Push-Button Method To Create Nanopores Using a Tesla-Coil Lighter

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ABSTRACT: Controlled dielectric breakdown (CDB) of silicon nitride thin films immersed in electrolyte solution has been used to fabricate single nanofluidic channels with ~10 nm and smaller diameters, nanopores, useful in single-molecule sensing and ionic circuit construction. A hand-held Tesla-coil lighter was used to form nanofluidic ionic conductors through a ~10 nm thick silicon nitride membrane. Modifications to the conventional approach were required by the low-overhead Tesla-coil-assisted method (TCAM): increased circuit resistance by including water in place of electrolyte and discrete rather than continuous voltage applications. The resulting ionic conductance could be tuned with the number of voltage applications. TCAM and conventional CDB produced nanopores with different conductance versus pH curves, suggesting different surface chemistry. Nevertheless, sensing experiments using the canonical test molecule, 4-DNA, produced signals comparable to translocation results through solid-state nanopores fabricated by other methods. Thus, the TCAM method offers flexibility in fabrication and in the properties and function of the nanoscale ionic conductors that it can generate.

INTRODUCTION

Nanopores have enjoyed decades of use and ongoing development as a platform for single-molecule sensing, with a strong focus on applications such as DNA sequencing but including other analytes and fundamental biophysical investigations. The most frequent experimental configuration relies on resistive-pulse sensing and has been referred to as a molecular-scale version of Coulter counting; analytes are electrophoretically passed through a <100 nm diameter, <100 nm long nanochannel, a nanopore, immersed in electrolyte solution, and analyte presence is revealed when it induces a measurable change in the nanopore conductance. The frequency of this occurrence is proportional to analyte concentration. More broadly, the nanopore can be thought of structurally as a nanoscale aperture or nanofluidic channel and functionally as an ionic circuit component. The rich application possibilities have inspired considerable effort in nanopore technology development to bring them to fruition. Thin-film silicon nitride (low-pressure chemical vapor deposition silicon nitride, SiNₓ) is a popular choice of material because it is robust, widely used, and can withstand a range of chemical and mechanical treatments. Although SiNₓ is a standard nanofabrication material, the small dimensions of the nanopores can nevertheless present considerable challenges to fabrication. SiNₓ nanopore fabrication efforts have largely depended upon the use of expensive and operationally demanding instrumentation such as transmission and (wet) scanning electron microscopes, helium ion microscopes, and large-scale accelerator facilities. Recently, controlled dielectric breakdown (CDB) was developed as a new nanopore fabrication method, free of the barriers associated with methods relying on complex and costly instrumentation and large-scale facilities. Application of a high field strength, typically ≤1 V/nm across a solution-immersed membrane (with solution on each side isolated from the other side by the membrane) yields a nanopore, with a number of operational benefits and monitoring possibilities emerging from this fabrication method and configuration. We were inspired by this successful effort and by the barriers to adoption of even such an elegant fabrication method that might emerge in the wide range of applications for nanopores, to ask if one could even more easily fabricate a nanopore, preferably “by hand” and with the push of a button. Our hypothesis was that we could, with sufficient consideration, use the Tesla-coil lighter as an exceptionally low-barrier tool to form nanopores in free-standing silicon nitride membranes.

Nanopore conductance analysis is a well-benchmarked method to approximate nanopore size and profile nanopore surface chemistry, and it directly characterizes a nanopore as an ionic circuit element. The method additionally complements the fabrication method by also being low overhead so that instrumentation eliminated from the fabrication workflow need not be reintroduced during characterization. In brief, a nanopore in electrolyte solution can be thought of as an ionic conductor, with its conductance determined by its dimensions and surface chemistry for a given solution composition. For a cylindrical nanopore of radius r₀ and total length L (here the length of the nanopore is taken to be equal to the SiNₓ
membrane thickness), the total nanopore conductance can be approximated as

\[
G = K \left( \frac{1}{\sigma L} + \frac{\mu I \Omega}{\kappa} \frac{2 \theta}{L} + \alpha 2 r_0 + \beta \frac{\mu \Omega}{L} \right)^{-1}
\]

where \( K \) is the solution conductivity, \( \sigma \) is the nanopore surface charge density, \( \mu \) is the surface counterion mobility, and \( \alpha \) and \( \beta \) are model-dependent parameters both set to 2 as in earlier work. \[35\] With known solution and surface parameter values, measurements of the conductance can be used to uncover effective nanopore sizes, \( r_0 \). Nanopores with ionizable surface species have \( \sigma = \sigma(pH) \) so that \( G \) can be tuned by pH (independent of geometrical parameters, here \( r_0 \) and \( L \)), and the resulting \( dG/dpH \) can yield insight into nanopore surface chemistry. To illustrate, it is conventional, in most instances, to treat the surface charge density of amphoteric SiN, nanopores as being governed by the monoprotic equilibrium

\[
\text{Si} - \text{R} - \text{OH}(\sigma = 0) \rightleftharpoons \text{Si} - \text{R} - \text{O}^- + \text{H}^+;
\]

\[
pK_a \approx -\log([\text{Si} - \text{R} - \text{O}^-][\text{H}^+] / [\text{Si} - \text{R} - \text{OH}])
\]

that would have \( \frac{dG}{dpH} \approx 0 \) when protonated in sufficiently acidic solutions, and \( \frac{dG}{dpH} > 0 \) when deprotonating in sufficiently basic solutions. The change in total conductance, with fixed \( K \) and \( r_0 \) but changing pH, arises from the surface chemistry through pH-dependent changes of \( \sigma \). We can approximate \[36\] \( \sigma \) for a monoprotic acidic-terminated surface as

\[
|\sigma| \approx \frac{C_{eff}}{\beta e W}\left(\frac{\beta e}{C_{eff}}\exp\left((pH - pK_a)\ln(10) + \ln(e\Gamma)\right)\right)
\]

with \( e \), \( \Gamma \), \( pK_a \), \( W \) the elementary charge, number of surface chargeable groups, dissociation constant of those groups, inverse of the thermal energy, effective Stern layer capacitance, and Lambert \( W \) function.

Translocation of the canonical test molecule, \( \lambda \)-DNA, through a nanopore provides additional nanopore size information and directly probes the molecular sensing performance of the nanopore. The change in nanopore conductance, \( \Delta G_{\lambda, DNA} \) due to translocation of \( \lambda \)-DNA (cross-sectional radius \( r_{0, \lambda, DNA} \), effective linear charge density \( q_{\lambda, DNA} \)) through the nanopore can be expressed as \[32,37\]

\[
\Delta G_{\lambda, DNA} = G - K \left( \frac{1}{\sigma_{\lambda, DNA}} + \frac{\mu I \Omega}{\kappa} \frac{2 \theta}{L} + \alpha 2 r_{0, \lambda, DNA} + \beta \frac{\mu \Omega}{L} \right)^{-1}
\]

where \( r_{0, \lambda, DNA} = \sqrt{r_0^2 - r_{\lambda, DNA}^2} \). Using eq 4 to solve \( \Delta G = \Delta G_{\lambda, DNA} \) for \( r_{\lambda, DNA} \) should yield a value consistent with the literature radius if translocation was successful. Furthermore, when measured with a nanopore of sufficient size, the conformational flexibility of \( \lambda \)-DNA allows it to translocate linearly or folded, with corresponding \( \Delta G = n \Delta G_{\lambda, DNA} \) (\( n = 1, 2, \text{etc}. \)): observation of these quantized peaks should thus be further evidence of successful nanopore formation supporting \( \lambda \)-DNA translocation. \[37,38\]

\section*{RESULTS AND DISCUSSION}

The Tesla coil was used to replace the entire CDB setup of Kwok et al. \[27\] Simply using the Tesla coil in place of a conventional voltage source for CDB in 1 M and even 10 mM KCl, however, was unsuccessful: post-CDB measurements of the cross-membrane conductance produced currents beyond the dynamic range of the current amplifier. Thus, crucial modifications were made to reduce the cross-membrane voltage drop provided by the Tesla coil, to allow for controlled pore formation. Fabrication was done in ultrapure water (K$^+$ ~ 18 MΩ cm) rather than in electrolyte medium (typically 1 M KCl with K$^+$ ~ 1 mΩ cm), and a 1 GΩ resistor was placed in series with the membrane and the Tesla coil (Figure 1). Straightforward timed voltage application was precluded by the Tesla-coil’s push-button operation with built-in circuit time out. The number of pulses, generated by a quick push-and-release of the button, required to generate a particular conductance value through the 11 ± 1 nm batch of membranes was reported in place of voltage application time (Figure 2). The minimum number of pulses needed to produce a reasonable conductance in the range of typical nanopore measurements was ~20. The continued increase in the through-membrane conductance with repeated voltage pulse applications was consistent with the increase of

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig1.png}
\caption{Cross-sectional view (through the PTFE custom holder) of the setup used to fabricate a nanopore through a nominally ~11 ± 1 nm thick SiN$_x$ membrane using a commercial Tesla-coil lighter. One of the electrodes of the Tesla-coil lighter was directly connected to a Ag/AgCl electrode and the other serially through a 1 GΩ resistor.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig2.png}
\caption{Growth of conductance through a SiN$_x$ membrane with a nominal thickness of 11 ± 1 nm with number of Tesla-coil pulses. Each pulse was applied to the membrane in ultrapure water, whereas conductance measurements were performed after exchanging water for 1 M KCl electrolyte buffered at pH ~ 7.}
\end{figure}
and durations (Fig. 3) of a nanopore (∼9 nm) fabricated by the Tesla-coil-assisted method (blue trace) through a SiN$_x$ membrane with a nominal thickness of ∼11 ± 1 nm. The solid lines show the linear fits made to raw data of each voltage polarity. The pH-conductance profiles of nanopores fabricated by (b) conventional CDB setup (∼12 nm) and (c) the Tesla-coil-assisted method (∼9 nm) through SiN$_x$ membranes with a nominal thickness of ∼11 ± 1 nm.

Figure 3. (a) Current−voltage curves of nanopores fabricated by the CDB setup (black trace) and the Tesla-coil-assisted lighter method (blue trace) through a SiN$_x$ membrane with a nominal thickness of ∼11 ± 1 nm. The solid lines show the linear fits made to raw data of each voltage polarity. The pH-conductance profiles of nanopores fabricated by (b) conventional CDB setup (∼12 nm) and (c) the Tesla-coil-assisted method (∼9 nm) through SiN$_x$ membranes with a nominal thickness of ∼11 ± 1 nm.

Figure 4. (a) Scatter plot of λ-DNA translocation events through a ∼9 nm TCAM SiN$_x$ nanopore with (b) discrete conductance changes consistent with zero (red), one (magenta), and folded (blue) λ-DNA translocations. (c) Histograms of event duration corresponding to λ-DNA translocations (gray) and the exponential fit (red).

Figure 4a shows a typical current−voltage curve observed for a nanopore fabricated through the Tesla-coil-assisted method (TCAM) with an estimated $r_0$ (eq 1) of ∼9 nm. Figure 3b shows a typical pH-conductance profile of a SiN$_x$ nanopore (∼12 nm) fabricated through the conventional CDB process. The behavior of $dG/dpH$ is consistent with the amphoteric nature of the SiN$_x$ surface.\(^{11,39}\) This curve profile can be attributed to the presence of a mixture of surface amine and hydroxyl functional groups, with the overall surface charge density dictated by the $pK_a$ values and relative abundances of the surface head groups.\(^{11,39}\) Briefly, when pH = $pI$, the surface charge is zero; when pH < $pI$, basic functional groups will protonate and impart a positive charge to the surface; and when pH > $pI$, acidic groups will deprotonate and impart a negative charge to the surface. This $dG/dpH$ trend produces changes to $G_{\text{surface}}$ that increase $G$ from its bulk-only minimum at the isoelectric point ($pI$). The $pI \sim 4.3 \pm 0.4$ (3 unique pores) using a fit to $G$ versus pH is consistent with a value of ∼4.1 reported in the literature.\(^{39}\) Figure 3c shows the pH-conductance profile of a nanopore (∼9 nm) fabricated by the Tesla-coil-assisted method: three unique nanopores exhibited an initial plateau ($\lambda \sim 0$ followed by $dG/dpH > 0$ consistent with monoprotic, rather than amphoteric, surface chemistry. It is possible that a plateau in conductance versus pH could arise from a charged surface already fully deprotonated at pH 2 (a diprotic surface with sufficient high $pK_a$, for example), but the conventional understanding of SiN$_x$ surface chemistry would make this an unlikely possibility. The $pK_a$ of the monoprotic surface chargeable groups of the nanopore surface was calculated by fitting the pH-conductance profile (using eqs 1 and 3 with $C_{\text{eff}}$ and $\Gamma$ free parameters minimizing $\chi^2 = \sum_i (G_i - G_{\text{fit}})^2 / \sigma_i^2$) to yield a best-fit value of ∼5.6 ± 0.5 (3 unique nanopores). These results illustrate that TCAM produces a functional ionic conductor with different pH-dependent conductances than by conventional CDB. The trend of the conductance with pH (Fig. 3) suggests that the Tesla coil generates a nanopore with different, ostensibly simpler, surface chemistry.

Nanopore measurements of λ-DNA translocation (0.125 nM in 4 M LiCl buffered to pH ~ 7) were used as an additional means to profile the Tesla-coil-assisted nanopores. A +600 mV potential was applied across the membrane to electrophoretically drive the λ-DNA through a ∼9 nm nanopore. Measurements were acquired at a rate of 100 kHz with 4-pole low pass Bessel filter built-in to the Axopatch 200B set to 10 kHz and extracted using a custom thresholding program written in Labview. Scatter plots showing the event magnitude means (Δ$G$) and durations (τ) are shown in Figure 4a. We created histograms of the current values within blockages that occurred after the addition of λ-DNA, plotted in Figure 4b. The resulting Δ$G$ profile shown in Figure 4b was fitted with the sum of three Gaussian functions, $g = \sum_i A_i \exp\left(-\lambda^2/2\sigma_i^2\right)$, with $A_i$, $\mu_i$, and $\sigma_i$ the amplitude coefficient, mean, and standard deviation, respectively, with all parameters left free. Qualitatively, the appearance of more than two peaks is consistent with the translocation of λ-DNA in linear and folded conformations. The first peak centered at Δ$G = 0$ ns corresponds to the open pore (baseline) current. The second peak was detected only in the presence of the λ-DNA and setting Δ$G = ΔG_{\text{DNA}}$ with the manufacturer-provided $L = 11 ± 1$ nm, we calculated $r_{\text{DNA}} \in [1.26, 1.37]$ (in nm), within the range of hydrated radii values reported for DNA.\(^{40–42}\) The third peak was centered at Δ$G = 2.03ΔG_{\text{DNA}}$, which is further evidence supporting the successful use of the Tesla-coil-assisted nanopore for translocation-based molecular sensing in that the nanopore is sufficiently large to accommodate the passage of folded-over λ-DNA. The event duration data shown as a histogram in Figure 4c was fit with a sum of two exponential decays $\phi^{\text{exp}} = \exp(-\tau/2\phi) \times (A_1 \exp(-\tau/\tau_1) + A_2 \exp(-\tau/\tau_2)) \theta$ that were truncated below the event duration mode, $\tau_{\text{mode}}$ before being convolved with the Gaussian, and with all parameters left free. Analysis of the event durations gives a ∼1000 μs time constant corresponding...
to a translocation speed of ∼20 ns/base pair, comparable to translocation speeds reported for nanopores fabricated by other means.¹³

### CONCLUSIONS

Here, we have demonstrated a portable, time- and cost-effective method (TCAM) to fabricate nanopores using a hand-held Tesla-coil lighter. The use of the Tesla-coil lighter required modifications to the conventional CDB configuration, principally inserting series resistance to compensate for the high fixed output voltage and applying a discrete number of voltage pulses in place of a continuously timed voltage. Given the need to add in series resistance to prevent uncontrolled pore formation in the ∼10 nm thick membranes, we expect that such a technique should be amenable for forming nanopore ionic conduction paths through thicker SiNₓ membranes than those employed here. The TCAM nanopores could successfully translocate the canonical C-DNA test molecule, with translocation characteristics similar to those through more conventionally fabricated nanopores. The nanopores showed fundamentally different surface chemistry, however, as shown in the shape of the conductance versus solution pH curve. In contrast to the amphoteric SiNₓ nanopore fabricated by CDB, which can be pH-tuned from both charge polarities through a neutral surface charge at the isoelectric point, these TCAM pores exhibited a flat response to pH in acidic solution over a fairly large range before an appreciable Gsurface onset in more basic solutions. Such behavior has two benefits. First, the nanopore conductance is independent of solution pH over a reasonably broad range, allowing the use of such a nanopore as a stable ionic conductor in a range of different solutions. Second, it allows, to an extent dictated by the presence of solution-available ionizable groups with suitable pKₐ within the analyte, tuning of anolyte charge by solution pH within the plateau range without appreciably changing the nanopore conductance. That this can occur without the need for the often difficult, and at least time-consuming, step of initial nanopore surface chemical modification, is especially salutary in terms of easing experimental burdens. Translocation characteristics of C-DNA through these nanopores were consistent with measurements in nanopores fabricated by other means, underscoring the utility of this fabrication method for molecular sensing, beyond simple ionic conduction. We note, however, that such a low-overhead fabrication route may be useful in other domains, including the straightforward fabrication of leak valves in vacuum science, nanochannels for fundamental condensed matter studies, or as solution apertures in nanoparticle synthesis where conventional nanopore instrumentation overhead might otherwise prove burdensome.¹⁵⁻¹⁶

### MATERIALS AND METHODS

Silicon nitride membranes on silicon frames (Norcada Inc, NT005Z, Lot # L45 with a nominal thickness of 11 ± 1 nm) were compressed between two silicone gaskets in a custom PTFE holder with two ∼500 µL sample wells.⁸ The electrodes of the Tesla-coil lighter (Tesla Coil Lighters, Amazon, ASIN: B01A02F714) were connected, in series with a 1 GΩ resistor (Newark Electronics, 66KK6871), to 1.0 mm diameter Ag/AgCl electrodes immersed in the sample wells of the PTFE holder containing ultrapure water (∼18 MΩ cm), as illustrated in Figure 1. Precautions appropriate to a high voltage power supply capable of igniting flammable materials should be observed.

After 18 pulses, the ultrapure water was exchanged with aqueous 1 M potassium chloride buffered at pH ∼7 with N-(2-hydroxyethyl)piperazine-N’-ethanesulfonic acid potassium salt to obtain a current–voltage (I–V) curve. All electrical measurements were carried out using an Axopatch 200B amplifier (Axon Instruments, Foster City, CA) in voltage clamp mode operated by custom Labview (National Instruments Corp., TX) programs. If the conductance remained ∼0 nS (no pore formation had appeared to take place), electrolyte was thoroughly exchanged with ultrapure water, and a small number of additional pulses (∼3–5) was applied. This process was continued until a pore, or a pore of desired size, was formed.

Curve fitting of data was performed using the NMinimize method of the NonlinearModelFit of Mathematica 11.0.1.0 (Wolfram Research, Champaign, IL).

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### ABBREVIATIONS

TCAM, Tesla-coil-assisted method; CDB, controlled dielectric breakdown

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