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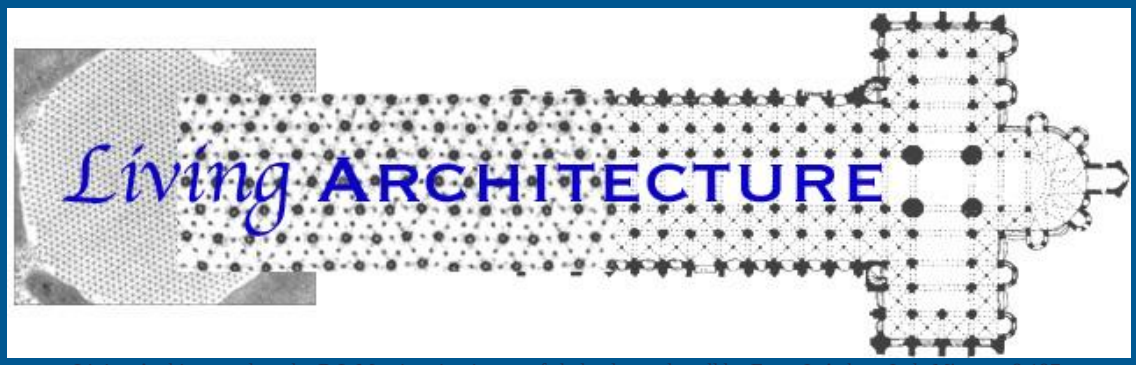


Living Architecture logo by R.L.Morris using image of skeletal muscle cell by From J. Auber, *J. de Microsc.* 8:197–232, 1969, available at http://www.ncbi.nlm.nih.gov/books/NBK26888/figure/A3068/?report=objectonly and image of floorplan of Basilica of Saint Sernin available on Laura Lyon's Romanesque Art Flashcards available at https://classconnection.s3.amazonaws.com/268/flashcards/716268/jpg/17-51330607485976.jpg

# Similarities Between Gap Junctions and the Peace Bridge in Northern Ireland

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# Similarities Between Gap Junctions and the Peace Bridge in Northern Ireland

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## Rule-to-Build By:

Assemble two monomers to create a dimeric bridge to allow passive transport across a gap.

## What:

The biological structure that upholds this principle are gap junctions which are made up of half-channels, and as a dimer comprised of two half-channels, allow passive transport of molecules between adjacent cells. The human-built structure that upholds this principle is the Peace Bridge in Northern Ireland which is a dimeric bridge assembled from two identical half-bridges, allowing pedestrian passage across the River Foyle.

## How:

Gap junctions allow for transport of ions and small molecules directly from cytoplasm to cytoplasm of adjacent cells (Mese et al, 2007). This intercellular communication is crucial for cell functioning in the tissues of multicellular organisms (Beyer and Berthoud, 2017). Gap junctions are extremely important due to their involvement in numerous biological processes in the cardiovascular, reproductive, and nervous system (Maeda et all, 2009). In the cardiovascular system, gap junctions allow communication between the cells in the myocardium, which is critical for aiding the propagation of an action potential in the heart (Nielson et al, 2012; Goldberg et al, 2004). Multiple connexins can be found in the tissues of both the male and the female reproductive system and throughout the nervous system, gap junctions are present in neurons and glial cells (Nielson et al, 2012). In the nervous system, gap junctions provide direct neuron-neuron communication (Nielson et al, 2012).

Gap junctions are intercellular channels that are formed by two hexameric structures called connexons, or hemichannels; this structure is illustrated in Figure 1 (Goodenough and Paul, 2009; Mese et al, 2007). The monomer of this intercellular channel, the connexon, is comprised of six subunits from a family of integral membrane proteins called connexins (Goodenough et al, 1996; Giepmans, 2004). The human genome contains 21 different connexin genes and they are expressed in almost all tissues, except for differentiated skeletal muscle, erythrocytes, and mature sperm cells (Nielsen et al, 2012). Connexins are structurally comprised of four transmembrane domains, with intracellular N- and C-termini and two extracellular loops (E1 and

E2) which provide continuity between the transmembrane domains (Figure 2) (Nielsen et al, 2012).

The connexon spans the plasma membrane of one cell and docks with a connexon of an adjacent cell (Figure 1) (Giepmans, 2004). When the connexons of two neighboring cells dock, it creates a 2-4 nm extracellular gap between the cytoplasms of the two cells, giving the junction its name (Mese et al, 2007). The intercellular channel formation is completed once a connexon finds a compatible partner connexon from a neighboring cell, creating a dimeric channel (Mese et al, 2007). Channels formed from identical connexons are called homotypic, but when channels are formed from connexons with different connexin composition, they are called heterotypic (Nielson et al, 2012). An individual connexon composed of one connexin type is called homomeric, while heteromeric connexons are composed of differing connexins (Nielson et al, 2012). So, between the possible channel combinations of homomeric/heteromeric and homotypic/heterotypic and the fact that the humans have 21 different connexins, and that connexons are made up of six connexins—the multitude of possible combinations is enormous (Nielson et al, 2012). But, not all combinations of connexins/connexons are able to form functional channels, *and* all connexin combinations may not be expressed in neighboring cells (Nielson et al, 2012). Connexon and gap junction combinations are illustrated in Figure 3. This complexity allows for an extremely versatile system for communication among cells (Levin, 2002).

Hemichannel gating, the opening/availability or closing/unavailability of the channel, is regulated in response to changes in voltage, calcium concentration, pH, phosphorylation, and protein interactions (Nielson et al, 2012). Gating in response to voltage, pH, etc. is used to determine the open probability of a channel—a measure of the percentage of time that the channel is open (Goldberg et al, 2004). It has been determined that most gap junction channels have a high open probability, therefore gap junction channels must have some selectivity that determines what can pass from cell to cell (Goldberg et al, 2004). The channel selectivity is determined and regulated at the mRNA level, by the transcription of connexin genes (Levin, 2002). Therefore, functional gap junction communication is dependent upon compatible hemichannels in the cytoplasms of neighboring cells, the selective permeability of the hemichannels, and the open probability of the gap junction (Levin, 2002).

The Peace Bridge in Derry, Northern Ireland spans the River Foyle, connecting the divided sides of the city (Figure 5). The bridge allows for transport of pedestrians and cyclists across the river. The Peace Bridge is constructed as a pair of self-anchored suspension bridges that each span half the river, meeting in the middle to create one continuous bridge (WilkinsonEyre, 2020). The half-bridges reach out across the river from opposite sides of the shore (WilkinsonEyre, 2020). Each single suspension bridge is a monomer that cannot carry traffic without the other half, similar to the way that one hemichannel cannot allow molecules to pass through without a compatible hemichannel partner (Figure 5) (WilkinsonEyre, 2020).

# Why:

Both gap junctions and the Peace Bridge create a dimeric bridge assembled of two monomers to bridge a gap between neighboring spaces, allowing passive transport across the gap. The architect, Wilkinson Eyre, designed the Peace Bridge as two identical parts meeting in the

middle to form a bridge is meant to symbolize unity between two politically and socially divided communities (WilkinsonEyre, 2020). The two halves of the bridge each span the riverside from opposite directions, reaching in the middle like a meeting of hands, a symbolic handshake (Figure 4) (IrelandsHiddenGems, 2020). The symbolic design of the bridge is an important piece to represent the physical and social regeneration of the once divided Protestant Waterside and Nationalist Bogside of Derry (WilkinsonEyre, 2020; IrelandsHiddenGems, 2020). The construction of the bridge was funded by the EU Peace III Programme which focuses on the creation of projects like the Peace Bridge that aim to unite the historically separated communities of Northern Ireland (WilkinsonEyre, 2020).

Gap junctions perform a similar function, uniting cells in the tissues of multicellular organisms through communication of neighboring cells from cytoplasm to cytoplasm. Gap-junctional communication (GJC) plays an important role in various aspects of normal tissue physiology (Levin, 2002). One of the most important roles that GJC plays is in embryonic morphogenesis (Levin, 2002). The complex mechanisms that underly embryo development require an elaborate web of information flow between cells (Levin, 2002). The multifaceted system of GJC is critical for information flow between cells during development (Levin, 2002). Aside from the role of GJC in embryonic development, GJC is also involved in the processes that distinguish normal cells from tumor cells (Levin, 2002). GJC contributes to coordinating tissue activity and morphogenesis through information flow, processes which are lost in tumors (Levin, 2002). Therefore, normal tissues possess a higher amount of GJC than tumor cells, allowing normal cells to be distinguished from tumor cells (Levin, 2002).

Like the Peace Bridge, gap junctions are not functional channels without a compatible partner to form a dimeric channel to allow cell-cell communication. Gap junctions span the plasma membrane of a cell to create a channel with an adjacent cell across extracellular space as the Peace Bridge connects the gap between two divided parts of the town of Derry.

# Figures:

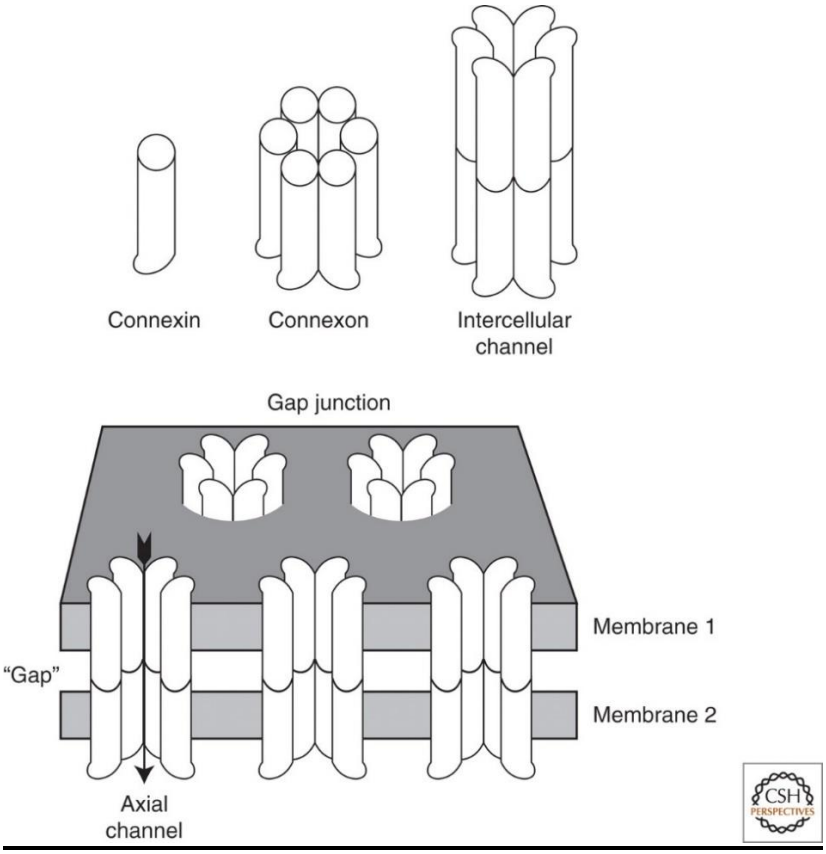


**Figure 1: Basic Structure of Gap Junction.** This diagram shows the structural levels of a gap junction. Individual connexins comprise a connexon which spans the plasma membrane of one cell. A connexon docks with a connexon of a neighboring cell, creating a dimeric channel across the plasma membranes of two cells, leaving an extracellular gap between the two cells. (Retrieved from Goodenough and Paul, https://cshperspectives.cshlp.org/content/1/1/a002576.full.pdf).

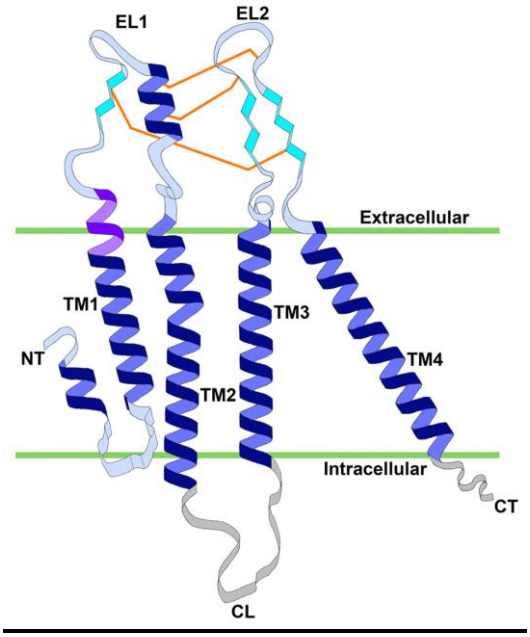


**Figure 2: Connexin Peptide Structure.** Illustration of how connexins are structured, made up of four transmembrane domains (labeled TM1-TM4). N- and C-termini are located in the intercellular region, and two extracellular loops (EL1 and EL2) are located in the extracellular region, providing continuity between the transmembrane domains. (Retrieved from Beyer and Bethoud, https://f1000research.com/articles/6-568).

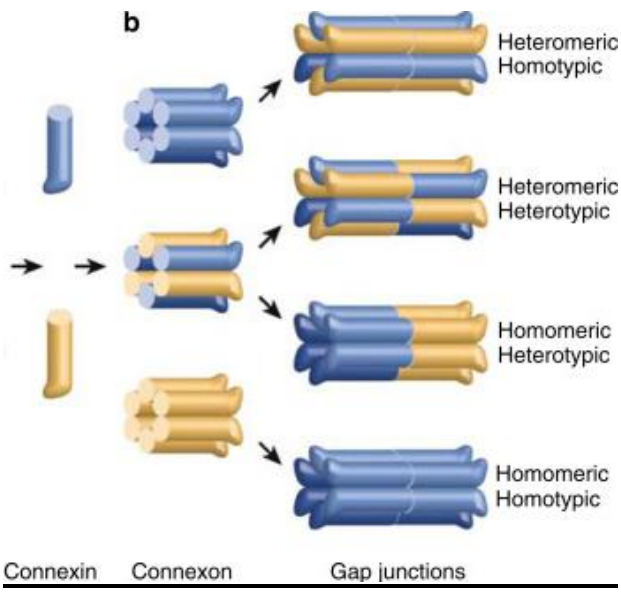


**Figure 3: Illustration of Connexin/Connexon Combinations.** Connexins make up connexons that create a gap junction when docked with a partner connexon from a neighboring cell. This diagram illustrates the combining of connexins to create homomeric and heteromeric connexons which then form into either homotypic or heterotypic gap junctions. (Retrieved from Mese et al, https://www.sciencedirect.com/science/article/pii/S0022202X15331821).

**Figure 4: Dimeric Architecture of The Peace Bridge.** Architectural design of the Peace Bridge, by Wilkinson Eyre. The bridge is constructed from two identical suspension half-bridges, each spanning half of the river. The half-bridges meet in the middle to create a whole bridge for passage across the River Foyle. (Retrieved from WilkinsoEyre, https://www.wilkinsoneyre.com/projects/the-peace-bridge).

**Figure 5: Uniting Forces.** Aerial image of the Peace Bridge which looks as though it is one continuous piece, although it is constructed of two identical halves that unite in the middle to form the functional bridge and symbolize unity between the politically divided halves of Derry. (Retrieved from WilkinsonEyre, https://www.wilkinsoneyre.com/projects/the-peace-bridge).

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