Addressing the Isomer Cataloging Problem for Nanopores in Two-Dimensional Materials

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ABSTRACT

Extended defects or nanopores in 2D materials can tailor their electronic, magnetic, and barrier membrane properties. However, the large number of possible lattice isomers of nanopores makes their quantitative study a seemingly intractable problem, confounding the interpretation of experimental and simulated data. Herein, we formulate a solution to this Isomer Cataloging Problem (ICP), combining electronic-structure calculations, kinetic Monte Carlo simulations, and chemical graph theory, to generate a catalog of unique, most-probable isomers of 2D lattice nanopores. The results demonstrate remarkable agreement with precise nanopore shapes observed experimentally in graphene and show that the thermodynamic stability of a nanopore is distinct from its kinetic stability. Triangular nanopores prevalent in hexagonal boron nitride are

also predicted, extending this approach to other 2D lattices. The proposed methodology should accelerate the application of nanoporous 2D materials by establishing specific links between experiment and theory/simulations, and providing a much-needed connection between molecular design and fabrication.

Extended defects or nanopores are inevitably present in real two-dimensional (2D) materials, such as transition metal dichalcogenides, graphene, and hexagonal boron nitride (hBN). They can also be used to tailor the optoelectronic,^{1,2} magnetic,³ electrochemical,⁴ and barrier⁵ properties of 2D materials. Indeed, the electronic structure of graphene at the edges is different from that of the pristine graphene basal plane.^{6,7} Moreover, a number of experimental studies have demonstrated the use of nanoporous graphene for gas^{9,10} and ionic sieving,^{11,5} and DNA sequencing.¹² Nevertheless, the identification of the molecular identity of an experimentally created nanopore¹³ is confounded by the exponentially-increasing number of possible nanopore shapes on a triangular lattice (e.g., graphene), such that the size of a nanopore is no longer a unique descriptor of the pore geometry. Topologically, each possible nanopore in graphene corresponds to a triangular “lattice animal” (or *polyiamond*). Borrowing results from the enumeration of polyiamonds,^{14,15} we observe that when $N=8$ carbon atoms are removed from the graphene lattice, there are only 66 possible nanopore isomers (i.e., nanopores of different shapes formed by removing exactly the same number of carbon atoms from the graphene lattice in a contiguous fashion). However, when $N=12$ carbon atoms are removed, there are 3226 possible nanopore isomers. At the atomic scale, small changes in pore shapes can lead to widely different macroscopically-observed properties, such as gas permeation fluxes and selectivities through nanopores.¹⁶ Therefore, the inability to link a given pore size with its molecular identity presents a gap between predictions of theory and simulations, and what can be realized experimentally. This gap could be closed by solving the “Isomer Cataloging Problem (ICP)”, which exists for all 2D lattice materials, and addresses the generation of a catalog of most-probable nanopore isomers in the 2D lattice.

The ICP currently hampers the connection between specific theoretical predictions and experimental studies in several important application areas of 2D materials. Emerging membrane technology based on 2D materials holds the potential to revolutionize the field of separations^{5,9-11,17} and osmotic power harvesting.^{18,19} Theoretical studies have provided insight into how magnetic,²⁰ optoelectronic,²¹ and transport^{17,22-24} properties depend on the specific atomic shapes and sizes of certain graphene nanopores. However, when an experiment reveals, e.g., a certain flux or activation barrier for transport of gases through a nanoporous 2D material sample, the likely question one would ask is: “what shapes and sizes of nanopores would lead to the observed transport?” Similar connection problems exist with magnetic, electronic, and optical defects, which necessarily form complex ensembles from processing.^{25,26} As the number of possible isomers increases exponentially with size (when $N=30$, there are around 400 billion nanopore isomers¹⁴), it is an insurmountable challenge to perform a mapping between simulation and experiment without addressing the ICP; using a solution to the ICP, one could consider only a small subset of the *most-probable* isomers (MPIs) of nanopores so as to obtain agreement of the theoretically-predicted physical observables with the appropriate experimental data.

Previously, simulation studies have combined transmission electron microscopy (TEM) imaging with kinetic Monte Carlo (KMC) simulations to demonstrate the prevalence of zigzag edges,²⁷ and qualitative agreement between simulated and experimentally observed nanopores, in graphene.²⁸ More recent work has used reactive molecular dynamics (MD) simulations to study defect creation in graphene under bombardment by noble gas ions, and has compared the results with experimental data in a qualitative fashion.²⁹ However, the use of MD simulations restricts the simulation to picoseconds of time, whereas etching of nanopores occurs on the time scale of minutes. Adopting a different approach, a few studies have investigated the thermodynamic

stability of graphene nanopores, by computing the energetics of formation of extended vacancies in graphene.^{20,30,31} However, as we show in this study, the thermodynamic stability of a nanopore is very different from its kinetic stability. In contrast to graphene, defect formation has not been widely studied even in this way for other 2D lattices.

In this paper, we present a solution methodology to the Isomer Cataloging Problem (ICP) and demonstrate its utility for two important 2D lattice systems: monolayer graphene and hBN. By generating, cataloging, and probabilistically ranking each potential isomer using a kinetic pathway analysis, we collapse the intractable isomer tree into the most-probable isomers for each vacancy number, such that the occurrence and observation of these isomers is most likely. We adopt a multi-scale modeling approach, which combines electronic-structure density functional theory (DFT) calculations with KMC simulations of the etching process.^{32,33} DFT calculations are used to determine the activation barriers for an exhaustive catalog of atomic rearrangements in the lattice. To enable high-throughput sorting of isomers from the list of stochastically generated nanopores, we develop a chemical informatics scheme based on graph-theoretic principles. Eventually, our algorithm is able to predict the few isomers that are reported experimentally in the literature with atomic level resolution, as well as the kinetics of the experimentally observed isomerization of nanopores.²⁵

Isomer Cataloging Framework

We consider defects with increasing vacancy number to catalog the stability and formation probability of each candidate nanopore, beginning with a graphene sheet having a monoatomic vacancy and using a KMC simulation framework to successively remove carbon atoms from the lattice, while allowing the edge atoms to relax via atomic rearrangements. Atomic rates were computed using an Arrhenius-type relationship: $r = \nu \exp\left(-\frac{E_a}{k_B T}\right)$, where r is

the rate of the physical process, ν is the atomic prefactor, E_a is the activation barrier for the process, k_B is the Boltzmann constant, and T is the absolute temperature of the system. Activation barriers for etching were determined using a combination of a quadratic reaction enthalpy (ΔH_r)–activation barrier (E_a) relationship³⁴ and DFT-calculated reaction enthalpies of etching. According to the Marcus reaction-rate theory for atom-transfer reactions,³⁵ which is able to accurately describe the relationship between reaction enthalpy and activation barrier for both endothermic and exothermic reactions (as compared to the linear Evans-Polanyi relationship³⁶):

$$E_a = E_a^0 \left(1 + \frac{\Delta H_r}{4E_a^0} \right)^2 \quad (1)$$

where E_a^0 is the intrinsic activation barrier for the set of reactions under consideration. We calculated reaction enthalpies for the etching of different types of atoms in nanoporous graphene: armchair, zigzag, and singly-bonded atoms,³⁷ as outlined in the Methods section. A zigzag atom (green atom in Fig. 1D) has 2 bonded neighbors, each of which possesses 3 bonded neighbors.³⁷ On the other hand, an armchair atom (green atom in Fig. 1E) has 2 bonded neighbors, one of which possesses 2/3 bonded neighbors and the other possesses 2 bonded neighbors.³⁷ The calculated reaction enthalpies are listed in Supplementary Table 1, in the presence of commonly encountered silicon etchant atoms.³⁸

Recent experimental work²⁵ systematically obtained high-resolution TEM images of nanopores in graphene, with a reported rate of 0.01 s^{-1} for the etching of the first four carbon atoms removed from the graphene lattice, in the presence of silicon contaminant atoms,³⁹ at a temperature of $500 \text{ }^\circ\text{C}$. Since the first four atoms to be etched from the graphene lattice are all zigzag atoms (see Supplementary Fig. 1), using an atomic prefactor (ν) of 10^{13} Hz (see Supplementary Information (SI) 2 for a discussion on the choice of the prefactor considered in our KMC simulations),⁴⁰ the experimentally observed etching rate of 0.01 s^{-1} corresponds to an

activation barrier of 2.301 eV for the etching of zigzag atoms. Using the enthalpy of etching listed in Supplementary Table 1 for a zigzag atom, we determine the intrinsic activation barrier, E_a^0 , to be 2.092 eV for graphene. Based on this value of E_a^0 , and the values of ΔH_r for the etching of armchair and singly-bonded carbon atoms, we tabulate the respective activation barriers for the etching of armchair and singly-bonded atoms in Supplementary Table 1. Atomic rearrangement (edge diffusion) rates were calculated using a prefactor (ν)⁴⁰ of 10^{13} Hz, and the associated activation energy barriers, determined using DFT-based nudged elastic band (NEB)⁴¹ calculations, as outlined in the Methods section. Rearrangements up to the nearest (N), next-nearest (NN), and next-to-next nearest (NNN) atomic sites to a carbon atom (Fig. 1A) in the graphene lattice were considered, starting and ending at one of these carbon atom types: singly-coordinated (1), doubly-coordinated armchair (2A), doubly-coordinated zigzag (2Z), or triply-coordinated (3).

Fig. 1 | Validation of calculated activation barriers for atomic rearrangements in the graphene lattice. (A) Illustration of the concept of nearest (N), next-nearest (NN), and next-to-next nearest (NNN) atomic sites, shown in red, green, and white color, respectively. (B-G) Molecular models depicting the initial (B, D, F) and final (C, E, G) states for the process of diffusion of a carbon

atom from a 2Z site to: a nearest 2Z site (B, C), next-nearest 2A site (D, E), and next-to-next nearest (F, G) 2Z site, with the diffusing atom shown in red (N), green (NN), and white (NNN) color, respectively. (H-K) Transmission electron microscopy (TEM) images (H-I) and corresponding molecular models (J-K), adapted from Ref. 25 (Copyright © 2014, American Chemical Society), of an experimentally observed transition occurring in the graphene lattice, which involves a series of three 2Z to 2Z NNN atomic movements, occurring over a period of 18 s.

The results of the barrier calculations are summarized in Table 1, and molecular models of example transitions starting at a 2Z site and ending at a N 2Z, NN 2A, and NNN 2Z site, respectively are depicted in Figs. 1B-C, 1D-E, and 1F-G. Examination of the data in Table 1 reveals that several of the atomic rearrangements are relevant only at high temperatures exceeding 1000 °C, due to activation barriers greater than 3 eV. We validated one of these barriers by direct comparison with experimental data from Ref. 25. The transition between the two nanopore states depicted in Fig. 1H and 1I (1J and 1K) took place in about 18 s at a temperature of 700 °C.²⁵ This transition can be effected through a set of three consecutive 2Z to 2Z NNN atomic movements. From Table 1, the barrier of one such transition is 2.856 eV, which compares well with the experimentally-deduced barrier of 2.66 eV (assuming a prefactor of 1×10^{13} Hz). Note that, with a prefactor of 1.309×10^{14} Hz, at a temperature of 700 °C, or an effective temperature of ~770 °C (which is possible due to heating of the lattice because of electronic collisions), with a pre-exponential factor of 1×10^{13} Hz, one would obtain exact agreement between experiment and simulation for this transition.

Equipped with experimentally-consistent edge diffusion barriers and etching rates, we carried out three different “*in silico* nanopore opening experiments”. In the first experiment, carbon atoms are removed from the graphene lattice one-by-one, and the atoms are not allowed to rearrange in between the etching steps. In the second *in silico* experiment, carbon atoms are allowed to diffuse along the nanopore edges, in between the etching steps, to consider the effect of atomic rearrangements. Finally, in the third experiment, atoms are not allowed to move in

between the etching steps, and etching rates are calculated using the theory of electron beam sputtering.⁴² All the *in silico* experiments were repeated 1000 times for each nanopore size considered (see SI4 for a discussion on the sufficiency of 1000 KMC runs in determining the frequencies of observation of the MPIs).

Table 1 | Activation barriers for rearrangements (edge diffusion) of carbon atoms starting from, and ending at, different types of sites in the graphene lattice, determined using CI-NEB calculations. N refers to nearest neighbor sites, NN refers to next-nearest neighbor sites, and NNN refers to next-to-next nearest neighbor sites. 1 refers to a singly-bonded site, 2A refers to a doubly-bonded armchair site, 2Z refers to a doubly-bonded zigzag site, and 3 refers to a triply-bonded site. To read the table, refer to the corresponding row for the source site, and to the corresponding column for the destination site. NP refers to an edge diffusion process which is not possible, and NC denotes that the NEB calculations did not converge. Diffusion events leading to a reduction in the number of bonded neighbors are highlighted in yellow.

N (eV)	1	2A	2Z	3
1 →	0	0	0	NP
2A →	0	2.691	1.372	NP
2Z →	0	7.409	1.211	NP
3 →	NP	NP	NP	NP
NN (eV)	1	2A	2Z	3
1 →	0	2.689	2.100	1.947
2A →	4.794	4.853	5.357	2.325
2Z →	3.463	3.580	6.593	2.906
3 →	0.872	5.580	2.906	3.479
NNN (eV)	1	2A	2Z	3
1 →	0	2.510	0.867	4.566
2A →	4.615	6.885	6.479	3.312
2Z →	1.091	4.666	2.856	NC
3 →	4.819	8.012	NC	5.336

In order to identify and catalog unique isomers and their respective probabilities from the results of the *in silico* experiments, we formulated a graph theoretic approach, which also takes into account the underlying symmetries of graphene (space group $p6mm$ with six-fold rotation and mirror symmetry). We consider the *antimolecule*, i.e., the molecule formed by the atoms removed from the 2D material lattice to form a nanopore, to be the representative molecular structure for that nanopore. In Fig. 2A-B, we depict an example nanopore formed by removing 6 carbon atoms from pristine graphene, along with the nanopore's antimolecule (shown in white color) and rim atoms (shown in yellow color). To find out if two nanopores are identical, we check if the molecular graphs associated with them (as embodied by the adjacency matrices⁴³ of the respective antimolecules) are isomorphic. Since bonds in 2D lattices are not freely rotatable (see Fig. 2C-D), we account for their relative orientations, as explained in the Methods section.

Fig. 2 | Distinguishing between and counting nanopore isomers in graphene. (A-B) Concept of an antimolecule. A nanopore in graphene, formed by removing 6 atoms from the lattice, is depicted in panel (A). Carbon atoms at the pore rim are shown in green color. The antimolecule of the pore depicted in (A) is shown in panel (B). The antimolecule atoms are depicted in white color. (C-D) Non-rotatability of bonds in the graphene lattice. The distinct pores depicted in panels (C) and (D) have antimolecules differing solely by the rotation of a single C-C bond. (E-J) Schematic depicting the sequential etching of carbon atoms to form a nanopore with 8 carbon

atoms removed from the graphene lattice. In each image, the atom about to be etched is depicted in red color. (K) Log plot of the number of isomers found in 1000 KMC runs, with (in blue color) and without (in green color) considering edge diffusion, versus the size of the nanopore. The total number of possible isomers, from counting of triangular lattice animals, is plotted in red color, versus the size of the nanopore.

Nanopores in Graphene

Fig. 2E-J depicts the sequential enlargement of a nanopore formed by removing 8 carbon atoms from the graphene lattice. We have carried out the KMC algorithm for up to 28 carbon atoms removed from the graphene lattice, distinguishing between non-identical nanopores to count the number of unique isomers obtained in 1000 KMC runs at a temperature of 500 °C (see SI5 for a discussion on how temperature does not change the shapes, or relative rank ordering, of the MPIs, but only alters their rates of formation). This data is graphically depicted in Fig. 2K, in green color for the first *in silico* experiment (without edge diffusion considered), and in blue color for the second *in silico* experiment (with edge diffusion considered) and shows that the number of isomers increases rapidly with the number of carbon atoms removed from the graphene lattice. In addition, Fig. 2K depicts the total possible number of isomers, in red color. It is noteworthy that the list of isomers generated in the KMC simulations is not exhaustive, and only represents a small fraction of the possible pores, which makes comparison with experimental data more straightforward. To this end, we have used the limited number of high-resolution TEM images available in the literature, plus five new TEM images, of graphene nanopores. The comparison is based on the following hypothesis: TEM images reported in the literature should be of the most abundant pores, since the finding and imaging of pores is a low probability event akin to finding a needle in a haystack. Accordingly, we report the top four MPIs of graphene nanopores formed by removing $N = 6, 7, 8, 10, 12, 13, 19,$ and 20 carbon atoms, as obtained from our KMC simulations in the first *in silico* experiment, in Fig. 3 (see

Supplementary Figs. 4–6 for other pore sizes). The corresponding results for the second *in silico* experiment are reported in Supplementary Fig. 7. In Fig. 3, we report the sizes (N) of the isomers considered, along with the number of isomers obtained in 1000 KMC simulations ($n_{iso,1000}$) as “ $4/n_{iso,1000}$ ”, implying that only the top four MPIs are depicted. Additionally, above each nanopore isomer in Fig. 3, we report its frequency of observation (in percent) in 1000 KMC simulations. Finally, wherever the simulated nanopore isomer directly corresponds to an observed experimental nanopore, we indicate the agreement with an orange border.

From a comparison of Fig. 3 and Supplementary Fig. 7, we conclude that: (i) the obtained MPIs offer striking agreement when compared to the limited TEM images of nanopores available in the literature, considering that anywhere between 12 and 593 nanopore isomers were obtained (see SI8 for a comment about the probabilities of the top four MPIs as a function of the size of the nanopore), and (ii) the inclusion of edge diffusion effects does not impact the relative abundance of the isomers considerably. An analysis based on the frequencies of observation of the MPIs is possible because the MPIs formed by removing an equal number of atoms from the graphene lattice have similar formation times (see SI9), indicating that none of the isomers are kinetically forbidden. On the other hand, the assumption that electron-beam scattering determines the etching rates precludes the observation of the experimentally-observed nanopore shapes in the simulated dataset (see SI10), providing *proof-by-contradiction* that electron-beam scattering theory does not accurately represent the physics of nanopore creation in the experimental studies considered, and supporting earlier hypotheses that silicon nanoparticle-catalyzed etching of graphene alters the kinetics of etching as compared to simple electron-beam sputtering.⁴²

Fig. 3 | Comparison of the results of the first *in silico* experiment (i.e., without including the effect of edge diffusion) with experimental TEM images available in the literature. The leftmost panel describes the sizes (N) of the isomers considered, and the number of isomers obtained in 1000 KMC simulations ($n_{iso,1000}$) as “4/ $n_{iso,1000}$ ”, the “4” implying that only the top four MPIs are depicted. The frequency of observation of each isomer in 1000 KMC simulations resulting in N -sized pores is reported in percent above each isomer. Wherever the simulated nanopore isomer

directly corresponds to an observed experimental nanopore, the agreement is indicated with an orange border and the corresponding experimental work is cited. Experimental data are taken from (a) Ref. 25 (b) this work (University of Oxford), (c) this work (Lockheed Martin Space), and (d) Ref. 38 (Copyrights © 2014 and 2015, American Chemical Society).

Thereby, MPIs can be utilized to falsify proposed mechanistic details even when the number of observed structures is low (see SI11 for further validation using *evidence-of-absence/less prevalence* of nanopore shapes not/less observed in experimental microscopy data). In some cases, however, we have observed that the nanopores observed using TEM are less frequent or are not seen in our simulated dataset, because our on-lattice simulation does not allow the formation of Stone-Wales defects⁴⁴ or 7- and 8-membered rings⁴⁵ (see SI12), thereby providing opportunities to improve our modeling framework.

To verify whether the simulated probability of nanopores correlates with their thermodynamic stability, we computed the geometry-optimized energies of formation of the MPIs using DFT calculations (see SI13 for calculations indicating that entropic and vibrational effects⁴⁷ are not significant). Supplementary Fig. 12 depicts a plot of the electronic formation energies of the top four MPIs formed by removing $N = 6, 7, 8, 10$, and 13 carbon atoms from the graphene lattice, without edge diffusion considered. The bars in Supplementary Fig. 12 (labeled 1st, 2nd, 3rd, and 4th) are arranged in decreasing order of the probabilities of occurrence of the isomers. It follows that, it is not necessary, given a nanopore size, for isomers which are more probable to have a lower formation energy. For example, the 1st MPI for $N=8$ has the highest formation energy (21.28 eV) amongst the four MPIs considered for $N=8$ (see SI14 for further evidence using *all* possible isomers for $N=6$). Therefore, more thermodynamically stable pores (i.e., those possessing lower formation energies) need not necessarily be more kinetically stable (i.e., more probable in the isomer tree).

Nanopores in Hexagonal Boron Nitride

Several experimental studies have observed nitrogen-terminated triangular defects in hBN under a TEM.^{26,48–51} It is known that the number of atoms removed from the hBN lattice to form a triangular nanopore should be a square number ($N = 1, 4, 9, 16, \dots$).⁵¹ We calculated the reaction enthalpies for etching of different types of B and N atoms in nanoporous hBN: armchair, zigzag, and singly-bonded, as outlined in the Methods section. These values are listed in Table 2, for etching in the presence and in the absence of silicon etchant atoms. Subsequently, the activation barrier was related to the reaction enthalpy using Eq. (1).

Table 2 | Enthalpies and activation barriers for the etching of different types of B and N atoms in the hBN lattice.

Type of Atom	Enthalpy of etching bare edge (eV)		Enthalpy of etching in the presence of a Si atom (eV)		Activation barrier for etching in the presence of a Si atom (eV)	
	B	N	B	N	B	N
Armchair	3.272	3.464	0.392	2.779	1.321	2.938
Zigzag	-0.302	-0.614	-1.458	1.949	0.506	2.304
Singly Bonded	0.167	-0.694	3.484	0.050	3.538	1.142

The value of E_a^0 was determined to be 1.116 eV, by fitting etching rates to a recent experimental dataset,⁵¹ as explained in SI15. Using the activation barriers for etching, as listed in Table 2, we used our combined graph-theoretic-KMC methodology to simulate the MPIs for $N=9$ atoms removed from the hBN lattice. Similar to graphene, only when the B/N etching rates are calculated in the presence of silicon contaminant atoms, the KMC simulations yield the experimentally observed nitrogen-terminated triangular defects (see the simulated pore shapes in Fig. 4 and Supplementary Fig. 14). As Fig. 4 shows, solely triangular shapes with nitrogen-

terminated edges are formed, comparing well with experimental findings. These results give further confidence that, with knowledge of lattice energetics alone, the proposed approach can find realistic isomers for 2D lattices.

Fig. 4 | Solution of the ICP for nanopores in monolayer hBN. (A) Molecular model of the only nanopore isomer obtained in 1000 KMC simulations, for a pore of size $N=9$. 100% of the observed pores (“1/1”) are triangular in shape and have edges terminated with nitrogen atoms. Nitrogen atoms are depicted in blue color and boron atoms are depicted in cream color. (B-E) Experimental TEM images, adapted from Ref. 48 (B), Ref. 49 (C), Ref. 50 (D), Ref. 26 (E), and Ref. 51 (F), demonstrating a prevalence of triangular nanopores in the hBN samples. (Copyright © 2009 and 2016 American Chemical Society, © 2015 Royal Society of Chemistry, © 2010 American Physical Society, and © 2017 Nature Publishing Group).

Conclusions

In this work, we have developed and demonstrated a solution to the ICP for graphene and hBN nanopores that should readily extend to other 2D systems. Combining *ab initio* calculations of etching and edge diffusion activation barriers with KMC simulations and chemical graph theory generates a nanopore catalog demonstrating remarkable agreement with experimental data. However, nanopore shapes simulated based on electron-beam scattering-derived etching rates do not agree with experimental data. We find that the thermodynamic stability of nanopores

is different than their kinetic stability. While experimentalists can use the approach developed herein to obtain insights into the atomic structures that could be present in their nanoporous 2D material samples, theorists could use this framework to rationally choose nanopore systems to work with. The methodology to solve ICPs presented herein improves understanding of the shape and size distributions of nanopores present in 2D materials, and could be extended to predict the role of pore termination and chemistry in nanopore formation.

Author Contributions

A.G.R., D.B., and M.S.S. formulated the solution to the ICP, including the isomer distinguishing methodology. A.G.R. carried out *ab initio* and KMC simulations and performed data analysis. K.S.S. assisted in formulating the isomer distinguishing methodology. J.S. prepared the graphene nanopore sample depicted as Fig. 3c. A.W.R. and J.H.W. contributed to understanding the kinetics of silicon-catalyzed etching of graphene nanopores and provided TEM images of graphene nanopores depicted as Fig. 3b. A.G.R., D.B., and M.S.S. wrote the manuscript. All authors commented on the final version of the manuscript.

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Competing Interest

The authors declare no competing interests.

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Methods

DFT Calculations. Electronic structure density functional theory (DFT) calculations for graphene were carried out using the mixed Gaussian and plane waves (GPW) approach,⁵³ as implemented in the open-source package cp2k.⁵⁴ For hBN, we utilized the Projector Augmented Wave (PAW) formalism,^{55,56} as implemented in the Vienna *Ab initio* Simulation Package (VASP).^{57,58} In both cases, spin polarization was taken into account, and due to large supercell sizes, reciprocal space sampling was limited to the Γ point in k -space. The Perdew-Burke-Ernzerhof (PBE)⁵⁹ generalized gradient approximation (GGA) functional was utilized to represent the exchange-correlation energy of the system. Vacuum space of about 20 Å was provided in the direction perpendicular to the graphene/hBN nanoribbon plane, as well as in the direction perpendicular to the nanoribbon edge. Molecular structures were geometry optimized so that the maximum force on any atom was less than 0.005 eV/Å. Enthalpies of etching (ΔH_{etch}) were determined using the relaxed energies as: $\Delta H_{etch} = (E_{edge-1} + E_{atom,bulk}) - E_{edge}$, where E_{edge} is the energy of the pristine edge, E_{edge-1} is the energy of the respective edge with one carbon (C), boron (B), or nitrogen (N) atom removed, and $E_{atom,bulk}$ is the energy of a single C, B, or N atom in the respective equilibrium phase. For carbon, the most-stable allotrope is graphite, for boron, it is the β -rhombohedral phase, and for nitrogen, it is the gaseous state. Accordingly, $E_{atom,bulk}$ for carbon is the energy of one carbon atom in the graphene lattice, for boron, it is the energy of one boron atom in the β -rhombohedral phase (whose unit cell contains 105 atoms), and for nitrogen, it is half the energy of a single isolated nitrogen

molecule (because gaseous densities are very low, we can assume an isolated molecule in our calculations). In the calculation of both E_{edge} and E_{edge-1} , a silicon atom was used to passivate the edge. It is well-known experimentally that silicon atoms are prominent impurities in CVD grown 2D material samples, and often contribute to etching of nanopores.^{25,38} Climbing image nudged elastic band (CI-NEB)⁶⁰ calculations were used to determine the activation barriers for various atomic rearrangements (edge diffusion processes) in the graphene lattice. Whenever possible, the CI-NEB calculations were well-converged such that forces in the direction perpendicular to the minimum energy path are less than 0.0005 Ha/Bo ($=0.0257$ eV/Å). Because the CI-NEB calculations were tedious to converge, for some cases, we were only able to converge to less stringent criteria. These criteria are documented in SI17. Formation energies of nanopores (ΔH_f) were calculated using DFT as: $\Delta H_f = (E_{pore} + NE_C) - E_{pristine}$, where N is the number of carbon atoms removed, $E_{pristine}$ is the energy of the pristine graphene lattice, E_{pore} is the energy of the graphene lattice with the pore atoms removed, and E_C is the energy of one carbon atom in the graphene lattice.

Details Regarding cp2k Calculations. In cp2k, the molecularly optimized (MOLOPT) triple zeta basis sets with two polarization functions (TZV2P)⁶¹ were used to describe the valence electrons in carbon and silicon atoms. Norm-conserving Godecker-Hutter-Tutter (GTH) pseudopotentials⁶² were used to describe the core electrons. The plane wave cutoff was set to a value of 450 Ry, with a relative cutoff of 60 Ry. Grimme’s D3 dispersion correction⁶³ was applied to account for van der Waals interactions. Fermi-Dirac smearing at a temperature of 300 K was utilized to speed up the convergence of the DFT calculations.

Details Regarding VASP Calculations. In VASP, a plane wave energy cutoff of 500 eV was utilized. Grimme’s D3 dispersion correction with Becke-Johnson damping⁶⁴ was applied to

account for the van der Waals interactions. Gaussian electron density smearing, with a width of 0.2 eV, was utilized to rapidly converge the DFT calculations. The projection operators were evaluated in real space, with fully automatic optimization of the projection operators.

KMC Simulations. Kinetic Monte Carlo (KMC) simulations³² based on Gillespie’s algorithm⁶⁵ were carried out using a code developed in MATLAB R2016b, at a temperature of 500 °C.²⁵ Note that three important modifications need to be accommodated in the standard KMC algorithm before simulating the formation of nanopores along with edge diffusion. The first is that the system should be prevented from getting stuck in “superbasins”³² during the course of the simulation, due to certain rates being much faster than the others (see Supplementary Table 1). For this purpose, if the system visits the same set of states repeatedly in the simulation, then, after a certain number of steps (say, 50), any one of the steps which takes the system out of the superbasin is selected with Gillespie’s probability. This is because, due to rapid kinetics, the system is equally likely to be in any of the states of the superbasin, and therefore, all the pathways which lead the system out of the superbasin are considered. This concept is explained with an illustration in Supplementary Fig. 15. Secondly, any atom cannot migrate to a site having no neighbors (because the enthalpy change involved in such a process, as documented in SI19, is massively endothermic). If any such “hanging” atom is created by the etching process, it can migrate to any neighbor, nearest-neighbor, or next-nearest neighbor site in a barrierless fashion. The third modification to the KMC algorithm is required because the *ab initio* calculated activation barriers for edge diffusion processes are “off-lattice”, in that they correspond to energetically minimized (using DFT) initial and final states, and therefore, do not correspond to atoms existing solely at the perfect crystal lattice positions. On the other hand, the KMC simulation is carried out in an “on-lattice” framework. As a result, we do not allow any edge

diffusion process, which results in a reduction in the number of bonded neighbors of a diffusing atom (these transitions are highlighted in yellow color in Table 1). Most of these transitions possess barriers which are much higher than 2.5 eV, and therefore, are anyway slower than the etching of atoms in the system. For transitions $2A \rightarrow 1$ (N) and $2Z \rightarrow 1$ (N), which possess a barrier of zero, the energy minimized initial and final states have the same energy, whereas the states before energy minimization necessarily do not possess the same energy, such that one of the states in the on-lattice representation is higher in energy than the other. This implies that, for the KMC simulation to remain as close as possible to the minimum potential energy surface, only those transitions having a zero barrier should be allowed, wherein the system lowers its energy, by increasing its number of bonded neighbors, in the corresponding on-lattice move. In other words, moves $1 \rightarrow 2A$ (N) and $1 \rightarrow 2Z$ (N) should be allowed, while moves $2A \rightarrow 1$ (N) and $2Z \rightarrow 1$ (N) should not be allowed. Further, transition $3 \rightarrow 1$ (NN), possessing a barrier of 0.872 eV, upon geometry optimization, corresponds to a 5-7 ring transformation at the edge (see SI17), and therefore, should not be included in the on-lattice description. Finally, we have observed that including transition $2Z \rightarrow 1$ (NNN), possessing a barrier of 1.091 eV, leads to simulated pore shapes which are significantly different from the experimentally observed shapes, and therefore, should be excluded from the rate catalog.

Isomer Distinguishing Methodology. We use a graph theoretic approach to compare the shapes of various nanopore isomers. To this end, the adjacency matrix of the antimolecule of a nanopore is used as its graph representation. The MATLAB Bioinformatics toolbox has in-built functions to determine whether two adjacency matrices are isomorphic. Because bonds in 2D materials are not freely rotatable, we also include the orientations of bonds in the antimolecule into the analysis. The graphene lattice consists of two hexagonally-arranged sublattices, labeled A and B.

As illustrated in Supplementary Fig. 16, there are three possible orientations for bonds originating at an A-sublattice carbon: bottom, top-left, and top-right, and three possible orientations for bonds originating at a B-sublattice carbon: top, bottom-left, and bottom-right. Since each A-sublattice carbon is connected to a B-sublattice carbon, only three of these orientations are sufficient to be included in the adjacency matrix of the antimolecule; we choose the bond orientations corresponding to the B-sublattice carbons, i.e., top, bottom-left, and bottom-right. To represent directionalities within the graph isomorphism framework, different edge lengths are assigned to differently-oriented bonds. Accordingly, a pre-determined number of fictitious atoms are introduced into the antimolecule and are inserted in between any two neighboring carbon atoms, as follows: (i) for a top-oriented bond, zero fictitious atoms are introduced, (ii) for a bottom-left-oriented bond, one fictitious atom is introduced, and (iii) for a bottom-right-oriented bond, two fictitious atoms are introduced. To account for the symmetry of graphene, as explained in SI20, the adjacency matrix of a given antimolecule is compared to the 12 symmetry-equivalent adjacency matrices of another antimolecule, to check for isomorphism. For hBN, we further ensure that two identical isomers have an equal number of B and N atoms removed, respectively.

Experimental Details for the Nanopores Labeled “b” in Fig. 3. Graphene was prepared using chemical vapor deposition, utilizing liquid copper as the catalyst.^{66,67} Copper (Cu) on tungsten (W) was placed in a split-tube furnace, where it was annealed at 1090 °C, with 200 standard cubic centimeters (sccm) argon (Ar) and 100 sccm 25% hydrogen (H₂) in Ar gas flow for 30-60 min, thereby melting the copper. The H₂/Ar flow was then decreased to 80 sccm and a 10 sccm methane (CH₄)/Ar mix (1% CH₄) was introduced into the furnace for 90 min. Subsequently, the sample was cooled to 1060 °C for 30 min under gas flow to fill in the graphene.⁶⁷ The graphene

was removed from the furnace and quickly cooled to room temperature under a H₂ and Ar atmosphere. A PMMA layer was spin coated on to the graphene/Cu/W stack before etching the metals. W was etched by attaching the sample as an anode in the electrolysis of 2 M NaOH solution with Cu as the cathode. The Cu was etched by floating the sample on 1 M ammonium persulfate solution, followed by extensive HCl, and DI water rinse stages to clean the graphene. The PMMA/graphene film was transferred to a TEM grid, and the PMMA was removed by baking in the ambient atmosphere at 350 °C overnight. Imaging was performed at 80 kV on Oxford's JEOL 2200MCO aberration corrected TEM, with single atom resolution images captured with the monochromator, using a 5 µm slit to reduce the beam energy spread to ~0.3 eV. A DENS solutions heating holder was used to heat the sample to temperatures of 500-700 °C to allow imaging of subnanometer pores before being filled. Images presented have been subjected to bandpass filtering and Savitzky-Golay smoothing. An upper estimate of the electron flux incident on the sample is $10^5 \text{ e nm}^{-2} \text{ s}^{-1}$, however insertion of the monochromator slit will act to reduce this flux.²⁵

Experimental Details for the Nanopore Labeled “c” in Fig. 3. The 8-carbon atom sized pore in graphene, labeled as “c” in Fig. 3, was generated by bombarding a graphene sample with Xeon ions (Xe⁺) with an energy of 500 eV, at ambient temperature. The irradiation chamber was evacuated to a pressure of 2×10^{-7} Torr a priori. Aberration-corrected scanning transmission electron microscopy (AC-STEM) imaging was performed using a Nion UltraSTEM100 operated at 60 kV accelerating voltage (60 pA probe current, 16 µs dwell time, 15.6 pm pixel size). Medium-angle annular dark-field (MAADF) images were acquired with a convergence semi-angle of 30 mrad and a collection semi-angle of 54–200 mrad. Prior to STEM imaging, the samples were baked for approximately 8 h under high vacuum at 160 °C in order to reduce

surface contamination. The AC-STEM image was post-processed using the Richardson-Lucy deconvolution algorithm available in MATLAB in order to generate the image shown in Fig. 3c.

Data Availability. The datasets generated during and/or analysed during the current study, including the XYZ files of the most-probable isomers, are available online at https://github.com/srgmit/nanopore_isomers, under the directory “catalog”.

Code Availability. The custom KMC and chemical graph theory code developed for this work in MATLAB is available online at https://github.com/srgmit/nanopore_isomers.

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