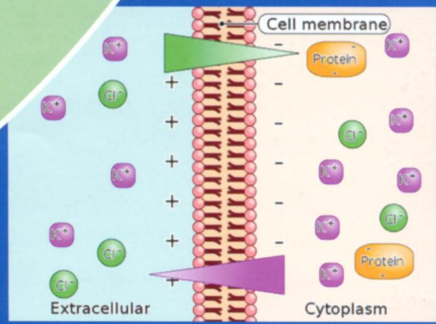
QUICK FIX

Gibbs-Donnan Effects & Traffic Between Fluid Compartments: A Digest for Students

SVEN KURBEL, M.D., SVJETLANA MARIĆ



This article is an attempt to devise a short text aimed at improving students' understanding of Gibbs-Donnan effects on fluid traffic between cellular and interstitial fluid and between interstitial fluid and plasma. The text is given to students as reading material for a discussion during seminars on microcirculation and lymphatics, usually scheduled for the following week. The students can use their textbooks (Guyton & Hall, 2000; Ganong, 2005) or other references (Schultz, 2003). Students are expected to understand the mechanisms behind the Donnan effect and, in case of any doubt, are encouraged to ask questions during seminars. They are also encouraged to try to calculate missing values from the Table (shaded fields in Table 1).

Seminar Tips

- Interstitial fluid is taken across the capillary wall by the Donnan effect of plasma proteins. At the same time, it is in balance with the cellular fluid due to opposed Donnan effects (of cytoplasmic proteins and of ECF sodium) (Leaf, 1959; Nguyen & Kurtz, 2006; Kurbel, 2008).

  Passive Gibbs-Donnan balance on the capillary wall would result in slightly higher electrolyte plasma values than reported. The lower actual data are probably results of water movement from ECF to compliant capillaries (circulatory volume is not restricted since blood vessels are not rigid).

- The only way for the cell to reach the osmotic equilibrium is to alter cell volume, until concentration of nondifusible intracellular ions (mainly charges on intracellular proteins) is equal to the ECF restricted ions (mainly Na+ ions, restricted by pumping out of cells) (Baumgarten & Feher, 2001).

- The achievement of electroneutrality requires that the sum of all anions equals the concentration of positive ions in the cell (mainly K^+). Negative charges on cytoplasmic proteins are the most stable component among ionized particles and other ions have to adapt to their concentration. Positive and negative

Analyze Table 1 and try to fill the empty fields. Note that the sum of anions must equal the sum of cations in the same fluid compartment, while products of ion pairs are often different on opposed sides of membranes.

Table 1. Examples of Gibbs-Donnan balances based on reference data. Students are expected to calculate values in gray cells on their own.

Concentrations in meq/L H_2O (based on Schultz, 2003)	Plasma	Capillary wall transport	Interstitial fluid	Cell membrane transport	Cellular fluid
Na^+	140.30	passive	136.80	<<< active	15.00
K^+	5.50	passive	5.36	active >>>	150.00
Cl^-	101.00	passive	112.30	passive	9.00
Other anions	44.80	no protein traffic	29.86	restricted traffic	156.00
Main other anions	bicarbs., proteins		bicarbs.		phosph., proteins
Gibbs-Donnan $Na^+ x Cl^-$	14170.30	equal? Y/N	15362.64	equal? Y/N	135.00
Gibbs-Donnan $K^+ x Cl^-$	555.50	equal? Y/N	602.24	equal? Y/N	1350.00
Skeletal muscle (concentrations in mmol/L)					
Na^+	142.86	Capillary wall transport	145.00	Cell membrane transport (based on Boron & Boulpaep, 2004)	12.00
K^+	5.24		4.50		150.00
Cl^-	105.00		116.00		4.20
Other anions	43.10		33.50		157.80
Gibbs-Donnan $Na^+ x Cl^-$	15000.00		16820.00		50.40
Gibbs-Donnan $K^+ x Cl^-$	550.00		522.00		630.00
Erythrocyte (concentrations in mmol/L)					
Na^+	145.00	Erythrocyte membrane transport (based on Hoffman, 1986)			11.00
K^+	4.50				140.00
Cl^-	116.00				80.00
Other anions	33.50				71.00
Gibbs-Donnan $Na^+ x Cl^-$	16820.00				880.00
Gibbs-Donnan $K^+ x Cl^-$	522.00				11200.00

soluble intracellular ions are all osmotically active and to achieve balance of osmotic forces on the cell membrane, the sum of their intracellular concentrations must equal the concentration of osmotically active extracellular particles.

- Described forces (osmosis and electric charges) force mobile chloride ions to move to ECF, leaving only a small quantity in the cell (Table 1).

  Higher intracellular chloride levels are found in some marine animals with high ECF sodium concentration due to immersion in sea water. For instance, almost four times, higher chloride concentration is reported in squid axons' cellular fluid (Na^+ - 50, K^+ - 400, Cl^- - 40)(Hodgkin, 1958).

  In cases of reduced ECF Na^+ concentration, even lower cytoplasmic chloride concentration can be expected, further reducing the ability to compensate osmotic or electrolyte changes and thus allowing the Donnan effect of charges on cytoplasmic proteins to prevail and lead to cell swelling.
- Erythrocytes are a probable exemption from the described situation. Since they float in protein rich plasma, the Donnan effect of their cytoplasmic proteins is reduced by the same effect of plasma proteins, so the role of ECF Na^+ is probably less important for maintenance of their cell volume (Kurbel, 2008). This seems to be in concordance with the fact that erythrocytes from several carnivores do not have a functional Na^+K^+-ATPase and probably use other ions to manage their volume (Sarkadi & Parker, 1991).●

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Text for Students

Gibbs-Donnan Effects & Microcirculation: Why Is It Important?

Proteins in plasma and intracellular fluid are negatively charged due to pH. Negative charges on cytoplasmic proteins cannot leave the cell and thus alter the cellular membrane ion balance due to the Donnan effect.

Concentration of these nondifusible charges (number of charges per volume of cytoplasm) is probably the main determinant of the Donnan effect, while the actual number of nondifusible protein molecules, their mass, shape, or exact amino acid compositions is less important.

Small ions adapt to this situation by passive diffusion aiming at a balanced situation in which products of paired ions' concentrations (one anion and one cation) are equal on both membrane sides, under the condition that further water movement is prevented by the fixed volume of neighboring fluid departments.

If depending only on the Donnan effect of cytoplasmic proteins, cells would start to swell due to the entrance of cations followed by water.

Active Na^+ pumping out of the cell is the main protective mechanism against occurrence of cellular edema due to the Donnan effect of cytoplasmic proteins.

The activity of Na^+K^+-ATPase makes Na^+ effectively restricted to the ECF pool, and thus sodium acts as another nondifusible ion sequestrated in the ECF pool, able to counterbalance the Donnan effect of intracellular macromolecules by its own Donnan effect.

This is a setting of the double Donnan effect:

> Charges on intracellular proteins are opposed by the effect of extracellular Na^+, leading to volume stability if Na^+K^+-ATPase works.
>
> The only way for the cell to reach osmotic equilibrium is to alter cell volume until concentration of nondifusible intracellular ions (mainly charges on intracellular proteins) is equal to the ECF restricted ions (mainly Na+ ions).

When considering ion traffic, as shown in Table 1, both the capillary wall and cell membrane can passively be passed only by Cl^- ions. Na^+ and K^+ pass the capillary wall with ease, but across the cell membrane, they are actively pumped against their chemical gradients. Active pumping makes their products with chloride ions on the cell membrane very different from the expected Gibbs-Donnan balance.

BIO

SVEN KURBEL, M.D., Ph.D. (sven@jware.hr), is in the Department of Physiology; and SVJETLANA MARIĆ, Ph.D., is in the, Department of Biology; both at Osijek Medical Facility, 31000 Osijek, Croatia.