.* **(2013)** 135: 17200-17208.
[3] Competition among Ca^{2+}, Mg^{2+}, and Na^{+} for ion channel selectivity filters: Determinants of metal ion selectivity. Todor Dudev & Carmay Lim,*J. Phys. Chem. B* (**2012)** 116: 10703–10714.
[4] Why voltage-gated Ca^{2+} and bacterial Na^{+} channels with the same EEEE motif in their selectivity filters confer opposite metal selectivity. Todor Dudev & Carmay Lim, *Phys. Chem. Chem. Phys.* (**2012)** 14: 12451–12456.