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2 **Influence of lactose on the diffusion of calcium ions at physiological temperature**

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25 **ABSTRACT**

26

27 Mutual diffusion coefficients for calcium chloride ($0.100 \text{ mol dm}^{-3}$) in aqueous
28 solutions containing lactose at various concentrations (from 0.005 to $0.200 \text{ mol dm}^{-3}$)
29 have been measured at $37 \text{ }^{\circ}\text{C}$ (physiological temperature), by using a conductimetric
30 cell coupled to an automatic system to follow the diffusion. This cell uses an open-
31 ended capillary method based on the measurement of the electrical resistance of a
32 solution placed inside the capillaries at recorded times. The analysis of the CaCl_2
33 diffusion coefficient values obtained suggests the presence of some CaCl_2 /lactose
34 aggregates in the media, which are influenced by the temperature.

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39 **Keywords:**

40 Lactose; Calcium chloride; Solutions; Mutual diffusion coefficient; Transport
41 properties.

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45 **1. Introduction**

46

47 Lactose, a disaccharide derived from the condensation of galactose and glucose, is not
48 only a technologically important compound, but also has biological, medical,
49 pharmaceutical, food and biomedical applications (Swartz, M.L., Bernhard, R.A., &
50 Nickerson, T.A., 1978; Sano, Y., & Yamamoto, S., 1993; Banipal, P.K., Banipal, T.S.,
51 Lark, B.S., & Ahluwalia, J.C., 1997; Moran, G.R., Jeffrey, K.R., Thomas, J.M., &
52 Stevens, J.R., 2000) due to its capacity to interact with different metal ions involved in
53 many biochemical reactions. It is the most important carbohydrate in milk of a large
54 number of mammals. Lactose intolerance is a dysfunction that leads to a reduced
55 calcium absorption, which can be associated with weight-bearing bones fractures,
56 particularly in female human subjects (Honkaner, R., Kröger, H., Alhava, E., Turpeinen,
57 P., Tuppurainen, M., & Saarikoski, S., 1997). As a result, people suffering from this
58 condition have to supplement their calcium ingestion to reach the adequate
59 physiological calcium levels.

60 Calcium plays a major role in bone structure and bone recalcification, which are
61 continuous processes declining with age. Osteopenia, or low mineral density of the
62 bones, must be addressed early since the calcium osteo-cycle is regulated by numerous
63 factors, vitamin D being the most important one (Lieben, L., & Carmeliet, G., 2013),
64 and skeletal metabolic diseases can cause a wide range of complications including pain,
65 fracture, and can even be lethal (Imel, E.A., DiMeglio, L.A., & Burr, D.B., 2014).

66 A positive association between lactose intake and the enhancing of the calcium osteo-
67 fixation, as well as the increasing of the trans-epithelial calcium transport was reported
68 by Armbrecht (Armbrecht, H.J., 1987). Work by Schaafsma et al. suggests that even

69 people with vitamin D-deficiency, the beneficial lactose effect can be noted (Schaafsma,
70 G., Visser, W.J., Dekker, P.R., & VanSchaik, M., 1987). Also, lactose was reported as a
71 superior carbohydrate in this role, when tested in calcium-deficient rats (Hämäläinen,
72 M.M., Knuutila, M., Svanberg, M., & Koskien, T., 1990).

73 Numerous studies regarding the thermodynamic properties of lactose binary aqueous
74 solutions have been performed. Nevertheless, transport data related to aqueous solutions
75 containing this sugar are scarce in the literature. The characterization of transport
76 properties, such as diffusion coefficients, is important to derive some type of structural
77 information on these aqueous systems. In fact, they provide a direct measure of
78 molecular mobility, an important factor to be considered when formulating sugar
79 matrixes.

80 We decided to extend our work concerning the experimental determination of diffusion
81 coefficients for systems containing lactose (Ribeiro, A.C.F., et al., 2006a; Ribeiro,
82 A.C.F., Gomes, J.C.S., Barros, M.C.F., Lobo, V.M.M., & Estesó, M.A., 2011a; Ribeiro,
83 A.C.F., Rita, M.B.B.J., Gomes, J.C.S., Lobo, V.M.M., & Estesó, M.A., 2011b;
84 Veríssimo, L.M.P., Gomes, J.C.S., Romero, C., Estesó, M.A., Sobral, A.J.F.N., &
85 Ribeiro, A.C.F., 2013a; Veríssimo, L.M.P., Valada, T.I.C., Ribeiro, A.C.F., Sobral,
86 A.J.F.N., Lobo, V.M.M., & Estesó, M.A., 2013b), by studying an aqueous lactose
87 system with added calcium chloride, having in mind a better understanding of both the
88 structure of these systems and the thermodynamic and transport behaviour of this
89 carbohydrate in those aqueous media. The main scope was to analyze the effect of the
90 lactose on the diffusion of calcium ions involved in many biological systems.

91 In a previous paper (Ribeiro, A.C.F., et al., 2011b) ternary mutual diffusion coefficients
92 (D_{11} , D_{22} , D_{12} and D_{21}) for aqueous solutions containing calcium ions in the presence of
93 lactose, at $T = 298.15$ K, were determined and analyzed. Then, we could conclude that

94 the diffusion of the calcium ions in the presence of lactose may be affected by the
95 eventual formation of different aggregate species resulting from various equilibria
96 taking place in these media. We have considered it interesting to evaluate the effect of
97 temperature on the formation of such aggregates, for which a temperature of 310.15 K
98 was selected to carry the analysis forward under physiological conditions.

99

100 **2. Materials and methods**

101

102 *2.1. Materials*

103 Lactose monohydrate (BDH Chemicals, UK > 97 %) and calcium chloride (Sigma-
104 Aldrich, Germany, *pro analysi* > 99.9 %) were used as received, without further
105 purification. The solutions, prepared in calibrated volumetric flasks using ultrapure
106 water obtained with a Millipore (Germany) water purification system (model Milli-Q
107 Advantage A10) $\{\kappa = (0.7-0.9) \times 10^{-4} \text{ S m}^{-1}\}$, were freshly prepared and de-aerated for
108 about 30 minutes before use.

109

110 *2.2. Mutual diffusion coefficients, D, measured by using the open-ended conductimetric* 111 *capillary cell*

112 The open-ended conductimetric capillary cell technique has been previously used to
113 obtain mutual diffusion coefficient values for a wide variety of electrolytes (e.g. (Agar,
114 J.N., & Lobo, V.M.M., 1975; Ribeiro, A.C.F., Lobo, V.M.M., Azevedo, E.F.G., Miguel,
115 M.G., & Burrows, H.D., 2001; Ribeiro, A.C.F., Lobo, V.M.M., & Natividade, J.J.S.,
116 2002; Ribeiro, A.C.F., Lobo, V.M.M., Azevedo, E.F.G., Miguel, M.G., & Burrows,
117 H.D., 2003; Ribeiro, A.C.F. et al., 2005; Ribeiro, A.C.F., et al., 2006b)). Therefore, this

118 method has been described in great detail in previous papers, along with various
119 operating conditions (Agar, J.N., et al., 1975; Veríssimo, L.M.P., et al., 2013), and only
120 the most relevant points will be indicated here. Basically, the technique consists of two
121 vertical capillaries each closed at one end by a platinum electrode (TE and BE, top and
122 bottom electrodes, respectively), positioned one above the other with the open ends face
123 to face at a distance of about 14 mm (Figure 1). The upper and lower tubes, surrounded
124 by a bulk solution of concentration c , are initially filled with solutions at concentrations
125 $0.75 c$ and $1.25 c$, respectively. This bulk solution (c concentration) is contained in a
126 glass tank ($200 \times 140 \times 60$ mm) immersed in a thermostatic bath at 37°C . Perspex
127 sheets, G, divide the tank internally and a glass stirrer, A, creates a slow lateral flow of
128 the ambient solution across the open ends of both capillaries. The experimental
129 conditions are such that the concentration at each of the open ends is equal to the
130 ambient solution value c , that is, the physical length of the capillary tube coincides with
131 the diffusion path. This means that the required boundary conditions described in the
132 literature to solve Fick's second law of diffusion are applicable (Agar, J.N., et al.,
133 1975). Therefore, the so-called Δl effect (Agar, J.N., et al., 1975) is reduced to
134 negligible proportions. In our apparatus, diffusion is followed by measuring the value of
135 the ratio ($w = R_t/R_b$), R_t and R_b being the electrical resistances of the upper and the lower
136 tubes, respectively. This w value is measured by using a digital voltmeter (Solartron,
137 UK, DVM 7061 with 6 1/2 digits). A power source (Elgar, USA, 121B/400SD) supplies
138 a 30 V sinusoidal signal at 4 kHz, stable within 0.1 mV, to a potential divider that
139 applies a 250 mV signal to the platinum electrodes in the top and bottom capillaries. By
140 measuring the voltages V' and V'' from both the top and the bottom electrodes with
141 respect to a central electrode, ME, the DVM can calculate w .

142 In order to measure the differential mutual diffusion coefficient D at a given
143 concentration c , the bulk solution of concentration c is prepared by mixing 1 l of ‘top’
144 solution with 1 l of ‘bottom’ solution, accurately measured.

145 Initially, the glass tank and the two capillaries are filled with c solution, immersed in the
146 thermostatic bath, and allowed to come to thermal equilibrium. The resistance ratio w
147 measured under these conditions ($w = w_\infty$) with solutions in both capillaries at
148 concentration c , accurately gives the quantity $\tau_\infty = 10^4 / (1 + w_\infty)$.

149 Afterwards, the capillaries are filled with the ‘top’ and the ‘bottom’ solutions, which are
150 then allowed to diffuse into the ‘bulk’ solution. Resistance ratio readings are
151 automatically recorded at various times, beginning 1000 min after the start of the
152 experiment, to determine the quantity $\tau = 10^4 / (1 + w)$ as τ approaches τ_∞ . The diffusion
153 coefficient is then evaluated by using a linear least-squares procedure to fit the data and,
154 finally, an iterative process is applied using 20 terms of the expansion series of Fick’s
155 second law for the present boundary conditions. The theory developed for this capillary
156 cell has been previously reported (Agar, J.N., et al., 1975).

157

158 **3. Results and discussion**

159

160 Diffusion coefficients, D , and their respective standard deviations, S_D , for CaCl_2
161 $0.100 \text{ mol dm}^{-3}$ in aqueous solutions containing lactose at various concentrations
162 ($0.005 \text{ mol dm}^{-3}$, $0.010 \text{ mol dm}^{-3}$, $0.025 \text{ mol dm}^{-3}$, $0.050 \text{ mol dm}^{-3}$, $0.100 \text{ mol dm}^{-3}$ and
163 $0.200 \text{ mol dm}^{-3}$) at $37 \text{ }^\circ\text{C}$ are shown in Table 1. For comparison, data at $25 \text{ }^\circ\text{C}$ (Barros,
164 M.C.F., et al., 2013) obtained with similar conditions are also included. For brevity, we
165 will indicate as 1 and 2 the lactose and CaCl_2 species, respectively (the solvent,

166 component 0, is not included). Each D value is the mean of at least four independent
 167 measurements. Since the error limits of our results should be close to the imprecision,
 168 the experimental uncertainty was 1-3%.

169 The following polynomial in $c_1^{1/2}$ was used to fit our data by a least squares procedure,
 170

$$D/10^{-9} \text{ m}^2 \text{ s}^{-1} = 1.454 - 0.252 c_1^{1/2} + 0.007 c_1 \quad (1)$$

$$R^2 = 0.998$$

171

172 where c_1 and D represent the concentration of lactose and the diffusion coefficient of
 173 cadmium chloride in the different aqueous solutions containing this carbohydrate,
 174 respectively. The goodness of the fit (obtained with a confidence interval better than 98
 175 %) was assessed by both the excellent correlation coefficient, R^2 , and the low standard
 176 deviation (< 1 %) found. Moreover, the limiting D^0 value calculated by extrapolating
 177 these experimental data to $c_1 \rightarrow 0$ ($D^0 = 1.454 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$) agrees well with the
 178 measured D value ($D = 1.440 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$) for solutions containing only CaCl_2 at
 179 $c_2 = 0.100 \text{ mol dm}^{-3}$ (deviation of 0.97 %) (Ribeiro, A.C.F., et al., 2008).

180 From the difference between the diffusion measurements for CaCl_2 at both temperatures
 181 in aqueous solutions in the presence and absence of lactose (measured as the percentage
 182 difference, $\Delta D/D$ %) (Table 1), it can be verified that the diffusion behaviour of calcium
 183 chloride in aqueous solutions is affected by the presence of the lactose molecules. In
 184 fact, for both temperatures and under the present experimental conditions, when lactose
 185 concentrations c are $\geq 0.05 \text{ mol dm}^{-3}$, the diffusion coefficient of CaCl_2 continuously
 186 decreases with increasing lactose concentration, especially at 25 °C, for which this
 187 percentage reaches the maximum difference (i.e., $\Delta D/D = -14.7$ %) at $0.200 \text{ mol/dm}^{-3}$ of

188 lactose. At 37 °C the behaviour observed is the same, although the values for the $\Delta D/D$
189 ratio are less than at 25 °C (i.e., $\Delta D/D = -6.7\%$ at $c_2 = 0.200 \text{ mol/dm}^{-3}$). It is also noted
190 that at concentrations $c < 0.05 \text{ mol dm}^{-3}$, the diffusion coefficient of CaCl_2 did not
191 significantly change at either temperature.

192 The decrease of the diffusion coefficients of calcium chloride with increasing
193 concentration of lactose in these media may be interpreted on the basis of the formation
194 of new species (e.g. ion pairs) resulting, mainly, from the interactions of Ca^{2+} cations
195 with lactose. This may lead to a reduced mobility of these species through the liquid
196 and, consequently, a lower diffusion coefficient value.

197 In relation to the small decrease found in the experimental D values of CaCl_2 in the
198 presence of lactose at 37 °C, at all concentrations studied (Table 1), one possible
199 explanation can be attributed to the decrease in the lactose/ Ca^{2+} interactions with the
200 increasing of the temperature; that is, the thermal motion destabilizes the associated
201 lactose/ Ca^{2+} structures.

202 In reality, the CaCl_2 /lactose/water (Callendar, R., & Leaist, D.G., 2006) system is a
203 ternary one, and the present technique measures changes of the electrical conductance
204 rather than changes of CaCl_2 concentration, which are not necessary the same, since
205 changes of the lactose concentration can alter the conductance of the system. Therefore,
206 we really have only measured the main diffusion coefficients (D_{11}). However, from the
207 experimental conditions used, we may consider this system as a pseudo-binary one and,
208 consequently, the measured parameters could be taken as the binary diffusion
209 coefficients, D .

210 Assuming that D is a product of both kinetic and thermodynamic factors (equation 2),
211 we suggest that both the thermodynamic factor and the kinetic factor decrease when we

212 move from a solution of pure CaCl_2 to a mixed solution containing both CaCl_2 and this
 213 carbohydrate. That is,

214

$$D_{OF} = F_M \times F_T \quad (2)$$

215

216 where

$$F_M = \overline{M} \left(\frac{|z_c| + |z_a|}{|z_c z_a|} \right) \frac{RT}{c} = (D^0 + \Delta_1 + \Delta_2) \quad (3)$$

217

218 and

$$F_T = \left(1 + c \frac{\partial \ln y_{\pm}}{\partial c} \right) \quad (4)$$

219

220 y_{\pm} represents the thermodynamic activity coefficient of the solute, D is the mutual
 221 diffusion coefficient of the electrolyte in $\text{m}^2 \text{s}^{-1}$, R is the gas constant in $\text{J mol}^{-1} \text{K}^{-1}$, T is
 222 the absolute temperature, z_c and z_a are the algebraic valences of the cation and the anion,
 223 respectively, and the last term in parenthesis is the activity factor, with y_{\pm} being the
 224 mean molar activity coefficient, c the concentration in mol/m^3 , and \overline{M} , in $\text{mol}^2 \text{s m}^{-3}$
 225 kg^{-1} , is given by

226

$$\bar{M} = \frac{1}{N_A^2 e_0^2} \left(\frac{\lambda_c^0 \lambda_a^0}{\nu_a |z_a| \lambda_c^0 + \nu_c |z_c| \lambda_a^0} \right) c + \bar{\Delta M}' + \bar{\Delta M}'' \quad (5)$$

227

228 In equation 5, the first and second-order electrophoretic terms, are equal to:

229

$$\bar{\Delta M}' = - \frac{c}{N_A} \frac{\left(|z_a| \lambda_c^0 - |z_c| \lambda_a^0 \right)^2}{\left(|z_c| \nu_c \lambda_a^0 + |z_a| \nu_a \lambda_c^0 \right)^2} \frac{\nu_c \nu_a}{\nu_c + \nu_a} \frac{k}{6\pi \eta_0 (1+ka)} \quad (6)$$

230 and

$$\bar{\Delta M}'' = \frac{\left(\nu_1 |z_2| \lambda_1^0 + \nu_2 |z_1| \lambda_2^0 \right)^2}{\left(\nu_1 |z_1| \lambda_2^0 + \nu_2 |z_2| \lambda_1^0 \right)^2} \frac{1}{(\nu_1 + \nu_2)^2} \frac{1}{N_A^2} \frac{k^4 \phi(ka)}{48\pi^2 \eta_0} \quad (7)$$

231

232 where η_0 is the viscosity of water in N/s/m², N_A is the Avogadro's constant, e_0 is the233 proton charge in coulombs, ν_c and ν_a are the stoichiometric coefficients, λ_c^0 and λ_a^0 234 are the limiting molar conductivities of the cation and anion, respectively, in m² mol⁻¹235 Ω^{-1} , κ is the 'reciprocal average radius of ionic atmosphere' in m⁻¹ (Harned, H.S., &236 Owen, B.B., 1964), a is the mean distance of closest approach of ions in m, ($a = 4.0 \times$ 237 10^{-10} m (Ribeiro, A.C.F., et al., 2008)). The values for $\phi(ka) = \left| e^{2ka} E_1(2ka) / (1+ka) \right|$

238 have been tabulated by Harned and Owen, and the other letters represent well-known

239 quantities (Harned, H.S., et al., 1964).

240 Thus, from equation (2) it can be seen that two different effects can control the diffusion
 241 process: the ionic mobility (F_M) and the gradient of the chemical potential (F_T).
 242 Concerning the first effect, and assuming identical considerations than those relative to
 243 the effect of the sucrose on the equivalent conductance of KCl (Lobo, V.M.M., &
 244 Gonçalves, L.C., 1982), we should accept a decreasing of 6.0 % in the limiting
 245 equivalent conductance of CaCl_2 in the presence of 0.1 mol dm^{-3} of lactose (3.4 % of
 246 lactose) at $25 \text{ }^\circ\text{C}$. That is, it would be $\Lambda^0 = 127.70 \times 10^{-4} \text{ m}^2 \text{ equiv}^{-1} \Omega^{-1}$, from which we
 247 may assume $\lambda_c^0 = 59.50 \times 10^{-4} \text{ m}^2 \text{ equiv}^{-1} \Omega^{-1}$ and $\lambda_a^0 = 76.35 \times 10^{-4} \text{ m}^2 \text{ equiv}^{-1} \Omega^{-1}$ at
 248 0.1 M lactose ($\lambda_c^0 = 55.93 \times 10^{-4} \text{ m}^2 \text{ equiv}^{-1} \Omega^{-1}$ and $\lambda_a^0 = 71.77 \times 10^{-4} \text{ m}^2 \text{ equiv}^{-1} \Omega^{-1}$ in
 249 pure water). Considering this value in the Onsager-Fuoss equations (2) to (5), we would
 250 get almost identical diffusion coefficients, D_{OF} , (Table 2) to that of 0.1 mol dm^{-3} CaCl_2
 251 in pure water, within the experimental error (in general, $\Delta D/D$ around 5 %) (Ribeiro,
 252 A.C.F., et al., 2008). Therefore, this slight variation of the equivalent conductances
 253 relative to pure water solutions cannot be responsible for the significant difference
 254 observed for diffusion in the range of concentrations $c \leq 0.1 \text{ mol dm}^{-3}$ of lactose (i.e.,
 255 $\Delta D/D < -15 \%$). Consequently, assuming that the presence of lactose does not
 256 significantly influence the ionic mobility of CaCl_2 , (confirmed by the very similar Δ_1
 257 values obtained by using limiting equivalent conductances of CaCl_2 , at both
 258 temperatures (Table 3)), we can conclude that the variation in D is mainly due to the
 259 variation of F_T (attributed to non-ideal thermodynamic behaviour) (Table 4). In fact, the
 260 very small values of Δ_1 obtained for the studied interval of concentrations, lead us to
 261 obtain very similar F_M values for the concentration range ($< 6.0 \%$), and so, we can say
 262 that the presence of lactose has little effect on F_M .

263 From the Onsager-Fuoss equation and our measurements of diffusion coefficients, we
264 have estimated the F_T values at both temperatures (Table 4), within the studied interval
265 of concentrations. Contrarily to the slightly increasing of F_M with concentration, the
266 presence of this carbohydrate leads to a significant decrease of the F_T values, when
267 compared with those estimated for an aqueous system containing only calcium chloride,
268 at 25 °C (Table 4). Due to the absence of literature values for the parameters necessary
269 to estimate D_{OF} at temperatures other than 25 °C, it was not possible to make a similar
270 analysis at 37 °C. Nevertheless, it was possible to infer the temperature effect on the
271 diffusion for this system. Thus, considering our experimental conditions (i.e., dilute
272 solutions), and by assuming that parameters such as viscosity, dielectric constant and
273 hydration in aqueous solutions, as well as complexation, (not taken into account in this
274 model) do not change with concentration, we can conclude that the variation in D is
275 mainly due to the variation of F_T (attributed to non-ideal thermodynamic behaviour).
276 The decreasing of the gradient of the free energy with concentration, F_T , for both
277 temperatures, leads us to assume that the eventual presence of solute–solute weak
278 interactions is being responsible by these observations.

279

280 **4. Conclusions**

281

282 From the values of D obtained it is possible to conclude that, over the concentration
283 range studied, the diffusion of CaCl_2 in aqueous solutions containing lactose at different
284 concentrations appears to be affected by the presence of this sugar. In fact, increasing
285 the lactose concentration in the medium is accompanied by a decrease in the diffusion
286 coefficient values for CaCl_2 , which is less accentuated at 37 °C than at 25 °C. This may
287 be the result of the existence of some association or aggregate formation between Ca^{2+}

288 and lactose. If such interactions exist in this region, they will be observed in two ways:
289 (i) a smaller mobility of the CaCl_2 /lactose aggregates, as a consequence of a steric
290 effect; (ii) a significant decreasing of the gradient of the chemical potential with the
291 lactose concentration, as a result of the non-ideal thermodynamic behaviour of the
292 system. At 37 °C, physiological temperature, this association is the calcium chloride
293 plus reduced due to a smaller decrease of both previous effects by the thermal motion.
294 Diffusion coefficients for calcium chloride, when obtained in the presence of lactose,
295 may provide the transport data necessary to model the diffusion behaviour for various
296 chemical and pharmaceutical applications.

297

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299

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303

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387

388 **Figure 1** – Schematic view of the Lobo’s open-ended capillaries conductimetric cell.

389 TE and BE are the top and the bottom Pt-electrodes, respectively; ME is the

390 medium Pt-electrode; G is a grid-bulkhead (in perspex); and A is a glass

391 stirrer.

392

ACCEPTED MANUSCRIPT

Table 1

Experimental diffusion coefficients, D , of aqueous systems containing lactose (1), and CaCl_2 (2) at 25 °C^{a)}

(Barros, M.C.F., et al., 2013) and 37 °C^{a)}.

$c_1 /$ / mol dm ⁻³ b)	$D \pm S_D /$ / (10 ⁻⁹ m ² s ⁻¹) c)	$D \pm S_D /$ / 10 ⁻⁹ m ² .s ⁻¹ c)	$(\Delta D/D) /$ / % d)	$(\Delta D/D) /$ / % d)
	(T =25 °C)	(T =37 °C)	(T =25 °C)	(T =37 °C)
0.200	0.947 ± 0.018	1.343 ± 0.010	-14.7	-6.7
0.150	1.001 ± 0.019 ^{e)}	1.359 ± 0.019	-9.8	-5.6
0.100	1.053 ± 0.020	1.372 ± 0.020	-5.1	-4.7
0.050	1.095 ± 0.021	1.400 ± 0.019	-1.4	-2.8
0.010	1.111 ± 0.028	1.430 ± 0.026	0.1	-0.7
0.005	1.112 ± 0.023	1.435 ± 0.020	0.2	-0.3
0.000	1.094 ± 0.008 ^{f)}	1.454 ± 0.008 ^{g)}	-1.4	1.0

^{a)} Uncertainty, $u(T) = 0.01$ °C. ^{b)} uncertainty, $u(c) = 0.001$ mol dm⁻³. ^{c)} D is the mean diffusion coefficient of 3 experiments and S_D is the standard deviation of that mean. ^{d)} $(\Delta D/D) / \%$ represents the deviation between the diffusion coefficients of the system (Lactose + CaCl₂ + H₂O), D , here measured and the diffusion coefficients, D_{Lit} , of the system (CaCl₂ + H₂O) at the indicated temperature (Ribeiro, A.C.F., et al., 2008). ^{e)} Interpolated value from data reported in reference (Barros, M.C.F., et al., 2013). ^{f)} Extrapolated value (when $c_1 \rightarrow 0$) for the diffusion coefficient of aqueous solutions of calcium chloride at $c_2 = 0.100$ mol dm⁻³ (Barros, M.C.F., et al., 2013). ^{g)} Extrapolated value (when $c_1 \rightarrow 0$) for the diffusion coefficient of aqueous solutions of calcium chloride at $c_2 = 0.100$ mol dm⁻³ from the values here obtained at 37 °C.

Table 2

Theoretical diffusion coefficients, D_{OF} , of the system ($\text{CaCl}_2 + \text{H}_2\text{O}$) at 25 °C, at different concentrations, c , using the limiting conductance value of the literature (Robinson, R.A, & Stokes, R.H., 1959) and estimated ones of CaCl_2 in aqueous solutions

$c/\text{mol dm}^{-3}$	$D_{\text{OF}}/10^{-9} \text{ m}^2 \cdot \text{s}^{-1}$ ^{a)}	$D_{\text{OF}}/10^{-9} \text{ m}^2 \cdot \text{s}^{-1}$ ^{b)}	$\Delta D_{\text{OF}}/D_{\text{OF}}$ % ^{c)}
	($T = 25$ °C)	($T = 25$ °C)	
0.150	1.180	1.130	-4.2
0.100	1.184	1.122	-6.2
0.050	1.182	1.129	-4.4
0.010	1.213	1.145	-5.9
0.005	1.233	1.162	-5.7

^{a)} Estimated values by using Onsager-Fuoss equation (3) and the limiting conductance value of CaCl_2 in aqueous solutions found in the literature (Robinson, R.A, & Stokes, R.H., 1959) (i.e., $\Lambda^0 = 135.85 \times 10^{-4} \text{ m}^2 \text{ equiv}^{-1} \Omega^{-1}$). ^{b)} Estimated values by using Onsager-Fuoss equation (3) and our estimated limiting conductance ($\Lambda^0 = 127.70 \times 10^{-4} \text{ m}^2 \text{ equiv}^{-1} \Omega^{-1}$), calculated from the Λ^0 value in pure water,

and assuming a drop of 6 % in that value in the presence of lactose. ^{c)} $(\Delta D/D) / \%$ represents the deviation between the diffusion coefficients obtained by using the Onsager-Fuoss equation (2) and the limiting conductance value in the literature (Robinson, R.A, & Stokes, R.H., 1959), and those obtained by the same model, but using our estimated limiting conductance of CaCl₂ in aqueous solutions, at the indicated temperature.

Table 3Electrophoretic factors, $\Delta_1 + \Delta_2$, estimated from equation (3) at 25 °C and 37 °C for aqueous lactose (1) + CaCl₂ (2) solutions

$c_1 /$ / mol dm ⁻³	$(\Delta_1 + \Delta_2) /$ /10 ⁻⁹ m ² s ⁻¹ ^{a)}	$\Delta(\Delta_1 + \Delta_2) / (\Delta_1 + \Delta_2)$ % ^{b)}	$(\Delta_1 + \Delta_2) /$ /10 ⁻⁹ m ² s ⁻¹ ^{c)}	$\Delta(\Delta_1 + \Delta_2) / (\Delta_1 + \Delta_2)$ % ^{d)}
	(T = 25 °C)	(T = 25°C)	(T = 37 °C)	(T =37 °C)
0.200	0.186	-0.5	0.184	-2.8
0.150	0.142	-0.7	0.152	2.8
0.100	0.156	-0.6	0.154	-2.9
0.050	0.137	0.7	0.136	-2.9
0.010	0.067	0.0	0.067	-2.9
0.005	0.044	0.0	0.044	-0.5
0.000	0.000	0.0	0.000	0.0

^{a)} Calculated values by using the Onsager-Fuoss equation (3) and our estimated limiting conductance value of CaCl₂ in aqueous solutions containing lactose at 25 °C ($\Lambda^0 = 127.70 \times 10^{-4} \text{ m}^2 \text{ equiv}^{-1} \Omega^{-1}$). ^{b)} $\Delta(\Delta_1 + \Delta_2) / (\Delta_1 + \Delta_2) \%$ represents the deviation between the electrophoretic factors obtained by using the Onsager-Fuoss equation (3) and our estimated value $\Lambda^0 = 127.70 \times 10^{-4}$

$\text{m}^2 \text{equiv}^{-1} \Omega^{-1}$, and those obtained by the same model, but using the limiting conductance value found in the literature (Robinson, R.A. & Stokes, R.H., 1959) ($\Lambda^0 = 135.85 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$), at 25 °C. ^{c)} Estimated values by using the Onsager-Fuoss equation (3) and our estimated limiting conductance value of CaCl_2 in aqueous solutions containing lactose ($\Lambda^0 = 161.91 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$), calculated from the Λ^0 value in pure water, and assuming a value drop of 6 % in the presence of lactose. ^{d)} $\Delta(\Delta_1 + \Delta_2) / (\Delta_1 + \Delta_2)$ % represent the deviation between the electrophoretic factors obtained by using the Onsager-Fuoss equation (3) and our estimated value ($\Lambda^0 = 161.91 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$), and those obtained by the same model, but using the limiting conductance value found in the literature (Robinson, R.A. & Stokes, R.H., 1959) ($\Lambda^0 = 172.24 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$), at 37 °C.

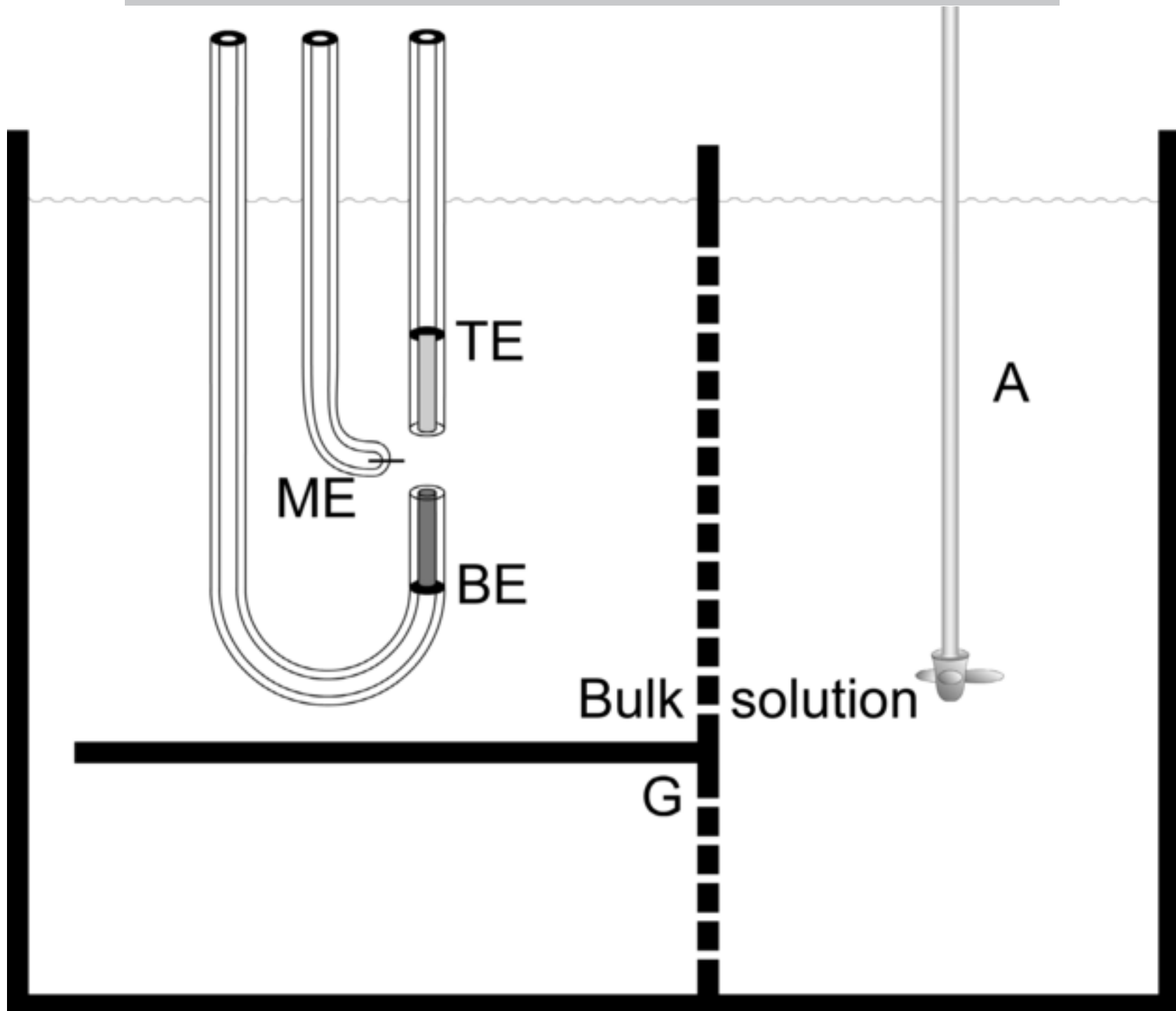
Table 4

Thermodynamic factors, F_T , for lactose (1) + CaCl_2 (2) aqueous solutions estimated from our experimental values of D and from equation (2), at 25 °C and 37 °C.

$c_1/$ / mol dm ⁻³	F_T ($T = 25$ °C)	$\Delta F_T/F_T$ ^{a)} % ($T = 25$ °C)	$\Delta F_T/F_T$ ^{b)} % ($T = 25$ °C)	F_T ($T = 37$ °C)	$\Delta F_T/F_T$ ^{c)} % ($T = 37$ °C)
0.200	0.657	5.6	-18.0	0.754	5.7
0.150	0.748	4.2	-6.0	0.777	5.7
0.100	0.776	4.7	-2.4	0.784	5.9
0.050	0.794	5.6	-1.5	0.808	5.9
0.010	0.840	6.0	-3.0	0.860	6.0
0.005	0.855	5.8	-4.3	0.875	6.2
0.000	1.000	0.0	1.0	1.000	0.0

^{a)} $\Delta F_T/F_T$ % represents the deviation between the thermodynamic factors estimated from our experimental values of D and from equation (2) at 25 °C, by using our estimated values $\lambda_c^0 = 55.93 \times 10^{-4} \text{ m}^2 \text{ equiv}^{-1} \Omega^{-1}$ and $\lambda_a^0 = 71.77 \times 10^{-4}$

$\text{m}^2 \text{equiv}^{-1} \Omega^{-1}$ and the corresponding values found in the literature (Robinson, R.A, & Stokes, R.H., 1959), i.e., $\lambda_c^0 = 59.50 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$ and $\lambda_a^0 = 76.35 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$. ^{b)} $\Delta F_T / F_T$ % represents the deviation between the thermodynamic factors estimated from our experimental values of D and from equation (2), at 25 °C and by using our estimated values $\lambda_c^0 = 55.93 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$ and $\lambda_a^0 = 71.77 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$, and those found in the literature (Robinson, R.A, & Stokes, R.H., 1959). ^{c)} $\Delta F_T / F_T$ % represents the deviation between the thermodynamic factors estimated from our experimental values of D and from equation (2) at 37 °C, by using our estimated values $\lambda_c^0 = 71.91 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$ and $\lambda_a^0 = 90.00 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$ and the values from the literature (Robinson, R.A, & Stokes, R.H., 1959), i.e., $\lambda_c^0 = 76.50 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$ and $\lambda_a^0 = 95.74 \times 10^{-4} \text{ m}^2 \text{equiv}^{-1} \Omega^{-1}$.



Research Highlights

- Calcium transport in lactose/calcium systems at 37 °C is affected by sugar concentration
- Association calcium/lactose is responsible of decreasing in diffusion coefficient values
- At 37 °C, the thermal motion difficult the stabilization of associated structures