Fig. S2. Cartoon representation of the crystal structure of the gap junction channel. (a) Cx26 is constituted by 12 connexin subunits assembled into 2 hemichannels forming the central axial pore (PDB ID: 5ER7) (12). The 2 hemichannels from adjacent cells (1 is in *grey* and the other is *multi-coloured* according to its constituent 6 subunits) interact through their extracellular loops to form the intercellular, dodecameric gap junction channel. The Phe142 residue (*green spheres in each subunit*), protrudes into the membrane bilayers lying at the exterior of the internal pore where the calcium ions bind (*black spheres*). (b) A single Cx26 subunit is shown in grey. Phe142, belonging to TM3, interacts by hydrophobic interactions with Pro87 of TM2 located at the bend in the helix. The cytosolic loop (IC2, residues 95–135), connecting TM2 and TM3, at the top with respect to the extracellular loops, is not displayed, as it is not visible in the relative crystal structure (PDB ID: 5ER7). Figure drawn with Pymol (The PyMOL Molecular Graphics System, Version 1.2r3pre, Schrödinger, LLC). Amino acid residues indicated by single letter code.