

### Chapter 3

#### Web Text Box 1

#### Can unpaired connexons open?

Historically, connexons were thought to function only as half of a complete gap junction channel. However more recently it has become clear that under certain experimental conditions unpaired connexons can open, providing a pathway between the cytosol and the extracellular medium. In particular, unpaired connexons open if calcium and magnesium ions are removed from the extracellular medium, while connexons formed of the connexin 46 isoform (but not other isoforms) open when cells are depolarized beyond +20mV. Could unpaired connexons open in the body under real physiological conditions? If unpaired connexons open for a significant period of time, the cell dies, and this does indeed seem to happen in some pathological conditions (see Saez et al. 2010. *Exp Cell Res* 316:2377). However a number of authors have proposed that opening of unpaired connexons occurs in healthy cells during their normal functioning, and plays an important role in intercellular signaling. The hypothesis is that by transiently opening some of its unpaired connexons a cell releases ATP, and that this ATP then acts as a transmitter, activating metabotropic cell surface receptors (see book page 269) on neighboring cells.

One influential paper that proposed a role for connexon-based ATP signaling in a particular tissue is Pearson et al. 2005. *Neuron* 46:73, while Spray et al. 2006. *Glia* 54: 758 is a useful skeptical review.