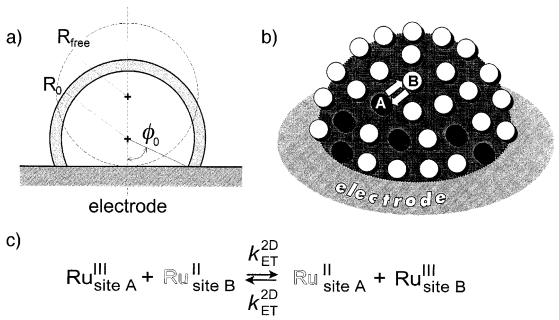

Figure 1. a) Schematized redox continuum showing the cross-section of an average PAMAM dendrimer molecule adsorbed onto a platinum ultra-microelectrode surface. The shaded area represents the thin shell ($d = 1.4$ nm) into which the 64 ruthenium redox centers are dispersed and where electron hopping diffusion takes place. The white zone located inside features the dendrimer covalent tethers. The circle shown in dashed line represents the size of the free dendrimer molecule in solution for comparison. b) Representation of the equivalent diffusion by electron hopping from a reduced (Ru^{II}, white, site B) towards an oxidized (Ru^{III}, black, site A) ruthenium bis-terpyridine moiety over the dendrimer hemispherical surface. c) Electron exchange reaction occurring between the Ru^{II} (white) and Ru^{III} (black) redox centers shown in (b).

Electrochemistry on a Few Molecules

Electrochemistry within a Limited Number of Molecules: Delineating the Fringe Between Stochastic and Statistical Behavior**

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Single molecule experiments attract an increasing interest in physical chemistry.[1,2] Indeed, the expectation of replacement of silicon by single molecules has stimulated investigations of molecular components.[3,4] In this context, electrochemistry provides an exceptional tool for monitoring electron transfer responses of a limited number of molecules.[2]

In this context, by using ultrafast voltammetry, we could recently analyze the dynamics of electron hopping inside an electroactive fourth-generation PAMAM dendrimer capped with 64 ruthenium(II) bis-terpyridine redox moieties.[5,6] In that case, each dendrimer could be oxidized progressively by the propagation of the electrochemical perturbation over the 64 redox centers distributed on its surface (Figure 1). However, about 10^6 molecules were adsorbed onto the ultramicroelectrode of micrometric radius, so that the analysis involved the averaging of about 64×10^6 individual events occurring in parallel. In a seminal experiment, Bard and coworkers reported the measurement of the electrochemical current provided by a single molecule trapped between two electrodes.[1] Even so, in this spectacular experiment a different kind of averaging was involved. Indeed, considering the time scale (about 1 s) of the method, this single molecule was involved in an electrochemical recycling during which it was continuously oxidized and reduced about 10^6 times so that the current resulted from the temporal averaging of a large series of fast sequential individual events. Both experiments involved temporal or spatial averaging of a large number of events so that in each case classical electrochemical formulations based on Fick's laws of diffusion could be used to analyze the experimental data. As electrodes of nanometer dimensions are presently available,[7–9] and considering that the electrochemical detection limits are continuously decreasing, one may expect soon the detection of electrochemical signals provided by a single molecule or a few ones. For example, in the "chronoamperograms" presented below (see Figure 2 and Figure 3), half of the charge (i.e. 32 electrons for each dendrimer), is passed within 25 ns, which would correspond to an average current of about 200 pA per dendrimer molecule. However, in the stochastic mode, and without any instrumental constraint the exchange of each electron should correspond to a much larger instant current, that is, $e/\Delta\tau_{et}$, where e is the charge of an electron and $\Delta\tau_{et}$ the life-time of the event. In the best electrochemical practice, the shortest sampling times, $\Delta\tau_{sampl}$, are in the range of a few nanoseconds[5,6] and are therefore expected to exceed most values of $\Delta\tau_{et}$. It follows that the largest instant currents in the stochastic mode are expected to be in the range of $e/\Delta\tau_{sampl}$, namely about 100 pA.

Under such conditions, the stochastic nature of each electrochemical event should be observable, thus leading to important deviations from the usual collective electrochemical laws (namely, statistical ones). Experimental investigation of such stochastic information is clearly warranted since it contains precious information about how molecules explore their phase domains, either concerning its transport or its reactivity.

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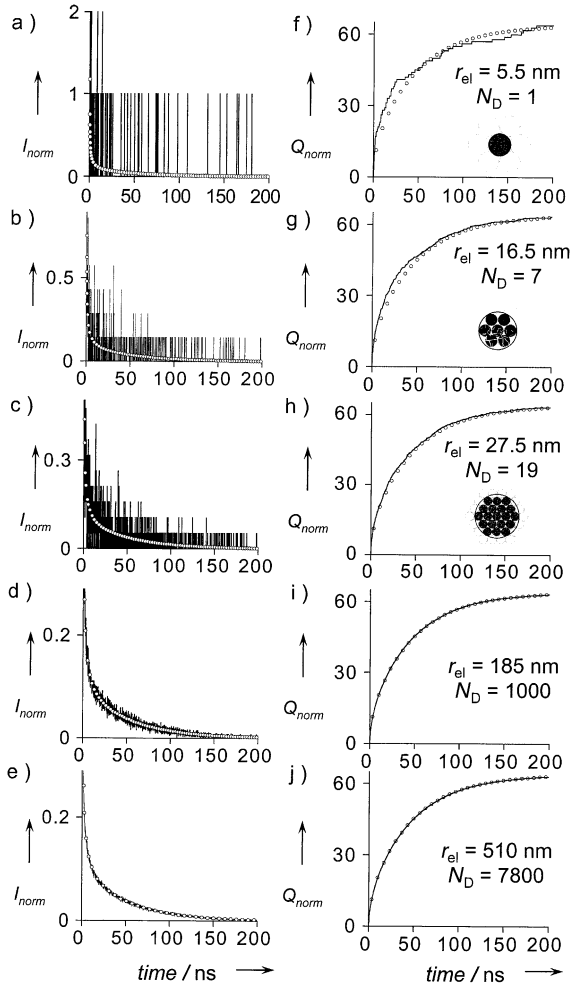

Figure 2. (a–e) Vertical thin lines: predicted variations of the normalized stochastic current (I_{norm}) versus time as a function of the number of dendrimers molecules adsorbed onto the electrode surface without considering any instrumental distortions. In each panel, $I_{norm} = I/N_D$ represents the current, I, normalized by the number of dendrimers, N_D. Vertical units are chosen so that one electron transferred during the time window interval of the simulation gives a current $I_{norm} = 1$ for $N_D = 1$, so that I_{norm} reflects the sequential electron count for the average "single" molecule during one 0.1 ns time window. These variations are superimposed onto the statistical electrochemical normalized current predicted for an infinite number of adsorbed dendrimers (open circles; same curve in each panel a–e). (f–j) Same as (a–e) but the electrochemical Faradaic charge ($Q_{norm} = ne/N_D$) normalized per dendrimer is considered, in which ne is the actual number of electrons transferred from the beginning of the experiment. $N_D = 1$ (a,f), 7 (b,g), 19 (c,h), 1000 (d,i), 7800 (e,j); see picture and/or legend in (f–j).

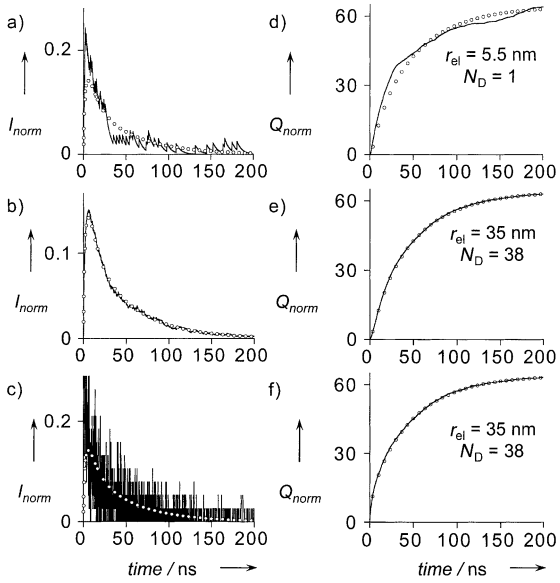

Figure 3. Effect of instrumental distortions. Solid lines: current (a–b) or charge (d–e) versus time variations considering an ultrafast potentiostat with a 6 ns time constant.[5,6,13,14] $N_D = 1$ (a,d), or 38 (b,e), see legend in (d–f). In (c, f) are shown the current and charge variations versus time in the absence of any instrumental distortion for $N_D = 38$ to emphasize the effect of instrumental filtering by comparison to (b, e) respectively. On each panel is superimposed the predicted result for an infinite population of dendrimers when the same instrumental distortion applies (open circles). Vertical current axis (namely, I_{norm} and Q_{norm}) in (a–c) are defined as in Figure 2.

Herein, we wish therefore to address theoretically this fundamental question through estimating the maximal number of events to be sampled so that stochastic electrochemical signatures may be detected within a determined experimental accuracy. We wish to develop this work in consideration of the specific example of our previous study on PAMAM redox dendrimers,[5,6] as this system is virtually commutable from completely statistical to totally stochastic, simply by decreasing the size of the electrode on which the array of dendrimers is adsorbed. Indeed, this controls directly the number of molecules addressable electrochemically.[7] To simplify the presentation we assume a perfect hexagonal pavement of the electrode though the true 2D-array is slightly distorted.[10] In solution, the dendrimer has a spheroidal shape with a diameter of approximately 10 nm, its 64 [$Ru^{II/III}$-(terpy)$_2$] (terpy = terpyridine) redox sites being distributed over its surface.[10] Upon adsorption, the dendrimer resembles a near hemisphere of radius R_0 and half angle $\phi_0 = 1.2$ rd, as described in Figure 1.[5,6] In each dendrimer molecule, all the 64 redox sites are covalently fixed to the dendrimer core by their dendritic polyamidoamide branches, so that they cannot diffuse "physically" to and from the electrode surface. Electrochemical contact between the dendrimer and the electrode may therefore only occur through the few redox sites distributed along the ring of the dendrimer shell in close contact with the electrode (see Figure 1 b). Propagation of the electrochemical perturbation over the dendrimer surface occurs then by "electron hopping"[11,12] between adjacent Ru^{II}/Ru^{III} redox centers (Figure 1 b,c). Thus, the status of the center (namely, Ru^{II} versus Ru^{III}) is propagated over the dendrimer shell by electron transfer between adjacent ruthenium centers without displacement of the centers themselves.[5,6]

Each center has several possibilities to cross-talk with its neighbors of appropriate redox state, so that the system is equivalent to the random-walk displacement of a fake particle representing the site status (Figure 1 b,c). Based on the Nernst-Schmoluchovski relationship between diffusion and random walk, this phenomenon is equivalent to diffusion over

the dendrimer shell.[6] Within one dendrimer molecule, these events are necessarily stochastic and are finite as there are only 64 centers and the phenomenon stops when all centers have their redox state commuted (namely, from Ru^{II} to Ru^{III} during an oxidative polarization, or from Ru^{III} to Ru^{II} during a reductive one). However, when an infinite array of dendrimer is adsorbed onto the electrode,[5,6,10] the series of events occurring within each dendrimer take place in parallel, so that a continuous statistical formulation becomes valid (Figure 1 a).[5,6] Conversely, upon decreasing the size of the electrode, the number of adsorbed dendrimers decreases and one may be able to evidence the basic stochastic nature of the phenomenon. Electrodes with radii of several tens of nanometers are now available,[7–9] so that the fundamental problem considered here is not far from being addressable experimentally.

To stress the effect related to the number of adsorbed dendrimers, we consider chronoamperometry, the simplest electrochemical technique. At $t = 0$, the electrode potential is poised at a value high enough to ensure a sufficient driving force so that at the electrode–dendrimer junction the commutation time can be considered as being instantaneous compared to the time required for propagation over the whole dendrimer shell, namely, several tens of ns. In agreement with the physical reality of the propagation phenomenon, we used a random-walk algorithm to account for the discrete nature of charge displacement, and we treated the processes occurring within each dendrimer through an individual simulation. Any selected number of simulations may be gathered together afterwards to account for the exact number of dendrimers supposedly adsorbed onto an electrode surface of any specific surface area.

We wished first to focus on the physicochemical significance of the measured current as a function of number of adsorbed dendrimers. We therefore assumed that the electrochemical equipment is perfect, that is, that there is no distortion of the signal. For only one adsorbed dendrimer, the electrochemical current shows a random and discontinuous succession of single electron-transfer events (Figure 2 a). Obviously each simulation produces a different pattern, however, Figure 2 a is representative of the most frequent ones. For a larger electrode, namely, where seven dendrimers can be adsorbed (Figure 2 b, which corresponds to an electrode of about 16.5 nm in radius), one still observes an important stochastic "noise" in the current though the classical shape of a chronoamperogram becomes already recognizable, with an increased probability of three or two simultaneous (namely, occurring within the same 0.1 ns sampling time window) events at initial times. This trend is pursued as the number of molecules increases (Figure 2 c–e), the current function approaches more and more closely the statistical one. For example, for an array of 7800 dendrimers (namely, an electrode of about 500 nm in radius) the stochastic nature of the phenomenon is no more clearly discernable. It amounts only to the introduction of a $\pm 10\,\%$ noise added onto the would-be classical electrochemical current, though observation of this later would require an infinite population.[5,6] (compare Figure 2 e). When one observes the electrochemical charge instead of the current (Figure 2 f–j) the stochastic noise is reflected by a series of staircase steps (e.g., Figure 2 f) whose fine structure rapidly vanishes when the number of adsorbed dendrimers approaches 20 (see Figure 2 h). This reflects the smoothing of the stochastic noise that arises from the integration. Nevertheless, the stochastic nature of the phenomenon is still reflected by a systematic misfit versus the statistical charge variation predicted for an infinite number of dendrimers, though this misfit is almost impossible to observe as soon as about 20 molecules are examined in parallel (Figure 2 h).

To be observed experimentally, the above results would require a perfect electrochemical instrumentation so that the apparatus did not introduce any filtering of its own. However, even with the fastest potentiostat available today,[13,14] a minimal time constant of about 6 ns is imposed by the electrochemical instrumentation.[14] This constant is obviously negligible with respect to the overall duration of the whole phenomenon (namely, a few 100 ns, see Figure 2, and Figure 3) but introduces a significant exponential tail[15] on each individual electron-transfer event as evidenced by the comparison between Figure 2 a and Figure 3 a. In this case, the stochastic noise becomes about $\pm 10\,\%$ of the statistical chronoamperogram for only 38 adsorbed dendrimers (Figure 3 b), although it is seen in Figure 3 c that for such a small number of molecules the real stochastic nature of the phenomenon would be definitely observable in absence of any instrumental distortions. Evidently, the same is true when the electrochemical charge is considered (Figure 3 d–f). Noteworthy, even for a single molecule the staircase nature of the charge variations is no more observable (Figure 3 d), though the stochastic reality of the phenomenon is still reflected by the deviation from the statistical curve. Therefore, experimentally, one may be led to believe that the electrochemical signal observed for a very minute quantity of molecules is very close to the average signal, though this would be an artifact reflecting only the characteristics of the apparatus and its distortions.

In conclusion, this particular example demonstrates that one should constantly bear in mind that a smooth current–time variations closely identical to that predicted by Fick's laws may not mean that the electrochemical signal for a few molecules is essentially similar to the usual statistical behavior, but may simply reflect instrumental distortions. Such considerations seem fundamental for subsequent analysis of experimental data relative to electrochemistry with limited number of molecules.

Experimental Section

In the random walk simulations, individual particle positions over the dendrimer shell (Figure 1) are referred by their spherical angular coordinates θ and ϕ. At each time iteration a direction is randomly chosen while Δl, the length of displacement, is maintained constant. The sampling frequency was fixed at $1/\Delta t = 10^{10}\ s^{-1}$, and the length of displacements of individual particles was chosen so that they agree altogether (namely, $\Delta l = 2(D\Delta t)^{1/2}$ with $D = 5 \times 10^{-6}\ cm^2 s^{-1}$) with the average equivalent diffusion coefficient value, D, which was measured experimentally for an array of about 10^6 adsorbed dendrimers.[5,6] D and k_{ET}^{2D}, the 2D-bimolecular rate constant of electron exchange (see its definition in Figure 1 c) are related by Equation (1):[5,6]

$$D = \frac{2\,k_{ET}^{2D}}{3\pi d} \quad (1)$$

in which d is the diameter of a ruthenium redox center (1.4 nm). Validity of the random-walk procedure was checked by two methods. First it was verified that without electrochemical reaction (namely, upon tracking the particle walks but without modifying the Ru^{II} or Ru^{III} status along the particle walk), the average population on the truncated sphere remained homogeneous when particles were allowed to move for duration times exceeding by several times the maximal times considered here. Second, the chronoamperometric current resulting from the averaging of 10^6 individual simulations (taken here as an infinite population) was compared to the statistical one obtained by solving the continuous analytical Fick's laws by finite differences as described elsewhere for voltammetry[5,6] though a chronoamperometric condition was imposed at the electrode dendrimer interface (namely, at $\phi = \phi_0$ in Figure 1 a). A perfect match was obtained except for the very first few events close to $t = 0$ where either the random walk or the finite differences solutions are not accurate by construction. It has to be underlined that a great advantage of this random walk formulation is to allow almost any further refinement of the model, that is, by incorporating real dynamics of the redox centers within their potential wells over the dendrimer surface which affects the local probabilities of electron exchange.[5,6] This was however outside the scope of the present paper.

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Keywords: dendrimers · electrochemistry · electron transfer · redox chemistry · single-molecule studies

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