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Research Article

Evaluation of the slip length in the slipping friction between background electrolytes and peptides through the modeling of their capillary zone electrophoretic mobilities

This work analyzes and discusses several physicochemical peptide chain properties that may generate partial or total BGE slip boundary conditions on the surface of peptides migrating as spherical and aspherical particles in CZE. A definition of the BGE slip length is presented that is able to account the effect of particle curvature through the associated metrical coefficients. This definition allows the distinction between partial and total BGE slip lengths. It is also shown that the BGE slip length must be variable on orthotropic aspherical particles surfaces.

Keywords:
Fluid slip boundary condition / Hydrophobic peptides / Partial and total slip lengths / Peptide effective electrophoretic mobility / Slip friction coefficient
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1 Introduction

Measurements of the effective electrophoretic mobility μ_p of peptides in different BGEs are useful to evaluate their electrokinetic and physicochemical properties and also to characterize their global chain structures, when coarse-grained modeling strategies are applied. In these regards different hypotheses and approaches in this line of research may be found for instance in [1–40]. Further estimations of transport properties like diffusion coefficient D, intrinsic viscosity [η], and BGE-chain friction coefficient f may be also obtained [3, 19, 28, 30–33, 36, 38]. With these purposes, one observes that CZE is a rapid and reliable technique providing effective experimental electrophoretic mobility μ_p^{exp} values at well-defined BGE properties like temperature T, electrical permittivity ε, viscosity η_s, ionic strength I and pH ([41–48] and citations therein).

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Abbreviations: AAS, amino acid sequence; **AHI**, average hydrophobicity index; **STN**, staphylococcal nuclease

In particular, the modeling of peptide effective electrophoretic mobility for global chain characterization purposes has increased steeply in the last years, and also has provided relevant information, mainly when models are based on theories developed through well defined and true physicochemical properties. These theories are already placed in a neat delimited range of parameter variations for their validity and applicability ([3, 5, 11, 30, 36, 38, 49–51] and citations therein). Therefore it is essential to differentiate between analytical theoretical developments, where for instance the polarization–relaxation phenomenon of ions around the migrating charged particle may be neglected [30, 36, 38, 52] and those containing in addition significant computational efforts allowing the description of quite nonlinear electrophoretic effects [3, 5, 11, 49–51]. Both proposals were shown to be useful in practice. Previously, we have found that a high number of CZE experimental runs of peptides published in the literature may be studied via the former approach, which applies for relatively low dimensionless zeta potentials ($e\zeta/k_BT$) < 2.5 and quite small particles with Stokes radius a_H within the range around 4–50 Å (Å $= 10^{-10}$ m), where Hückel asymptote of Henry theory applies [30, 38, 49, 50, 53, 54]. Here, e is the elementary charge, ζ is the particle zeta (electrokinetic) potential and k_B is Boltzmann constant. In this regard, the different linear branches of Henry theory for spherical particles of radius a_H and Debye–Hückel parameter $\kappa = (2e^2 I N_A 10^3/\varepsilon k_B T)^{1/2}$ must be clearly distinguished; N_A being Avogadro constant.

In fact as long as $(e\zeta/k_BT) < 5/2$ and $\kappa a_H < 3$ involving a 1–1 symmetric BGE, one can assume that ion polarization–relaxation is negligible for spherical and rather aspherical particles generating Henry–Hückel asymptotic response [18, 20, 27, 29, 30, 32, 36] where the dimensionless effective electrophoretic mobility $(3e\mu_p\eta_s/2\varepsilon\Omega k_BT)$ becomes quite insensitive to values $\kappa a_H < 3$ [38, 50]; here Ω is the particle asphericity. In particular, for spherical particles ($\Omega = 1$), the dimensionless effective electrophoretic mobility as a function of $(e\zeta/k_BT)$ for around $\kappa a_H > 3$ and still relatively low dimensionless zeta potentials keeps yielding linear branches above the Hückel asymptote, until the Helmholtz–Smoluchowski linear regime is achieved at the extreme branch $\kappa a_H \to \infty$ [55, 56]. This last result has major applications to relatively high radii of charged colloidal particles. Nevertheless for around $(e\zeta/k_BT) > 5/2$ and $\kappa a_H > 3$, nonlinear phenomena are expected.

Here, in particular, we propose to analyze several physicochemical chain properties generating the partial or total BGE slip boundary condition on the surface of peptide particles migrating in CZE. For this purpose, it is relevant to use the friction ratio $\Omega = f_o/f$ defined before in [30, 32], where f is the actual friction coefficient between BGE and particle and $f_o = 6\pi\eta_s a_H$ is the friction coefficient of the equivalent spherical particle involving the BGE nonslip boundary condition on the particle surface. The designation "friction ratio" for Ω is adopted throughout the present work allowing us to refer generically to different hydrodynamic phenomena, and still without losing previous physical meanings when the BGE nonslip boundary condition applies in aspherical particles already described in [20, 29, 30, 32, 36, 38]. Thus, in previous works Ω was also designated "shape orientation factor" or simply "asphericity."

For the present analysis of BGE slip on peptides, experimental effective electrophoretic mobility data yielding $\Omega > 1$ through the perturbed Linderstrøng–Lang capillary electrophoresis model are considered only (see model details in [18, 27, 30, 32, 36] and a summary in the Supporting Information). Therefore, here we study μ_p^{exp} values of peptides reported in [57] at pH 2.5, I = 35.3 mM, and T = 22°C, that may present the BGE slip boundary condition. Supporting Information Table I-1 depicts the amino acid sequence (AAS) of 102 peptides (both oligo- and polypeptides) studied in [57] indicating their average hydrophobicity index (AHI) to allow then a proper discussion in Section 3. In this table, one visualizes those peptides having $\Omega > 1$. In this same framework, the staphylococcal nuclease (STN) is analyzed as a protein case study for pH 8.9, I = 14 mM, and T = 25°C, where the protocol pH is approaching the protein p*I* 9.63 giving $\Omega > 1$ (the μ_p^{exp} value was reported in [58]). We expect to illustrate that under specific conditions involving BGE and AAS, other hydrodynamic phenomena may appear in the electrophoresis of certain types of peptides, even when ion polarization–relaxation may be neglected.

The manuscript is organized as follows. Section 2 presents theoretical aspects required to model μ_p when the BGE slip boundary condition is considered on the migrating particle surface. Section 3 analyzes peptide physical characteristics required for applying the BGE slip boundary condition when $\Omega > 1$. Concluding remarks and proposals for further researches are also provided.

2 Theory

2.1 Modeling peptide effective electrophoretic mobility in the Henry–Hückel branch

As a consequence of the matching between Henry theory and Hückel asymptotic response for around $\kappa a_H < 3$, a good estimation of the peptide effective electrophoretic mobility at the Henry–Hückel branch is [18, 20, 29, 30, 32, 36, 38]:

$$\mu_p = \Omega \frac{eZ}{f_o(1+\kappa a_H)} f_H(\kappa a_H) \quad (1)$$

where Z is the peptide effective charge number and $f_H(\kappa a_H)$ is Henry function satisfying $f_H(0) = 1$ and $f_H(\infty) \to 3/2$. Equation (1) defines the "equivalent spherical model" that we have used previously to study proteins and peptides, and further details may be found in [20, 30, 38]. Consequently, spherical and aspherical particles satisfying this constraint yielded $\Omega = 1$ and $\Omega \neq 1$, respectively. We found in general that $1/2 < \Omega < 3/2$ approximately, for peptides and proteins depending mainly on the AAS and basic protocol properties. Further, it was also showed that orthotropic aspherical particles translating with an average angle Θ less than 55°, which is formed between the main particle axis of revolution and the direction of the external applied electrical field, were appropriate particle shapes when $\Omega > 1$, as described in [20]. Alternatively, it is clear that another hydrodynamic situation yielding $\Omega > 1$ is also possible involving specifically a partial or total BGE slip boundary condition on the particle surface, and hence an analytic expression for Ω may be found as will be explained in Section 2.3.

Within this framework it is important to visualize from [18, 20, 29, 30, 32, 36] that Eq. (1) is an approximation to μ_p^{exp} in the Henry–Hückel branch when the equivalent spherical model with radius a_H is defined so that this spherical particle has the same effective charge number Z and also approximates the zeta potential of the actual aspherical particle. In addition, the actual hydrated particle volume must equal the equivalent sphere volume $4\pi a_H^3/3$. It is then clear that the friction ratio $\Omega = f_o/f$ depends on particle hydration $\delta = \{(a_H/a_c)^3 - 1\}v_p/v_w$ (water mass/peptide mass) where a_c is the peptide compact radius defined in [20] and v_p and v_w are the peptide and water-specific volumes, respectively. Nevertheless analytical treatments of the several possible hydrodynamic phenomena occurring simultaneously in peptide migrations described through Ω may be quite complex, and this is not the purpose of the present work. Here, we are trying to keep our analysis within the framework of simple analytical expressions to study in particular the friction ratio when a partial or total BGE slip occurs mainly on a spherical particle, which may be relevant to interpret the experimental

effective electrophoretic mobility of peptides. Thus, when the BGE slips on the particle, one obtains $\Omega = f_o/f > 1$ and $f_o > f$. Here, the importance of Hückel asymptotic result $\mu_p^{exp} \approx \Omega\, e\, Z/f_o$ matching Eq. (1) for decreasing dimensionless zeta potentials must be visualized to use then f available from previous studies [59]. Further, from [30, 32], proteins and relatively large peptides (high number N of amino acid residues) for pHs far from their pI values present the opposite situation yielding $\Omega = f_o/f < 1$ and $f_o < f$. Thus when $\Omega < 1$ the migrating particles are hydrodynamically more dissipative than the equivalent spherical particle of radius a_H.

Throughout this work, several peptide properties already defined and described in our previous works [18, 20, 30, 32] are also used. They are summarized in the Supporting Information where a list of symbols is also included. Therefore the electrical state of peptides is described through effective charge number Z, positive and negative charge numbers Z_+ and Z_-, total charge number $Z_T = Z_+ + |Z_-|$, and near molecule pH designated pH* due to the charge regulation phenomenon [18]. Also through the hydrated chain fractal model [32, 36, 38] the packing g_p and friction g_f fractal dimensions are defined (Supporting Information). One finds that $1 < g_p < 3$ from linear to spatial chain packing within the hydrated particle domain, and $1/3 < g_f < 1$ from collapsed to free draining chain conformations. In this framework, for rather high number N of amino acid residues, collapsed conformations can destabilize toward the so called hybrid chain regime when $|Z| > \sqrt{Z_T}$ (see details in [32, 36]). Also the number of water molecules per chain is $H = \delta M/18$ that is evaluated through the peptide hydration function described in [27, 29, 30, 32]; M is the peptide molar mass.

2.2 BGE slip on spherical and aspherical orthotropic particles

It is clear that in the Henry–Hückel linear branch, dissimilar values of $\Omega = f_o/f$ may be obtained through several hydrodynamic phenomena, like for instance those generated through different particle shapes and their average orientations [20] as well as for those involving partial or total BGE slip on the particle surface. Therefore within this branch, an orthotropic aspherical particle has an average friction ratio $\Omega = \alpha\Omega^{//} + (1-\alpha)\Omega^{\perp}$, where $\Omega^{//} = f_o/f^{//}$ and $\Omega^{\perp} = f_o/f^{\perp}$ are associated with BGE-particle friction coefficients $f^{//}$ and $f^{\perp}$ defined when this particle translates parallel and perpendicular to the revolution axis, respectively. Here $\alpha = \cos^2\Theta$, and in particular $\Theta \approx 55°$ for gravitational particle sedimentation, a situation not generally found in CZE [20]. In particular when the BGE slip boundary condition applies, the slip friction ratio is designated Ω_{slip}. In general, the average slip friction coefficient $f_{slip} = f_o/\Omega_{slip}$ is very sensitive to hydrodynamic BGE behavior around the particle migration and hence the fluid mechanic problem may become quite complex [60, 61] (see also [20] for the effect of orientation on aspherical particles when $f = f_o/\Omega$). For our purposes it is clear that Ω_{slip} and f_{slip} are conceptually different from Ω and f representing dissimilar hydrodynamic phenomena.

2.3 BGE slip boundary condition on orthotropic particles

An interesting historical synopsis concerning the origin of fluid slip boundary condition on a given surface may be found in [62] and more recently in [63]. Here in particular the fluid slip boundary condition refers to the kinematics constraint of the BGE velocity vector $\mathbf{v}$ evaluated on the hydrated peptide particle. Therefore, this boundary condition for a Newtonian BGE and a given particle is expressed in the invariant tensor form as follows:

$$\beta_{slip}\mathbf{v}\cdot\mathbf{e}_t = \eta_s\,(\mathbf{e}_n\cdot\dot{\gamma}\cdot\mathbf{e}_t) \tag{2}$$

with the constraint $\mathbf{v}\cdot\mathbf{e}_n = 0$, where $\dot{\gamma} = \nabla\mathbf{v} + \nabla\mathbf{v}^T$ is the BGE rate of deformation tensor, $\mathbf{e}_n$ is the unit vector perpendicular to the interface, while $\mathbf{e}_t$ is the corresponding orthogonal tangential unit vector. In Eq. (2), β_{slip} is the slip coefficient [59] having units $N\ s\ m^{-3}$. In particular for a flat interface Eq. (2) gives the tangential velocity $v_t = b_{slip}\,\partial v_t/\partial n$ where $v_t = \mathbf{v}\cdot\mathbf{e}_t$ while n refers to normal coordinate values. In particular $b_{slip} = \eta_s/\beta_{slip}$ is the slip length [61, 63, 64]. For a spherical particle of radius a_H and by using spherical coordinates (r, θ, ϕ), Eq. (2) yields $v_\theta = b_{slip}(\partial v_\theta/\partial r)_{r=a_H}$ with $v_t \equiv v_\theta$ and $n \equiv r$, where:

$$b_{slip} = \eta_s \Big/ \left(\beta_{slip} + \frac{\eta_s}{a_H}\right) \tag{3}$$

In Eq. (3), the slip length is still a constant that depends on the particle radius a_H. For high radius values $b_{slip} \to \eta_s/\beta_{slip}$ and the slip length for a flat particle surface is consistently recovered. Further the friction coefficient of a sphere translating in a Newtonian fluid satisfying the slip boundary condition is well known [59, 65] which in the Henry–Hückel branch readily provides $\Omega_{slip} = (\beta_{slip}a_H + 3\eta_s)/(\beta_{slip}a_H + 2\eta_s)$; here when $\beta_{slip} \to 0$ one gets $\Omega_{slip} = 3/2$, which is the value for total BGE slip in a spherical particle giving $b_{slip} = a_H$. Also $\Omega = 3/2$ is obtained for a slender cylinder with BGE non slip boundary condition [52] moving parallel to the external applied electrical field indicating thus a clear conceptual distinction between Ω_{slip} and Ω. In fact one value is due to a spherical particle with a total BGE slip boundary condition while the other comes from a slender cylinder and its extreme orientation ($\Theta \to \pi/2$). In addition, $\Omega_{slip} \to 1$ for $\beta_{slip} \to \infty$ and the classical Stokes flow with the BGE non-slip boundary condition is recovered ($\Omega = 1$ and $b_{slip} = 0$). Therefore, the peptide diffusion coefficient may be estimated from $D = (k_B T\Omega_{slip}/6\pi\eta_s a_H)$ and the intrinsic viscosity is $[\eta] = (5/2)(v_p + \delta v_w)(\beta_{slip}a_H + 2\eta_s)/(\beta_{slip}a_H + 5\eta_s)$ (see also [30, 38, 59].

For orthotropic particles, however, metrical coefficients involved in Eq. (2) indicate that a well-defined slip length

must be variable on the particle surface as deduced after a considerable algebraic procedure to obtain:

$$b_{slip} = \eta_s \Big/ \left(\beta_{slip} - \eta_s \frac{\partial h_2}{\partial q_1}\right) \tag{4}$$

where an orthogonal coordinate system of revolution (q_1, q_2, q_3) is used with metrical coefficients (h_1, h_2, h_3) and BGE velocity field $v_1(q_1, q_2)$, $v_2(q_1, q_2)$, and $v_3 = 0$ (see [59] for basic definitions). In particular for a prolate spheroid of major a and minor c radii, one finds that $q_1 \equiv n$, $q_2 \equiv t$, and $q_3 \equiv \varphi$ are the normal, tangential, and rotational coordinates, $v_1 = v_n$, $v_2 = v_t$, and $h_1 = h_2 = a\,E_x(\sinh^2 n + \sin^2 t)^{-1/2}$, giving the expression:

$$b_{slip} = \frac{\eta_s}{\{\beta_{slip} + \eta_s \sinh n_o \cosh n_o / [a\,E_x(\sinh^2 n_o + \sin^2 t)^{3/2}]\}} \tag{5}$$

where $E_x = \sqrt{1 - (c/a)^2}$ is the eccentricity with a spheroidal surface defined through $n_o = (1/2)\ln(a + c)/(a - c)$. Here, $0 \le n \le \infty$, $0 \le t \le \pi$ and $0 \le \varphi \le 2\pi$. Therefore b_{slip} is varying on the particle surface and takes a maximum value b_{slip}^{max} at $t = \pi/2$ (Section 3). Finally, when the prolate spheroid is translating parallel to its axis of symmetry the slip friction ratio is $\Omega_{slip} = \Omega_{slip}^{//}$ with $\alpha = 1$. At present numerical values for $f_{slip}^{//}$ can be readily found as a function of $\eta_s/c\beta_{slip}$ and ratio a/c in [60, 61]. We show below that this type of fluid–particle situation may be useful to explain rather high values of $\Omega_{slip} > 3/2$ found for some peptides. Thus these results are physically viable when asphericity and BGE slip manifest together as shown in Section 3. Nevertheless this specific subject is under intensive research at present (see for instance [60, 61, 64, 66] and citations therein) and will deserve further consideration in future works to seek for simpler expressions and correlations.

For the numerical evaluations of peptide case studies proposed here with $\kappa a_H < 1$, we follow the same conceptual framework used in the perturbed Linderstrøng–Lang capillary electrophoresis model [18, 20, 27, 29, 30, 32, 36, 38] (see further details in the Supporting Information concerning the use of van der Waals volumes of amino acid residuals). For particles with high κa_H values including also the consideration of fluid slip at the particle surface see [64, 67].

3 Results and discussion

Table 1 presents numerical values of main model parameters including β_{slip} and b_{slip} for peptides with $1.017 < \Omega_{slip} < 1.330$ indicating that partial BGE slip may occur. All the peptides in this table are hydrophobic with an AHI varying from 0.84 to 10. One also observes that the slip length values obtained in the range $0.10 < b_{slip} < 2.53$ Å are consistently smaller than the corresponding spherical particle radius a_H. For instance, peptide No. 7 has $\Omega_{slip} \approx 1.330$, $a_H = 5.13$ Å, and $b_{slip} = 2.53$ Å, indicating a partial BGE slip of around 50% of the total BGE slip. This last condition is achieved when $\Omega \to 3/2$ and hence $b_{slip} = a_H$. Since one of the main physicochemical characteristics of these peptides is their hydrophobic nature, it is possible to explain the BGE slipping through the "cage effect" [68] where water molecules near the BGE-peptide interface reorder through hydrogen bonds without a significant interaction with the peptide amino acid residues. Thus beyond this rather ordered structural water layer on the particle surface, the random hydrogen bonds of water molecules in the BGE bulk are recovered far from the hydrophobic particle. On the contrary, when the BGE nonslip boundary condition is satisfied, in general the interfacial interaction between water molecules and peptide is due to the hydrophilic nature of amino acid residues exposed to the BGE. Accompanying the hydrophobic nature of peptides in Table 1, it is clear that they are rather short with $N \le 5$, presenting a quite linear packing within the hydrated particle domain ($g_p < 2$). Further for relatively high hydrophobic peptides (No. 7 and 10) and conformations rather collapsed ($g_f \le 0.4$ below Flory-theta condition) the higher slip lengths are obtained. Thus the chain tendency to the free draining conformations yields lower b_{slip} values despite the hydrophobicity may be high (see for instance peptides No. 14, 16, 19). These characteristics of peptides suggest that their modeling by including partial BGE slip on the assumed spherical particles is one of the physically viable phenomena where the hydrophobic nature of the AAS is relevant. Interesting is to point out here that most of the peptides reported in Table 1 cannot be modeled as spherical particles with BGE nonslip boundary conditions because the hydration values become unphysical ($\delta < 0$) yielding $a_H < a_c$ (similar results were already reported and discussed in [20]).

Those peptides belonging to the 102 ones in Supporting Information Table I-1 no reported in Table 1 are classified by groups here, which have the following characteristics for their exclusion in this last table. Group I: Peptides No. 26, 28, 30, 33–40, 42–51, 53–61, 63, 66, 69, 71–81, 83, 86, 87, 90–93, 96, and 98–102 in Supporting Information Table I-1 possess low to high hydrophilic chains ($-10 < AHI < 0$) with $\Omega < 1$ for which the BGE slip boundary condition does not apply because $f > f_o$. These peptides have relatively high N with abundant hydrophilic chain centers interacting with the BGE and thus increasing f. Also they present $g_p > 2$ indicating a spatial chain distribution in the hydrated particle domain. Group II: Peptides No. 17, 18, 20, 21, 24, 62, 68, 70, 82, 85, 94, and 95 in Supporting Information Table I-1 are low to high hydrophilic chains $N \le 6$ with $1 < \Omega < 3/2$ (see Supporting Information Table I-2), presenting a quite linear packing within the hydrated particle domain ($g_p \le 2$). Thus, $f < f_o$ because these particles are aspherical (slender cylinders) and move oriented at $\Theta < 55°$ (see also [20]). These hydrophilic peptides have $\Omega > 1$ as a consequence of their asphericity and average orientation in relation to the external applied electrical field in CZE. Other characteristics of this group leading consistently to this physical situation are their rather open conformations (several of them with $g_f \ge 1/2$) and also having $|Z| > \sqrt{Z_T}$ in the hybrid chain regime [32, 36]. In this group, for instance, one finds peptides AAA, AAAA, and AAAAA with low hydrophilicity (AHI is

Table 1. Numerical results of main model parameters for low to high hydrophobic peptides with $N \leq 5$ modeled as spherical particle with BGE slip boundary condition (see Eq. (3))

No.	AAS (*N*)	AHI	a_H (Å)	p*I*	pH*	Z	δ	g_p	g_f	Ω_{slip}	$\beta_{slip} \times 10^{-6}$ (N s m^{-3})	b_{slip} (Å)
2	FD (2)	0.84	5.25	3.90	2.87	0.83	0.65	1.23	0.50	1.239	4.04	1.65
7	VV (2)	4.09	5.13	5.65	2.90	0.89	0.75	1.23	0.40	1.330	1.95	2.53
8	FG (2)	3.80	4.90	5.65	2.93	0.88	0.65	1.18	0.53	1.245	4.12	1.59
9	FA (2)	4.45	5.07	5.65	2.91	0.89	0.64	1.20	0.49	1.268	3.31	1.86
10	LL (2)	9.69	5.29	5.65	2.89	0.89	0.66	1.29	0.39	1.303	2.39	2.30
11	FV (2)	7.05	5.20	5.65	2.90	0.89	0.54	1.30	0.48	1.218	4.82	1.45
12	FL (2)	9.85	5.28	5.65	2.89	0.89	0.51	1.33	0.50	1.189	6.04	1.23
13	MM (2)	4.59	5.26	5.65	2.89	0.89	0.57	1.30	0.46	1.233	4.25	1.59
14	FF (2)	10.00	5.24	5.65	2.89	0.89	0.40	1.39	0.54	1.135	10.06	0.82
15	YY (2)	2.50	5.73	5.65	2.86	0.90	0.67	1.21	0.58	1.184	5.84	1.29
16	WW (2)	9.69	5.75	5.65	2.85	0.90	0.50	1.31	0.64	1.086	16.19	0.54
19	FFF (3)	10.00	5.73	5.65	2.86	0.90	0.27	1.86	0.52	1.017	96.24	0.10
22	YGGFL (5)	3.47	6.29	5.65	2.82	0.90	0.42	1.99	0.46	1.063	21.47	0.42
23	YGGFM (5)	2.46	6.28	5.65	2.82	0.90	0.40	1.99	0.48	1.037	38.62	0.24

For the meaning of all symbols presented, please see the text, where they are first defined, or the total list of symbols in the Supporting Information.
Protocol data are pH = 2.5, I = 35.3 mM, and T = 22°C. From the numerical algorithm $1 < \Omega_{slip} < 3/2$ and $H_d = 0$ in the particle hydration function.

Table 2. Numerical results of main model parameters for low hydrophilic peptides with $N = 2$ modeled as prolate aspherical particles oriented at $\Theta = 0$ with BGE slip boundary condition

No.	AAS (*N*)	AHI	c (Å)	p*I*	pH*	Z	g_p	g_f	$\Omega^{//}_{slip}$	$\beta_{slip} \times 10^{-6}$ (N s m^{-3})	b^{max}_{slip} (Å)
4	GG (2)	−2.4	3.63	5.65	2.96	0.87	0.98	0.29	1.659	2.75	2.91
5	AA (2)	−1.1	3.88	5.65	2.93	0.88	1.04	0.30	1.584	2.58	3.11
6	PG (2)	−1.3	3.96	5.65	2.92	0.88	1.01	0.36	1.546	2.52	3.17

For the meaning of all symbols presented, please see the text, where they are first defined, or the total list of symbols in the Supporting Information.
Protocol data are pH = 2.5, I = 35.3 mM, and T = 22°C. From the numerical algorithm $\Omega_{slip} > 3/2$, while $H_d = 0$ in the particle hydration function. Here, b_{slip} is a function of position and the maximum slip length b^{max}_{slip} is at $t = \pi/2$. Numerical data $f^{//}_{slip}$ are from [60] at a/c ≈ 2.

Table 3. Numerical results of main model parameters for low hydrophilic peptides with $N = 2$ of Table 2 modeled as spherical particles with total BGE slip boundary condition by reducing hydrations to obtain $\Omega_{slip} \approx 3/2$

No.	AAS (*N*)	H_d	a_H (Å)	pH*	Z	δ	g_p	g_f	Ω_{slip}	$\beta_{slip} \times 10^{-6}$ (N s m^{-3})	b_{slip} (Å)
4	GG (2)	−3.5	4.15	3.01	0.86	0.76	1.13	0.30	1.498	0.019	4.12
5	AA (2)	−2.4	4.65	2.95	0.87	0.85	1.13	0.30	1.498	0.020	4.61
6	PG (2)	−1.5	4.85	2.93	0.88	0.99	1.06	0.36	1.497	0.021	4.80

For the meaning of all symbols presented, please see the text, where they are first defined, or the total list of symbols in the Supporting Information.
Protocol data are pH = 2.5, I = 35.3 mM, and T = 22°C. The numerical algorithm uses $H_d < 0$ in the particle hydration function.

around −1.1) and rather compact conformation ($g_f < 0.4$). These AHI and g_f values suggest the study of these peptides also as spherical particles with BGE slip boundary condition as reported in Supporting Information Table I-3 where once more the slip lengths are consistent with theoretical equations described above ($b_{slip} < a_H$). In general this group shows that either BGE slip and/or asphericity may be the causes yielding $\Omega > 1$. Group III: Peptides DD and EE in Supporting Information Table I-1 coded as No. 1 and 3 are high hydrophilic with AHI = −8.30. However, these peptides have $\Omega = 1.062$ and 1.221, respectively. Here the remarkable physical situation is that they have p*I* 3.63 and p*I* 3.87 that are rather closed to the corresponding pH* 2.84 and pH* 2.86, respectively (the protocol pH is 2.5) yielding an "effectively hydrophobic chain," indicating also that chain hydrophobic nature depends on pH (see results below in relation to STN near its p*I*). Thus peptides DD and EE at the protocol pH and through our calculations yield $b_{slip} \approx 0.35$ and 1.54 Å,

respectively, with $b_{slip} < a_H$, when a spherical particle with BGE slip boundary condition is assumed. In addition, since these two particles have $N = 2$, $g_p \approx 1.08$ and 1.14 (linear packing) and $g_f \approx 0.83$ and 0.59 (these values are above the Flory-theta condition toward the free draining response [38]) one should also expect in part a hydrodynamic effect of fairly aspherical particles oriented with $\Theta < 55°$. Therefore they are also considered as cylinders in Supporting Information Table I-2. Group IV: Peptides GG, AA, and PG, with code No. 4, 5, and 6 in Supporting Information Table I-1, are low hydrophilic having AHI ≈ -2.4, -1.1, and -1.3). Here, the relevant physical aspect is that they have $\Omega \approx 1.659$, 1.584, and 1.546, which are higher than the maximum value $\Omega \approx 3/2$ obtained for a slender cylinder at $\Theta \approx 0°$ with BGE non-slip boundary condition [52]. We found that the particles representing these peptides may be, for instance, a prolate spheroid with BGE slip boundary condition translating parallel to the external applied electrical field (see Eq. (4) and (5) and Table 2). In fact from Section 2.3 it is clear that $\Omega_{slip} = \Omega^{//}_{slip}$ with $\alpha = 1$. In addition values of $f^{//}_{slip}$ can be found from numerical solutions as a function of $\eta_s/c\beta_{slip}$ and ratio a/c as reported in [60]. Here one must also observe that b_{slip} changes with the position on the surface particle. Table 2 shows that the maximum values of slip length obtained satisfy consistently $b^{max}_{slip} < c$. Alternatively, peptides No. 4, 5, and 6 may be also studied as spherical particles with BGE slip boundary condition when their hydrations are slightly reduced as indicated in Table 3 through the values assigned to H_d in the particle hydration function (Supporting Information). The appropriate estimation of peptide hydrations is a difficult problem, and the hypotheses introduced in the peptide hydration function H may be quite approximate for $H_d = 0$ when peptides are considered, taking into account that in general one does not refer to native states of these rather short chains. Group V: Peptides coded No. 25, 27, 29, 31, 32, 41, 52, 64, 65, 67, 84, 88, 89, and 97 in Supporting Information Table I-1 are hydrophobic with AHI > 0 and $\Omega < 1$ (Supporting Information Table I-4), and hence the BGE slip boundary condition does not apply because $f > f_o$ despite their average hydrophobicity. These hydrophobic peptides are hydrodynamically dissipative aspherical particles having a spatial packing $g_p > 2$, and g_f values around the Flory-theta condition. Since the number of amino acids residues is relatively high ($7 < N < 18$) their "effective" chain hydrophobicity (AHI > 0) includes ionizing and polar groups that increase the friction between BGE and peptide giving and effective friction ratio $\Omega < 1$. Based on the discussion above, the "cage effect" of water molecules is not achieved. It is interesting to point out that in Supporting Information Table I-4 one can also find several peptides (No. 25, 27, 64, 65, 67) in the collapsed state ($|Z| < \sqrt{Z_T}$) because their effective charges are relatively low ($|Z| < 1$). Nevertheless it is expected that their ionizing and/or polar groups are placed at the outer particle domain causing also a major chain interaction with the BGE (higher f and $\Omega < 1$).

Concerning μ_p^{exp} of STN at pH 8.9 and 25°C as a protein case-study, we found pH* 9.21 that was quite close to p*I* 9.63 generating a collapsed globule state with $g_f \approx 1/3$, a chain spatial packing $g_p \approx 2.61$ within the hydrated particle domain and a relatively small radius $a_H \approx 19.8$ Å, thus behaving as a rather hydrophobic chain. This result is consistent with the description already presented above for Group III where pH*$\rightarrow$ p*I*, even in the case the STN has a high N =149. In fact when this protein is modeled as a spherical particle with partial BGE slip boundary condition and $H_d \approx 0$, one gets $\Omega_{slip} \approx 1.323$, $\beta_{slip} \approx 4.97\,10^{-5}$ $N\,s\,m^{-3}$ and $b_{slip} \approx 9.47$ Å (around 48% of total slip). We also showed previously in [30] that for pH 2.8, I = 5.5 mM, and 25°C this protein is denatured giving $\Omega < 1$, and hence generating a high dissipative particle by increasing substantially its hydration, which is of course the opposite physical situation from that found when the chain has a hydrophobic nature.

Finally, results for spherical particles also indicate that $D = k_B T/(4\pi\eta_s a_H)$ when the BGE total slip occurs. Then D may differ by a factor 3/2 from the classical Stokes–Einstein diffusion due to slip. A similar analysis for the intrinsic viscosity indicates that $[\eta] = (v_p + \delta v_w)$ for BGE total slip, giving directly the average hydrated peptide specific volume (see also additional calculations in Supporting Information Table I-5 for $1 < \Omega < 3/2$).

4 Concluding remarks

Different hydrodynamic phenomena may occur in the BGE kinematics around peptides and proteins when these particles translate in CZE. One of them is specifically associated with the partial or total BGE slip at the peptide particle surface in the Henry–Hückel branch. The BGE slip may occur at least in the following situations: (i) The AAS of the peptide has a predominantly hydrophobic nature. (ii) The peptide pH* is close to the p*I*. (iii) Low hydrophilic short peptides that can be represented as aspherical particles translating at $\Theta < 55°$. It is also clear that further research concerning the evaluation of the BGE slip on aspherical particles is required to deepen present studies through simpler correlations.

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