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Simulation of Fast-Scan Nanogap Voltammetry at Double-Cylinder Ultramicroelectrodes

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Abstract

High temporal resolution of fast-scan cyclic voltammetry (FSCV) is widely appreciated in fundamental and applied electrochemistry to quantitatively investigate rapid dynamics of electron transfer and neurotransmission using ultramicroelectrodes (UMEs). Faster potential scan, however, linearly increases the background current, which must be subtracted for quantitative FSCV. Herein, we numerically simulate fast-scan nanogap voltammetry (FSNV) for quantitative detection of diffusing redox species under quasi-steady states without the need of background subtraction while maintaining high temporal resolution of transient FSCV. These advantages of FSNV originate from the use of a parallel pair of cylindrical UMEs with nanometer-wide separation in contrast to FSCV with single UMEs. In FSNV, diffusional redox cycling across the nanogap is driven voltammetrically at the generator electrode and monitored amperometrically at the collector electrode without the transient background. We reveal that the cylindrical collector electrode can reach quasi-steady states $\sim 10^4$ times faster than the generator electrode with identical sizes to allow for fast scan. Double-microcylinder and nanocylinder UMEs enable quasi-steady-state FSNV at hundreds volts per second as practiced for in-vivo FSCV and megavolts per second as achieved for ultra-FSCV, respectively. Rational design and simple fabrication of double-cylinder UMEs are proposed to broaden the application of nanogap voltammetry.

Fast-scan cyclic voltammetry (FSCV) is a powerful electrochemical method to monitor rapid dynamics of heterogeneous electron transfer (1) and neurotransmitter release (2) at high temporal resolution. FSCV at >100 V/s is routinely used for real-time monitoring of neurotransmitters in the brain at sub-millisecond resolution (3). Ultra-FSCV at $\sim 10^6$ V/s was developed to resolve the kinetics of extremely fast electrode reactions at nanosecond resolution (4). Faster potential scan, however, linearly increases a background current based on double-layer charging at the electrode/solution interface (5) and electrolysis of the electrode surface (6). The transient background is suppressed by using an ultramicroelectrode (UME) to minimize the iR drop, but often exceed a response to the diffusing redox species. This diffusional response also becomes transient with fast scan, but grows only with the square-root of scan rate (7). Accordingly, FSCV is typically used for the study of redox molecules adsorbed on (3) or tethered to (4) the electrode surface to yield a transient response that is proportional to scan rate (6). A background voltammogram, however, must be subtracted for quantitative FSCV, which is limited to differential measurement of concentration changes in vivo (8).

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Herein, we report on finite element simulation of fast-scan nanogap voltammetry (FSNV) to quantitatively detect diffusing redox species at high temporal resolution of FSCV without the need of background subtraction. Specifically, we simulate diffusional redox cycling across a nanometer-wide gap between a parallel pair of cylindrical UMEs with identical sizes (Figure 1). With this setup, the generator electrode voltammetrically electrolyzes a redox reactant, O, at a fast scan rate to obtain a current response with the high background. By contrast, a constant potential is applied to the collector electrode to amperometrically detect the product, R, without the transient background. Subsequently, background subtraction is not needed for quantitative analysis of a nanogap voltammogram based on the amperometric collector response against the cycled generator potential (9) (10). Only slow scan at 0.1 V/s, however, has been used to characterize nanogap electrochemical cells (11, 12). Moreover, double-cylinder UMEs only with micrometer-wide gaps have been reported (13-15) to assess steady-state theories (16, 17) at slow scan rates.

In this work, we predict that quasi-steady states are achieved by FSNV of diffusing redox species at up to hundreds volts and megavolts per second using double-microcylinder and nanocylinder UMEs, respectively. We adapt a previous model of chronoamperometry (18) for FSNV to reveal that local redox cycling between nanogap sides of double-cylinder electrodes (red and blue arrows in Figure 1A) quickly reaches quasi-steady states to allow for fast scan while a voltammetric response at the solution side of the generator electrode (black arrows) is still transient. A quasi-steady-state collector response is determined by a ratio between gap width and cylinder radius and can be enhanced by using longer cylinders even with a smaller radius to facilitate fast current measurement. Simulation results are obtained using general dimensionless parameters (18) and related to actual currents, scan rates, and sizes for double-cylinder UMEs that we propose to fabricate from double-disk-like UMEs (19, 20). The proposed method requires neither nanolithography (21, 22) nor nanoscale scanning electrochemical microscopy (SECM) (23, 24) in contrast to other nanogap cells (11, 12) to widen the application of nanogap voltammetry.

Model

Here, we consider FSNV at a parallel pair of cylindrical electrodes with the identical radius, r , and length, L , and a narrow separation, g (Figure S-1 in Supplementary Material). Geometrically, our model is equivalent to the model used for simulation of chronoamperometry at double-hemi-cylinder electrodes (18) owing to the symmetry of double-cylinder electrodes with respect to the x -axis. In this work, we simulate voltammetric responses not only at generator and collector electrodes, but also at nanogap and solution sides of each electrode (Figure 1) in contrast to the previous study (18).

We employ a commercial package for finite element simulation (COMSOL version 5.3a, COMSOL, Burlington, MA) to solve a 2D diffusion problem at double-cylinder electrodes in the solution containing a redox species, O. This reactant participates in a n -electron transfer reaction as given by

We assume the identical diffusion coefficient, D , for species O and R so that the diffusion problem needs to be solved only for the reactant. Diffusional mass transport of the reactant is represented by

$$\partial c_O / \partial t = D(\partial^2 c_O / \partial x^2 + \partial^2 c_O / \partial y^2) \quad (2)$$

where c_O is the local concentration of the reactant at (x, y) in solution. The reactant is voltammetrically electrolyzed at the generator electrode to yield the boundary condition based on the Butler–Volmer kinetics (25) as

$$D(\partial c_O / \partial \mathbf{n}) = -v_{\text{et}} \quad (3)$$

with

$$v_{\text{et}} = k^0 \{ c_O \exp[-\alpha n F (E_g - E^{0'}) / RT] - (c_0 - c_O) \exp[(1 - \alpha) n F (E_g - E^{0'}) / RT] \} \quad (4)$$

where $\mathbf{n}$ is a vector with a length of r and is normal to the surface of the generator electrode at the point of interest, v_{et} is the heterogeneous electron-transfer rate, k^0 is the heterogeneous standard electron-transfer rate constant, α is transfer coefficient, E_g is the potential of the generator electrode, $E^{0'}$ is the formal potential of the redox couple, and c_0 is the bulk concentration of the reactant, O. We employ large k^0 values to obtain reversible voltammetric responses at generator and collector electrodes unless mentioned otherwise.

We simulate current responses at generator and collector electrodes, i_g and i_c , respectively, by solving eq 2 with boundary conditions including eq 3 at the generator electrode. The boundary condition for diffusion-limited regeneration of the reactant at the collector electrode is given by

$$c_O = c_0 \quad (5)$$

This boundary condition implies that the potential of the collector electrode, E_c , is positive enough with respect to $E^{0'}$. Other boundary conditions are shown in Figure S-1 (Supplementary Material). We employ dimensionless parameters (Supplementary Material and Results and Discussion) to simulate normalized currents at generator and collector electrodes, I_g and I_c , respectively, as given by (18)

$$I_g = i_g / n F D L c_0 \quad (6)$$

$$I_c = i_c / n F D L c_0 \quad (7)$$

Normalized currents at nanogap and solution sides of generator and collector electrodes are also simulated. The reliability of our simulation was validated for chronoamperometry at single-cylinder UMEs (26) as reported in the previous study (18) (Supplementary Material).

Results and Discussion

Scan Rates and Geometric Parameters.

In this work, we consider double-cylinder UMEs with a micrometer or nanometer radius and a nanometer-wide gap to simulate quasi-steady-state FSNV at up to hundreds volts or megavolts per second, respectively. The gap width is normalized against the cylinder radius to yield one of key dimensionless parameters (18) as

$$G = g / r \quad (8)$$

Another key dimensionless parameter is the normalized scan rate given by

$$\sigma = r^2 n F v / D R T \quad (9)$$

where v is the scan rate of generator potential. Actual cylinder radii are used to calculate gap widths and scan rates from the corresponding dimensionless parameters (Table 1).

We consider the radii and gap widths of double-cylinder UMEs (Table 1) that we propose to fabricate from double-disk-like UMEs. Specifically, a pair of independent carbon-disk UMEs with gap distances of $<1 \mu\text{m}$ was fabricated by filling each channel of a theta glass capillary with a carbon fiber, pulling the assembly using a pipet puller with a heating coil, and mechanically polishing the tip end (19). The glass sheath of double-disk carbon-fiber UMEs may be etched in a HF solution to expose double-microcylinder UMEs with a desirable length. A typical carbon-fiber radius of $3.5 \mu\text{m}$ (3) is considered in our model to yield a gap width of $0.35 \mu\text{m}$ with $G = 0.1$. Similarly, double-microcylinder UMEs with wider gaps ($G = 1$) may be fabricated from double-disk carbon-fiber UMEs with micrometer-wide gaps (19, 27), which are too wide to establish redox cycling for FSNV (see below).

We also propose that double-nanocylinder UMEs with nanogaps may be fabricated from double carbon nanoelectrodes obtained by pyrolysis of a carbon source inside a theta quartz nanopipet (20). Double-nanocylinder UMEs may be obtained by etching the insulating sheath of double carbon nanoelectrodes in a HF solution as demonstrated for fabrication of single-cone carbon nanoelectrodes with precisely controlled lengths of $5 \mu\text{m}$ – $175 \mu\text{m}$ (28). The geometry of double carbon nanoelectrodes is semielliptical (20) and tapered (28), but idealized in our model to yield a pair of 35 nm -radius cylinders with a gap width of $G = 0.1$ or 1 . A narrow gap width of 3.5 nm with $G = 0.1$ is still wide enough to prevent direct electron tunneling between generator and collector electrodes (29). Our simple model neglects long-range electron transfer through redox species in the narrow gap (30) and the migration of redox species through electrical double layers at the electrodes (12).

Simulation of FSNV at double-microcylinder and nanocylinder UMEs employs the identical σ values of 300, 3, and 0.03, which correspond to very different scan rates for the respective UMEs (Table 1). The highest σ value of 300 is equivalent to a fast scan rate of 400 V/s at the double-microcylinder UMEs as practiced for in-vivo FSCV with single carbon-fiber UMEs (3). By contrast, the highest σ value at the double-nanocylinder UMEs reaches an ultrafast scan rate of 4 MV/s, which is the highest scan rate achieved for FSCV by using single disk UMEs (31, 32). Accordingly, the lowest σ value of 0.03 at the double-nanocylinder UMEs maintains a fast scan rate of 400 V/s as realized for in-vivo FSCV using single-cone carbon nanoelectrodes (28). By comparison, the same σ value yields a slow scan rate of 0.04 V/s for the double-microcylinder UMEs as typically employed for nanogap voltammetry (11, 12).

It should be noted that the normalized scan rate is related to the normalized duration of the entire simulation, τ_e , given by eq S-3 in Supplemental Material as

$$\tau_e = 2F\Delta E / \sigma RT \quad (10)$$

where E is a difference between initial and switching potentials. Eq 10 with $E = 0.5$ V yields $\tau_e = 0.13$, 13, and 1300 for $\sigma = 300$, 3, and 0.03, respectively. These time regimes match those examined in the previous study of double-hemi-cylinder electrodes (18), where chronoamperograms were reported at τ_e values of up to 10 and at steady states (i.e., $\tau_e \rightarrow \infty$). Our simulation of FSNV, however, provides a new insight that the collector electrode reaches quasi-steady states much faster than the generator electrode to allow for fast scan (see below).

FSNV at Double-Cylinder UMEs with Narrow Gaps ($G = 0.1$).

We employed the finite element method to demonstrate that quasi-steady-state FSNV is enabled even at $\sigma = 300$ when the gap of double-cylinder UMEs is narrow, i.e., $G = 0.1$ (Figure 2A). This σ value corresponds to 400 V/s and 4 MV/s at 3.5 μm - and 35 nm-radii cylinder electrodes, respectively (Table 1). At $\sigma = 300$, the collector electrode yielded a limiting current during the reverse scan (red dashed line) to ensure quasi-steady states despite large hysteresis in comparison with the forward wave (red solid line). This hysteresis is due to the finite time required for the redox product, R, to diffuse from the generator electrode to the collector electrode across the gap (Figure 1A). In fact, the collector response was delayed from the generator response during the forward scan (blue solid line). Noticeably, peak-shaped transient responses were obtained at the generator electrode even during the reverse scan (blue dashed line), thereby indicating that only the collector response reached quasi-steady states at $\sigma = 300$.

An intermediate scan rate of $\sigma = 3$ also yielded a quasi-steady-state voltammogram with small hysteresis at the collector electrode in addition to a peaked-shape transient voltammogram at the generator electrode (Figure 2B). This slower scan rate is still relevant to FSNV, because it corresponds to a fast scan rate of 40 kV/s at 35 nm-radius double-cylinder UMEs with a 3.5 nm-wide gap (Table 1). The normalized limiting current at the collector electrode changed only by $\sim 25\%$ from -3.5 to -4.4 as σ decreased by two orders of magnitude from 300 to 3. The scan-rate dependence of the limiting current is weak and

opposite to that of a transient response, thereby ensuring quasi-steady states at the collector electrode. By contrast, the generator response was transient during the entire potential cycle as indicated by the peak-shaped negative response during the reverse scan as well as by lower peak currents at $\sigma = 3$ than at $\sigma = 300$. Again, only the collector electrode reached quasi-steady states at $\sigma = 3$.

Quasi-steady state responses were obtained at both generator and collector electrodes with $\sigma = 0.03$ (Figure 2C) to demonstrate that the collector electrode reached quasi-steady states $\sim 10^4$ times faster ($\sigma = 300$) than the generator electrode. A low σ value of 0.03 still corresponds to a fast scan rate of 400 V/s at the double-nanocylinder UMEs (Table 1). The slow scan rate yielded a high collection efficiency of 0.90 as defined by an absolute ratio of a normalized limiting current of -4.7 at the collector electrode with respect to that of 5.2 at the generator electrode. High collection efficiency at the slow scan rate is anticipated from the previous simulation study (18), which yielded high collection efficiency at steady states. Importantly, our simulation revealed that lower collection efficiency at faster scan rates (or shorter time regimes) is mainly due to a larger transient response of the generator electrode and is irrelevant to FSNV, which measures a quasi-steady-state collector response.

Current Distributions at Generator and Collector Electrodes with Narrow Gaps ($G = 0.1$).

Voltammetric responses at nanogap and solution sides of generator and collector electrodes with $G = 0.1$ were simulated to demonstrate that the collector response reaches quasi-steady states much faster than the generator response because of the slow decay of the current response at the solution side of the generator electrode. The normalized current at each side of generator and collector electrodes (Figure 1A) was simulated against generator potential to yield a pair of voltammograms for each electrode at $\sigma = 300$, 3 , and 0.03 (Figures 3A, C, and E, respectively). In these plots, the polarity of the collector response was inverted to compare the absolute collector response with the generator response during the forward scan. Additionally, we simulated the concentration profile of the reactant, O, at the respective scan rate (Figures 3B, D, and F) to visualize a diffusion layer of the reactant, which is complementary to that of the product with a concentration given by $c_0 - c_O$.

The highest scan rate of $\sigma = 300$ yielded a quasi-steady-state voltammetric response at the nanogap side of the collector electrode (red lines in Figure 3A), which evidences that quasi-steady-state redox cycling was established between nanogap sides of generator and collector electrodes. Redox cycling occurred between local regions of the nanogap sides as demonstrated by the simulated concentration profile of the reactant, O (Figure 3B). Accordingly, the generator response at the nanogap side (blue lines in Figure 3A) was still transient and dominated by the reactant diffusing from solution. Moreover, the potential scan was too fast for solution sides of generator and collector electrodes to participate in redox cycling. No current response was obtained at the solution side of the collector electrode (magenta lines), whereas a transient voltammetric response at the solution side of the generator electrode was unaffected (black lines). Overall, both nanogap and solution sides of the generator electrode yielded transient responses at $\sigma = 300$ when a quasi-steady-state response was obtained at the collector electrode without a contribution from the solution side.

Remarkably different responses were obtained at nanogap and solution sides of the generator electrode at $\sigma = 3$ (Figure 3C). In this case, a voltammetric response at the nanogap side of the generator electrode reached quasi-steady states to nearly match a voltammetric response at the nanogap side of the collector electrode, thereby yielding a high collection efficiency of 0.91 determined from limiting currents. By contrast, a voltammetric response at the solution side of the generator electrode was still transient and peak-shaped during both forward and reverse scans. These results indicate that a transient generator response at $\sigma = 3$ (Figure 2B) was attributed to a transient response at the solution side of the generator electrode, which was too far from the collector electrode to participate in redox cycling. In fact, only a small current response was obtained at the solution side of the collector electrode, which was also too far from the generator electrode. Moreover, the diffusion layer at the generator electrode extended nearly to the entire surface of the nanogap side of the collector electrode, but yet to its solution side (Figure 3D). A larger area of the nanogap side of the collector electrode contributed to redox cycling at $\sigma = 3$, thereby yielding a higher collector response (Figure 2B) than at $\sigma = 300$ (Figure 2A).

Eventually, the entire assembly of double-cylinder electrodes reached quasi-steady states at $\sigma = 0.03$. Voltammetric responses at each side of generator and collector electrodes showed a sigmoidal shape with negligible or small hysteresis (Figure 3E). Voltammetric responses at nanogap sides of generator and collector electrodes nearly overlapped with each other to yield a remarkably high collection efficiency of 0.97 determined from limiting currents. By contrast, the current response at the solution side of the generator electrode was higher than that at the solution side of the collector electrode, thereby yielding a lower overall collection efficiency of 0.90 for the entire double-cylinder electrodes (Figure 2C). A simulated concentration profile (Figure 3F) shows that the solution side of the collector electrode was only partially exposed to the redox product, R, produced at the generator electrode, whereas its solution side was fully exposed to the redox reactant, O, in solution.

Importantly, we found that the solution side of the generator electrode makes no influence on the collector response and, subsequently, on FSNV. This finding implies that the fabrication of double-cylinder UMEs is simplified without affecting FSNV by exposing the entire surfaces of generator and collector electrodes as proposed by removing the insulation sheath of double-disk-like UMEs (19, 20). Specifically, the solution side of the generator electrode was insulated in our model to prevent a redox reaction (Figure S-3 in Supplemental Material). The resultant collector response was affected negligibly at $\sigma = 300$ and 3 (Figures S-3A and B, respectively) and barely noticeable at $\sigma = 0.03$ (Figure S-3C). By contrast, the generator response was significantly reduced at $\sigma = 300$ and 3 to improve collection efficiency, which is irrelevant to FSNV. A very small insulation effect on the generator response was observed at $\sigma = 0.03$, where the current response of the solution side of the generator electrode was already very low without insulation (Figure 3E).

FSNV at Double-Cylinder UMEs with Wide Gaps ($G = 1$).

We investigated the effects of gap width on FSNV by considering double-cylinder UMEs with wider gaps ($G = 1$). These gaps were still narrow enough to yield a substantial collector response at $\sigma = 30, 3$, and 0.03 (Figure 4), but not at $\sigma = 300$ (data not shown). This result

indicates that a 3.5 μm -wide gap of the double-microcylinder UMEs with $G = 1$ is too wide for FSNV at the corresponding scan rate of 400 V/s (Table 1), thereby requiring a nanometer-wide gap to achieve sub-millisecond resolution of in-vivo FSCV (3). A 35 nm-wide gap of the double-nanocylinder UMEs with $G = 1$ is also too wide to enable ultra-FSNV at 4 MV/s (Table 1), which requires a narrower gap (e.g., $G = 0.1$ in Figure 2A). The current response of a collector electrode with a wide gap ($G = 1$) became substantial when the normalized scan rate was decreased to $\sigma = 30$ (Figure 4A), which corresponds to 40 V/s and 400 kV/s for double-microcylinder and nanocylinder UMEs, respectively, with cylinder radii listed in Table 1. The collector response was delayed from the generator response during the forward scan, which is attributed to the time required for the redox product, R, to diffuse across the wide gap from the generated electrode to the collector electrode. The resultant collector response was transient without reaching a limiting value even during the reverse scan.

Quasi-steady-state FSNV was enabled by the collector electrode with $G = 1$ at $\sigma = 3$ and 0.03 (Figures 4B and C, respectively). The respective σ values correspond to fast scan rates of 40 kV/s and 400 V/s at the double-nanocylinder UMEs listed in Table 1. As σ decreased from 3 to 0.03, a limiting current at the collector electrode increased only from -1.1 to -1.4 to ensure quasi-steady states. By contrast, the generator response did not reach quasi-steady states even at $\sigma = 0.03$ as demonstrated by a slightly negative response during the reverse scan. These results indicate that the collector electrode reached quasi-steady states at least 100 times faster ($\sigma > 3$) than the generator electrode ($\sigma < 0.03$) with wider gaps ($G = 1$).

Current Distributions at Generator and Collector Electrodes with Wide Gaps ($G = 1$).

Mechanistic insights into FSNV with wider nanogaps ($G = 1$) were gained by simulating voltammetric responses at nanogap and solution sides of generator and collector electrodes (Figure 5). In these plots, the polarity of the collector response was inverted for a comparison with the generator response. Interestingly, transient voltammetric responses at both sides of the generator electrode were nearly identical at $\sigma = 30$ while the current response at the nanogap side of the collector electrode was significant (Figure 5A). The collector response indicates that this scan rate was slow enough for the redox product, R, to diffuse across the wider gap from the generator electrode to the collector electrode. By contrast, the generator response was unaffected, because this scan rate was too fast for the original reactant, O, regenerated at the collector electrode to return to the generator electrode across the wide gap. Accordingly, the collector response at $\sigma = 30$ was based on the time-of-arrival mechanism (33) rather than the redox-cycling mechanism. In fact, the diffusion layer at the generator electrode barely overlapped with the nanogap side of the collector electrode (Figure 5B).

The establishment of redox cycling across the wider gap required slower scan rates of $\sigma = 3$ and 0.03, thereby enhancing current responses at nanogap sides of both generator and collector electrodes (Figures 5C and E, respectively). In fact, the corresponding diffusion layers at the generator electrode significantly overlapped with the nanogap side of the collector electrode (Figures 5D and F). The efficiency of redox cycling, however, was still low at $\sigma = 3$ as indicated by a peak current and a lower limiting current at the nanogap side of

generator and collector electrodes, respectively. Finally, redox cycling became efficient enough at $\sigma = 0.03$ to obtain quasi-steady-state responses with small hysteresis at nanogap sides of both generator and collector electrodes with a high collection efficiency of 0.87 (Figure 5E). At this scan rate, solution sides of generator and collector electrodes also participated in redox cycling, but showed large voltammetric hysteresis. Moreover, a peak-shaped transient response was obtained at the solution side of the generator electrode to render the entire generator response transient even at $\sigma = 0.03$ (Figure 4C).

It should be noted that the voltammetric response of the collector electrode with $G = 1$ was also barely affected by insulating the solution side of the generator electrode (Figure S-4 in Supplemental Material). Accordingly, the entire generator electrode may be fully exposed to simplify the fabrication of double-cylinder UMEs for FSNV. Lower collection efficiency based on a higher response at the fully exposed generator electrode is irrelevant to FSNV, which measures the collector response.

Effects of Cylinder Radius on FSNV.

Advantageously, a collector electrode with a smaller cylinder radius reaches quasi-steady states faster without compromising sensitivity when a constant ratio of the cylinder radius against the gap width, i.e., G , is maintained. Accordingly, double-nanocylinder UMEs enable quasi-steady-state FSNV at up to megavolt per second (Table 1) to yield a limiting current that is as high as obtained with the micrometer counterpart, thereby facilitating ultrafast current measurement. A smaller cylinder radius decreases not only the active electrode area, but also the gap width to increase the flux across the gap and, subsequently, maintain a constant collector response. Importantly, a collector response can be used to determine the bulk concentration of the redox reactant, which is electrolyzed at the generator electrode, not at the collector electrode. A limiting current at a collector electrode, $i_{c, \text{lim}}$, is proportional to the bulk concentration, c_0 , as given by eq 7

$$i_{c, \text{lim}} = nFDLc_0I_{c, \text{lim}} \quad (11)$$

where $I_{c, \text{lim}}$ is the dimensionless limiting current determined by G for a given σ value. $I_{c, \text{lim}}$ with $G = 0.1$ increased only by ~35% (Figure 2) as σ decreased from 300 to 0.03, where $I_{c, \text{lim}}$ with $G = 1$ was lower and varied by a factor of ~3 (Figure 4).

In addition, the cylinder radius affects the reversibility of FSNV as detailed in Supplementary Material. The reversibility of FSNV at the collector electrode is controlled by the dynamics of electron transfer at the generator electrode (eq 4) and mass transport across the nanogap. The reversibility of FSNV is apparent, because the regeneration of the reactant at the collector electrode is diffusion-limited (eq 5). When a constant gap-radius ratio, G , is maintained, FSNV becomes less reversible with a smaller cylinder radius, which narrows a gap to enhance mass transport across the gap. By contrast, the reversibility of FSNV is nearly independent of scan rate, which controls transient mass transport at the solution side of the generator electrode, but weakly affects quasi-steady-state mass transport across the gap. Practically, reversible FSNV is expected for fast redox couples, e.g., ferrocene compounds and $\text{Ru}(\text{NH}_3)_6^{3+}$ (34-39), at the double-cylinder UMEs listed in Table

1 with the exception of those with the narrowest 3.5 nm-wide gap. Fast mass transport across a nanogap is advantageous to mitigate interferences by slow redox couples, e.g., ascorbic acid in the brain (2).

Comparison between FSNV and FSCV.

FSNV will complement FSCV by eliminating the need of background subtraction to enable some applications, which may also compensate the lower sensitivity of quasi-steady-state FSNV in comparison with transient FSCV as detailed in Supplementary Material. Briefly, the FSNV response of the double-cylinder UMEs listed in Table 1 is up to 14 times lower than the FSCV response of single-cylinder UMEs with identical sizes. Moreover, ultra-FSCV at 4 MV/s is ~23 times more sensitive than ultra-FSNV when the respective techniques employ 2.5 μm -radius single-disk UMEs (31, 32) and 175 μm -long double-cylinder UMEs with 35 nm radius and 3.5 nm-wide gap (20, 28) for ultrafast scan as listed in Table 1. Nevertheless, no background response of FSNV is crucial for various applications as represented by in-vivo determination of a basal concentration of neurotransmitters (8). In this application, FSNV of neurotransmitters adsorbed on the electrode surface (3) will yield an enhanced transient response (36). Moreover, the kinetics of extremely fast electrode reactions will be determinable more reliably by ultra-FSNV than ultra-FSCV with the high background (31, 32), where a higher reactant concentration can be used to enhance an ultra-FSNV response. It, however, should be noted that a higher FSNV response increases the iR drop, which is as large as in FSCV (Supplementary Material) and must be compensated for ultrafast scan (31, 32).

Conclusions

In this work, we employed the finite element method to predict that double-cylinder UMEs with nanometer-wide gaps will allow FSNV to quantitatively detect diffusing redox species at high temporal resolution of transient FSCV under quasi-steady states without the need of background subtraction. It should be emphasized that we simulated FSNV only under quasi-steady states as demonstrated by the noticeable scan-rate-dependence of limiting currents and hysteresis in contrast to true steady states (i.e., $\tau_e \rightarrow \infty$) considered in the previous study (18). Specifically, we predict that double-microcylinder UMEs will enable FSNV at hundreds volts per second as practiced for in-vivo FSCV in the brain using single carbon-fiber UMEs (3). Moreover, ultra-FSNV at megavolts per second will be feasible using double-nanocylinder UMEs with narrower gaps to reach nanosecond resolution as demonstrated by ultra-FSCV using single-disk UMEs (31, 32). The cylindrical collector electrode can reach quasi-steady states $\sim 10^4$ times faster than the generator electrode with identical sizes to simultaneously yield quasi-steady-state and transient voltammograms, respectively, at fast scan rates as observed by SECM-based nanogap voltammetry with a UME tip and a macroscopic substrate at slow scan rates (10, 36-39). The versatile model (18, 40) adapted for FSNV in this study will accommodate the adsorption of redox species on the electrode surface (36, 41, 42) to simulate transient FSNV for in-vivo-detection of adsorbed neurotransmitters, e.g., dopamine and serotonin (3) using adsorption isotherms reported in the literature (43).

This study provides valuable information to rationally design double-cylinder UMEs for FSNV. A quasi-steady-state response is obtained faster at the collector electrode with a smaller gap–radius ratio, G , and can be enhanced by using longer cylinders even with a smaller radius to facilitate fast current measurement. While steady-state collection efficiency is useful to determine a gap–radius ratio (18), the improvement of collection efficiency at a slower scan rate is mainly due to a decay of the generator response, which is irrelevant to FSNV, thereby allowing for the exposition of the entire cylinder surfaces to simplify electrode fabrication. In fact, we proposed to fabricate double-cylinder carbon UMEs for FSNV by removing the insulating sheath of double-disk-like carbon UMEs (19, 20). Double-cylinder carbon UMEs thus fabricated may be implantable in the brain with minimal tissue damage (44) and electrode fouling (45) to enable sensitive FSNV of adsorbed neurotransmitters in vivo (3). Advantageously, FSNV will be minimally interfered by ascorbic acid, one of the most common interfering species for in-vivo FSCV (2), because the irreversible interfering species is oxidized at the generator electrode and hydrolyzed in the nanogap to become redox-inactive at the collector electrode (46–48). More broadly, a simple method for fabrication of nanogap electrodes will be useful for other electrode materials to promote the application of nanogap voltammetry at both fast and slow scan rates.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

(A) Orthogonal cross-section of a parallel pair of cylindrical UMEs with the identical radius and length as voltammetric generator and amperometric collector electrodes in a solution containing a redox species, O. Dotted lines separate nanogap and solution sides of each electrode. Blue and red arrows indicate redox cycling between nanogap sides of the double-cylinder UMEs. Black arrows indicate the electrolysis of the original redox species at the solution side of the generator electrode. (B) Potentials of generator and collector electrodes, E_g and E_c , respectively, during FSNV.

Figure 2. Voltammetric responses of generator (blue) and collector (red) electrodes with narrow gaps ($G = 0.1$) during forward (solid) and reverse (dashed) scans of generator potential.

Figure 3.

(A, C, E) Voltammetric responses at nanogap (blue and red) and solution (black and magenta) sides of generator and collector electrodes, respectively, with narrow gaps ($G = 0.1$) during forward (solid) and reverse (dashed) scans of generator potential. (B, D, F) Concentration profiles of the reactant, O, at the switching potential.

Figure 4.

Voltammetric responses of generator (blue) and collector (red) electrodes with wide gaps ($G = 1$) during forward (solid) and reverse (dashed) scans of generator potential.

Figure 5.

(A, C, E) Voltammetric responses at nanogap (blue and red) and solution (black and magenta) sides of generator and collector electrodes, respectively, with narrow gaps ($G = 1$) during forward (solid) and reverse (dashed) scans of generator potential. (B, D, F) Concentration profiles of the reactant, O, at the switching potential.

Table 1.

Geometric Parameters and Scan Rates for FSNV Simulation.

UME	r	g		v^a		
		$G = 0.1$	$G = 1$	$\sigma = 300$	$\sigma = 3$	$\sigma = 0.03$
double microcylinder	3.5 μm	0.35 μm	3.5 μm	400 V/s	4 V/s	0.04 V/s
double nanocylinder	35 nm	3.5 nm	35 nm	4 MV/s	40 kV/s	400 V/s

^aCalculated by solving eq 9 with $D = 6 \times 10^{-6} \text{ cm}^2/\text{s}$.