

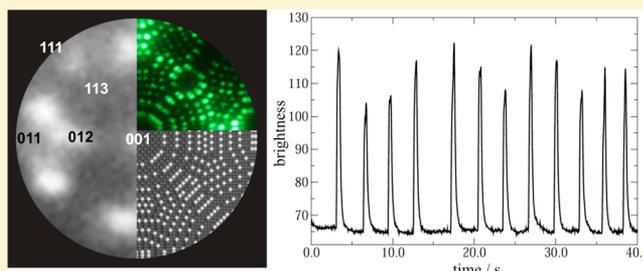
Fluctuating Dynamics of Nanoscale Chemical Oscillations: Theory and Experiments

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ABSTRACT: Chemical oscillations are observed in a variety of reactive systems, including biological cells, for the functionality of which they play a central role. However, at such scales, molecular fluctuations are expected to endanger the regularity of these behaviors. The question of the mechanism by which robust oscillations can nevertheless emerge is still open. In this work, we report on the experimental investigation of nanoscale chemical oscillations observed during the $\text{NO}_2 + \text{H}_2$ reaction on platinum, using field electron microscopy. We show that the correlation time and the variance of the period of oscillations are connected by a universal constraint, as predicted theoretically for systems subjected to a phenomenon called phase diffusion. These results open the way to a better understanding, modeling, and control of nanoscale oscillators.



Chemical reactions are at the heart of a vast amount of self-organized phenomena found in both animate and inanimate systems. Such behaviors include, but are not limited to, the coexistence of multiple stationary states, the emergence of oscillations, and the chaotic evolution of concentrations in space and time. These emerging organizations play a central role in the dynamics of reactive systems ranging from tabletop experiments to industrial applications to biological cells.

The constructive role played by nonequilibrium reactions in the development of a macroscopic order has been clarified and put on a firm theoretical basis by Prigogine and co-workers.¹ Because of the intrinsically nonlinear character of their macroscopic kinetics, chemical reactions can destabilize the states emanating from equilibrium, which form the so-called thermodynamic branch. This destabilization can lead to the sudden appearance of new behaviors, among which one can encounter the aforementioned complex phenomena.

The above macroscopic approach has been used successfully to assess the origin of many nonlinear phenomena, including, in particular, oscillations observed in heterogeneous catalysis and in living cells.^{2–4} In both of these cases, however, chemical reactions take place in extremely small systems. The diameter of catalytic particles ranges from a few to about a hundred nanometers, and that of a biological cell is typically on the order of the micrometer. At such a scale, the atomic structure of matter manifests itself in the form of important molecular fluctuations, which affect the time evolution of all observables. These fluctuations could in principle modify or altogether destroy the self-organized phenomena. It is thus crucial to understand the role that they play in nanoscale dynamics.

If much effort has been devoted to unveil the properties of fluctuations in systems at or close to thermodynamic equilibrium, much less is known about fluctuations in far-from-equilibrium systems, where the self-organization takes place. Theoretical studies of such noisy systems have been developed since the 1970s,^{5,6} and several effects have been investigated, such as noise-induced bistability,⁷ transitions between coexisting states induced by external or internal noise,^{8–12} stochastic resonance,^{13–17} or variability and robustness in gene expression.^{18–20} The studies performed thus far and the conclusions drawn from them rely almost exclusively on the use of stochastic approaches. In this framework, one assumes that the reactive processes can be modeled as random events, so that the statistics of the concentrations and their fluctuations is captured by a relatively simple evolution equation for the probability to find the system in a given state.

Experimental verifications of the validity of the stochastic approach for nanoscale reactions have lagged behind for a long time. Recent advances in experimental techniques have however allowed the study of far-from-equilibrium systems at the nanoscale. In particular, the discovery of nonlinear behaviors with field electron and field ion microscopes has opened new perspectives.^{11,21–25} The metallic tip used in such microscopes has a radius of curvature of about 20 nm at the apex. The dynamics of reactions can be followed in regions

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comprising only a few hundred adsorption sites, a size for which molecular fluctuations are expected to play an important role.

The purpose of this work is to report on experimental results supporting fundamental assumptions of the stochastic theory used to describe nanoscale noisy oscillators. The question of the role played by fluctuations is pivotal for understanding the robustness of chemical clocks at the nanometric scale. We focus in particular on the phase diffusion induced by noise. According to this mechanism, the phase of the oscillator undergoes a random walk of Gaussian character, which is justified by the central limit theorem. Moreover, noisy oscillations are expected to lose their synchrony as periods repeat. This loss of synchrony can be characterized by the correlation time, which is defined as the damping time of the temporal autocorrelation function of the signal. Theory predicts a universal relationship between phase diffusion and the correlation time of oscillations, which we aim to test experimentally.

The experiments were carried out in a stainless steel field emission microscope with a base pressure of 10^{-10} mbar. Details about the setup and principles of the methods can be found elsewhere.²⁶ The platinum field emitter tips were prepared by electrochemical etching and subsequently cleaned in a ultrahigh vacuum chamber by cycles of field evaporation, thermal annealing, and ion sputtering, as described in ref 27. Figure 1 shows an image of the surface of the resulting sample obtained by field ion microscopy at low temperature.

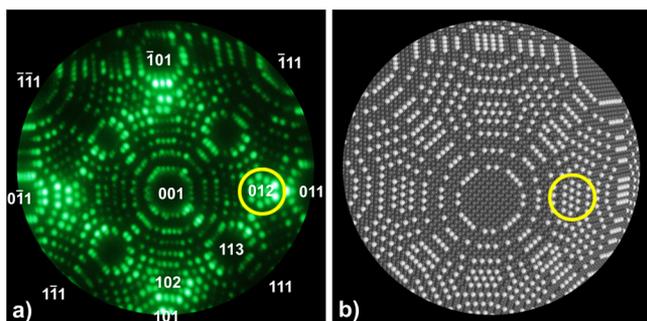


Figure 1. (a) A micrograph of a (001)-oriented Pt sample, imaged by field ion microscopy at low temperature (40 K), with $F = 44 \text{ V}\cdot\text{nm}^{-1}$ and $p_{\text{He}} = 2 \times 10^{-5}$ mbar. The diameter of the visible area is approximately 35 nm. The tip presents different facets and channels, corresponding to different crystallographic planes and directions. The region of interest, in which the brightness has been followed in real time during the reaction, corresponds to a (012) facet and is shown in each figure. (b) A top view of a ball model for the apex of the Pt samples used in the experiments. The protruding atoms appear brighter to facilitate comparison with the previous micrograph.

Field electron microscopy (FEM) was used to monitor the ongoing reaction. Typically, the procedure consisted of heating the sample to 390 K and then applying a field of about $4 \text{ V}\cdot\text{nm}^{-1}$. A mixture of nitrogen dioxide (98% purity) and dihydrogen (99.9996% purity) was then admitted into the chamber. The partial pressures were measured by a Bayard–Alpert gauge. The values that we report take into consideration the gas correction factors. The dynamics of the reaction was followed by filming a phosphor screen, which collects the output of a multichannel plate used to amplify the electronic signal emitted from the tip sample. The video recording device

has a time resolution of 40 ms digitized with a dynamic range of 8 bits.

The time series used for the statistical treatments correspond to variations of the brightness of the image as measured by the gray level over a fixed region of interest, from which the background brightness was subtracted. The region of interest that we followed corresponds to one of the {012} facets and extends over approximately 10 nm^2 (see Figure 1). The first return times were computed as the time it takes for the signal to cross its average brightness during an oscillation, on the way up. Statistics obtained with different definitions of the first return time (for example, the crossing time during a decrease of the intensity of the signal) were tested and shown to lead to no discernible differences with the results presented here. The histograms were obtained by using Scott's normal reference rule²⁸ for the width of the bins. The (unbiased) autocorrelation functions were calculated with the corresponding Matlab built-in function. The correlation times (see later in the text) were obtained by a linear regression of the logarithm of the maxima of the autocorrelation function.

We started the experiments by setting a constant pressure of NO_2 and then increasing the pressure of H_2 . The surface was in each case monitored for several minutes to detect kinetic instabilities. These experiments revealed that highly regular oscillations of the brightness could be observed above a critical pressure of H_2 , $p_{\text{H}_2}^c$ (see Figure 2a). FEM micrographs of the oscillating behavior are not shown here but can be found in previous publications (see, for example, ref 40). The first oscillations (i.e., those observed just beyond the critical pressure) have a relatively large amplitude and a low frequency. Both the amplitude and the period tend to fluctuate, however. This feature is not surprising in view of the very small size of the system under investigation. We will come back to this important point later on. As the distance from the critical pressure increases, the mean amplitude of the oscillations remains constant to some extent. The mean frequency increases, as pictured in Figure 2b. Note that when the NO_2 pressure is larger than the one used for the depicted results, the frequency presents a maximum that is observed at a well-defined pressure, and after which, it slowly decreases. In all cases, in the vicinity of the critical pressure, the mean frequency scales as $\nu \propto (\text{cst} - \ln \mu)^{-1}$, where $\mu = (p_{\text{H}_2} - p_{\text{H}_2}^c)/p_{\text{H}_2}$, which is consistent with the transition being a homoclinic bifurcation.²⁹

The oscillations that we observe are due to the fact that the catalytic surface is an open reactor, in which nonlinear chemical processes are taking place. Potential chemical mechanisms explaining these oscillations are discussed elsewhere.^{27,40} Here, we want to assess in detail the variability of the oscillating process itself. More precisely, our objective is to verify whether the statistical properties of the fluctuating oscillations respect universal features, as predicted by stochastic theories.

The dynamics of reactive systems at the nanoscale is usually assessed on the basis of a chemical master equation.⁶ In such an approach, the reactions are seen as Markovian stochastic processes satisfying well-defined physicochemical constraints. The study of oscillating reactions has shown that fluctuations affect both the amplitude and the periodicity of the process. In the macroscopic limit, where the effects of fluctuations can be neglected, oscillating reactions define a limit cycle in the phase space spanned by the concentrations of the different species. One can then define a first return time as the time taken by the system to come back to a given point on the cycle. In the

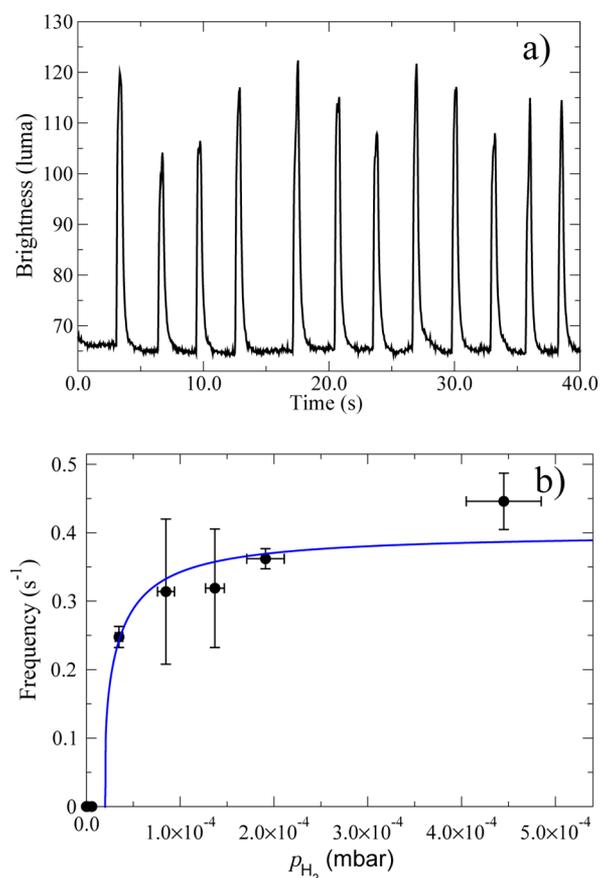


Figure 2. (a) Oscillations of the brightness of the image observed in the region of interest depicted in Figure 1, for a temperature of 390 K, $p_{\text{NO}_2} = 5.43 \times 10^{-6}$ mbar, $p_{\text{H}_2} = 8.48 \times 10^{-5}$ mbar, and an applied field of $4.0 \text{ V}\cdot\text{nm}^{-1}$. (b) Bifurcation diagram plotting the frequency of the oscillations as a function of the pressure of H_2 . All other control parameters are the same as those in (a). The line is a best fit obtained with $\nu = 0.54 \times (1.35 - \ln \mu)^{-1}$ (see the text for more details).

macroscopic limit, this time is equal to the period of the oscillations.

For smaller systems where noise manifests itself, a phenomenon called phase diffusion has been reported.^{30–34} The spontaneously occurring fluctuations induce a diffusion of the trajectories along (i.e., tangentially to) the limit cycle. As a

consequence, the first return time is a statistically distributed quantity. Starting from the master equation for a homogeneous system, it has been shown that in the weak noise limit (where the master equation actually reduces to a Fokker–Planck equation), the first return time T has a Gaussian distribution

$$P(T) = \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left[-\frac{(T - \langle T \rangle)^2}{2\sigma^2}\right] \quad (1)$$

In this formula, $\langle T \rangle$ is the mean period of the noisy limit cycle and σ^2 the variance of the distribution. This prediction is valid for a fully developed cycle, in other words, when the system evolves far away from any bifurcation point. The variance of the first return time is related to the amplitude of the noise $\epsilon = 1/\Omega$, where Ω is proportional to the system size by^{35–38}

$$\sigma^2 = \epsilon F \quad (2)$$

In this equation, F is a function that critically depends on the details of the mechanism and on the rates of the reactions taking place in the system. It is thus highly system-specific.

The phase diffusion is also known to affect the shape of the temporal autocorrelation function

$$C(t - t') \equiv \frac{\langle X(t)X(t') \rangle - \langle X(t) \rangle \langle X(t') \rangle}{\langle X^2(t) \rangle - \langle X(t) \rangle^2} \quad (3)$$

in which $X(t)$ is the brightness in the region of interest at a given time. The brackets represent averaging over time. This function measures how strongly correlated two measurements performed at a temporal distance $t - t'$ are during the oscillations. It has been predicted that $C(t - t')$ presents damped oscillations in the case of a noisy limit cycle, first for specific examples of simple reactions^{32,39} and then in a more general fashion.^{36,37} More precisely, it has been shown that the envelope of this function decreases exponentially as $e^{-t/\tau}$ with a decay rate given by

$$\tau = \frac{\langle T \rangle^3}{2\pi^2 \epsilon F} \quad (4)$$

Like the variance of the first return time, this quantity depends on the details of the reactions through the system-specific function F . Despite these specificities, it appears that all of the fluctuating oscillations that comply with the hypotheses of the stochastic approach should be such that the product of their relative variance and their relative decay rate is a constant

Table 1. Selected Experimental Time Series Summarizing the Conditions and the Measurements for the Experiments Retained in the Statistical Treatments^a

experiment	p_{NO_2} (mbar)	p_{H_2} (mbar)	period (s)	τ (s)	σ (s)
1	5.43×10^{-6}	3.48×10^{-5}	4.04	11.5	0.251
2	5.43×10^{-6}	1.91×10^{-4}	2.76	145.2	0.128
3	5.43×10^{-6}	4.45×10^{-4}	2.24	23.36	0.249
4	5.36×10^{-6}	1.57×10^{-4}	4.28	8.5	0.49
5	5.36×10^{-6}	2.41×10^{-4}	2.96	6.8	0.38
6	3.64×10^{-6}	1.05×10^{-4}	3.05	185.7	0.044
7	3.64×10^{-6}	1.46×10^{-4}	2.71	821.2	0.0230
8	3.64×10^{-6}	2.10×10^{-4}	2.36	109.4	0.057
9	3.64×10^{-6}	4.00×10^{-4}	5.900	87.5	0.322
10	2.16×10^{-6}	2.00×10^{-4}	8.90	49.2	0.73
11	2.16×10^{-6}	2.18×10^{-4}	10.42	26.8	1.03
12	2.16×10^{-6}	2.44×10^{-4}	13.52	32.0	1.49

^aIn each case, the temperature is 390 K.

$$\left(\frac{\sigma^2}{\langle T \rangle^2}\right) \left(\frac{\tau}{\langle T \rangle}\right) = \frac{1}{2\pi^2} \quad (5)$$

We extracted the statistics of numerous experiments in order to verify the above predictions. The oscillations observed just after crossing the critical pressure were discarded in order to account for the fact that the aforementioned results hold far from bifurcation points. The 12 selected experiments are listed in Table 1. Histograms of four of the chosen experiments are shown in Figure 3. The experiments correspond to different

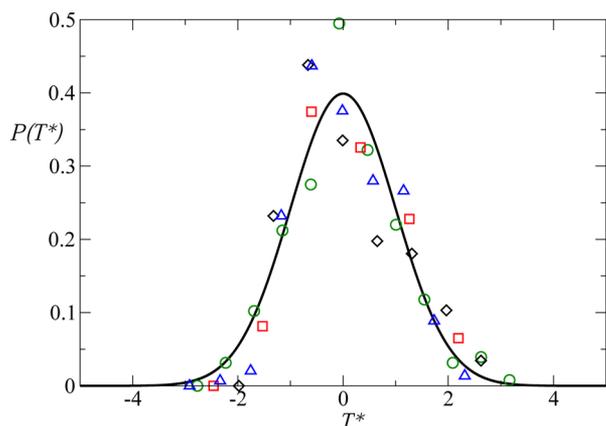


Figure 3. Centered probability distribution for the rescaled and centered period, $T^* = (T - \langle T \rangle)/\sigma$, taken from four experiments performed at four different pressures of NO_2 . Experiments 1, 4, 8, and 10 appear, respectively, as black diamonds, green circles, blue triangles, and red squares. The plain curve is a normal distribution, the mean and variance of which are 0 and 1, respectively.

partial and total pressures and sometimes different platinum tips. The corresponding oscillations have different shapes, and their average periods differ. It nevertheless appears that in all cases, the first return time closely follows a normal distribution, as predicted by the Fokker–Planck equation.

The autocorrelation functions were also extracted from these experiments. They indeed consist of damped oscillations, as reported earlier.⁴⁰ The correlation time was obtained by fitting each of the decaying envelopes of these oscillations with an exponential function. By combining these results with the variance and the mean of the first return times, σ^2/T^2 and τ/T were calculated. Figure 4 shows a plot of the logarithm of these two quantities. The best linear fit of these data gives an intercept of -2.6 ± 0.7 and a slope of $-(0.9 \pm 0.1)$. The theoretical approach based on the Fokker–Planck equation predicts that

$$\ln \frac{\tau}{\langle T \rangle} = \ln \frac{1}{2\pi^2} - \ln \frac{\sigma^2}{\langle T \rangle^2} \approx -2.98 - \ln \frac{\sigma^2}{\langle T \rangle^2} \quad (6)$$

Our results thus confirm the predictions of the stochastic description in the weak noise limit.

Our goal was to investigate the fluctuating dynamics of nanoscale oscillating reactions through high-precision measurements performed by a microscope with nanometric lateral resolution. The experimental data and their subsequent statistical treatment form the first reported evidence that stochastic approaches can indeed be used to assess the noisy behavior of chemical clocks. They confirm that phase diffusion is a key phenomenon affecting the regularity and hence the

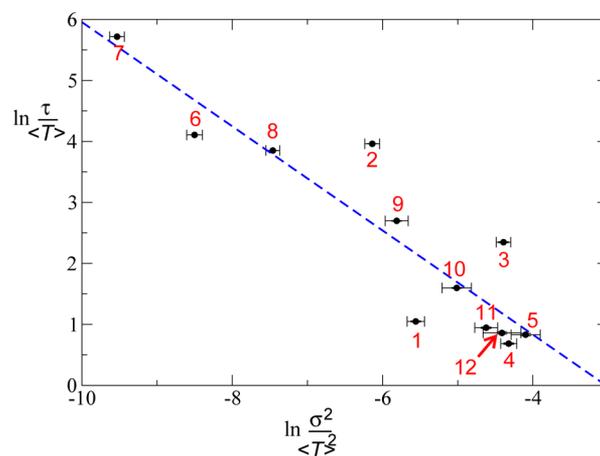


Figure 4. Logarithm of the relative lifetime as a function of the logarithm of the relative variance of the period of oscillations. The points correspond to the selected periodic behaviors (see Table 1). The dashed line is the best linear fit of the data. Its intercept and slope are consistent with the proposed scaling, as discussed in the text.

robustness and the controllability of chemical reactions at such scales.

We plan to assess the universal character of these results by studying other oscillating reactions with the same technique (such as the $\text{NO}_2 + \text{H}_2$ or the $\text{O}_2 + \text{H}_2$ reactions on rhodium). Future work should also address the issue of the determination of nonuniversal aspects of such systems. Besides the understanding of the reaction mechanism at the origin of oscillations, several issues remain open, in particular, the determination of the noise amplitude $\epsilon = \Omega^{-1}$, which is related to the system size. One of the basic assumptions of the theoretical results that we used is that the system under consideration is well-mixed. The robustness of the oscillations that we observed suggests that the number of particles involved in the phenomenon is larger than what can be found on the single monitored facet. This observation implies that a mechanism of synchronization exists, which is able to couple different parts of the sample so that ϵ is effectively small. The nature and the efficiency of such coupling should be investigated in detail.

The variance and the correlation time of oscillations are determined by the function F , which depends on the chemical mechanistic details of the oscillations. Our results suggest that information on these nonuniversal features can be extracted using time series analysis. The validity of proposed chemical mechanisms could be assessed not only from the predictions that they lead to concerning the average behavior of the system but also from the very structure of the fluctuations around such an average.

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Notes

The authors declare no competing financial interest.

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REFERENCES

- (1) Glansdorff, P.; Prigogine, I. *Thermodynamic Theory of Structure, Stability, and Fluctuations*; Wiley-Interscience: London, 1971.
- (2) Imbihl, R.; Ertl, G. Oscillatory Kinetics in Heterogeneous Catalysis. *Chem. Rev.* **1995**, *95*, 697–733.
- (3) Goldbeter, A. *Biochemical Oscillations and Cellular Rhythms*; Cambridge University Press: Cambridge, U.K., 1996.
- (4) Epstein, I. R.; Pojman, J. A. *An Introduction to Nonlinear Chemical Dynamics*; Oxford University Press: New York, 1998.
- (5) Nicolis, G. Fluctuations around Nonequilibrium States in Open Nonlinear Systems. *J. Stat. Phys.* **1972**, *6*, 195–222.
- (6) Nicolis, G.; Prigogine, I. *Self-Organization in Nonequilibrium Systems*; Wiley: New York, 1977.
- (7) Fichthorn, K.; Gulari, E.; Ziff, R. Noise-Induced Bistability in a Monte Carlo Surface-Reaction Model. *Phys. Rev. Lett.* **1989**, *63*, 1527–1530.
- (8) Horsthemke, W.; Lefever, R. Phase Transition Induced by External Noise. *Phys. Lett. A* **1977**, *64*, 19–21.
- (9) Smythe, J.; Moss, F.; McClintock, P. V. E. Observation of a Noise-Induced Phase Transition with an Analog Simulator. *Phys. Rev. Lett.* **1983**, *51*, 1062–1065.
- (10) Erdmann, U.; Ebeling, W.; Mikhailov, A. S. Noise-Induced Transition from Translational to Rotational Motion of Swarms. *Phys. Rev. E* **2005**, *71*, 051904.
- (11) Suchorski, Yu.; Beben, J.; James, E. W.; Evans, J. W.; Imbihl, R. Fluctuation-Induced Transitions in a Bistable Surface Reaction: Catalytic CO Oxidation on a Pt Field Emitter Tip. *Phys. Rev. Lett.* **1999**, *82*, 1907–1910.
- (12) Suchorski, Yu.; Beben, J.; Imbihl, R.; James, E. W.; Liu, D.-J.; Evans, J. W. Fluctuations and Critical Phenomena in Catalytic CO Oxidation on Nanoscale Pt Facets. *Phys. Rev. B* **2001**, *63*, 165417.
- (13) Benzi, R.; Sutera, A.; Vulpiani, A. The Mechanism of Stochastic Resonance. *J. Phys. A* **1981**, *14*, L453–L457.
- (14) Nicolis, C. Solar Variability and Stochastic Effects on Climate. *Solar Phys.* **1981**, *74*, 473–478.
- (15) Guderian, A.; Dechert, G.; Zeyer, K.-P.; Schneider, F. W. Stochastic Resonance in Chemistry. 1. The Belousov–Zhabotinsky Reaction. *J. Phys. Chem.* **1996**, *100*, 4437–4441.
- (16) Förster, A.; Merget, M.; Schneider, F. W. Stochastic Resonance in Chemistry. 2. The Peroxidase–Oxidase Reaction. *J. Phys. Chem.* **1996**, *100*, 4442–4447.
- (17) Hohmann, W.; Müller, J.; Schneider, F. W. Stochastic Resonance in Chemistry. 3. The Minimal-Bromate Reaction. *J. Phys. Chem.* **1996**, *100*, 5388–5392.
- (18) McAdams, H. H.; Arkin, A. Stochastic Mechanisms in Gene Expression. *Proc. Natl. Acad. Sci. U.S.A.* **1997**, *94*, 814–819.
- (19) Barkai, N.; Leibler, S. Circadian Clocks Limited by Noise. *Nature* **2000**, *403*, 267–268.
- (20) Gonze, D.; Halloy, J.; Goldbeter, A. Robustness of Circadian Rhythms with Respect to Molecular Noise. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 673–678.
- (21) van Tol, M. F. H.; Gilbert, M.; Nieuwenhuys, B. E. Oscillatory Behaviour of the Reduction of NO by H₂ over Rh. *Catal. Lett.* **1992**, *16*, 297–309.
- (22) Gorodetskii, V.; Block, J. H.; Ehsasi, M. Oscillations in the Carbon Monoxide Oxidation on Platinum Surfaces Observed by Field Electron Microscopy. *Appl. Surf. Sci.* **1992**, *67*, 198–205.
- (23) Gorodetskii, V.; Drachsel, W.; Block, J. H. Imaging the Oscillating CO-Oxidation on Pt-Surfaces with Field Ion Microscopy. *Catal. Lett.* **1993**, *19*, 223–231.
- (24) Voss, C.; Kruse, N. Oscillatory Behavior in the Catalytic Reduction of NO and NO₂ with Hydrogen on Pt field Emitter Tips. *Appl. Surf. Sci.* **1996**, *94/95*, 186–193.
- (25) Visart de Bocarmé, T.; Bär, T.; Kruse, N. In Situ Dynamic Study of Hydrogen Oxidation on Rhodium. *Ultramicroscopy* **2001**, *89*, 75–82.
- (26) Gaussmann, A.; Kruse, N. CO-Induced Structural Changes of Pd Particle Surfaces. *Catal. Lett.* **1991**, *10*, 305–315.
- (27) Barroo, C.; De Decker, Y.; Visart de Bocarmé, T.; Kruse, N. Complex Oscillation Patterns during the Catalytic Hydrogenation of NO₂ over Platinum Nanosized Crystals. *J. Phys. Chem. C* **2014**, *118*, 6839–6846.
- (28) Scott, D. W. On Optimal and Data-Based Histograms. *Biometrika* **1979**, *66*, 605–610.
- (29) Gaspard, P. Measurement of the Instability Rate of a Far-from-Equilibrium Steady State at an Infinite Period Bifurcation. *J. Phys. Chem.* **1990**, *94*, 1–3.
- (30) Tomita, K.; Ohta, T.; Tomita, H. Irreversible Circulation and Orbital Revolution: Hard Mode Instability in Far-from-Equilibrium Situation. *Prog. Theor. Phys.* **1974**, *52*, 1744–1765.
- (31) Kitahara, K. The Hamilton–Jacobi-Equation Approach to Fluctuation Phenomena. *Adv. Chem. Phys.* **1975**, *29*, 85–111.
- (32) Walgraef, D.; Dewel, G.; Borckmans, P. Nonequilibrium Phase Transitions and Chemical Instabilities. *Adv. Chem. Phys.* **1982**, *49*, 311–355.
- (33) Kurrer, C.; Schulten, K. Effect of Noise and Perturbations on Limit Cycle Systems. *Physica D* **1991**, *50*, 311–320.
- (34) Vance, W.; Ross, J. Fluctuations near Limit Cycles in Chemical Reaction Systems. *J. Chem. Phys.* **1996**, *105*, 479–487.
- (35) Nicolis, G.; Gaspard, P. Toward a Probabilistic Approach to Complex Systems. *Chaos, Solitons Fractals* **1994**, *4*, 41–57.
- (36) Gaspard, P. Trace Formula for Noisy Flows. *J. Stat. Phys.* **2002**, *106*, 57–96.
- (37) Gaspard, P. The Correlation Time of Mesoscopic Chemical Clocks. *J. Chem. Phys.* **2002**, *117*, 8905–8916.
- (38) Nakanishi, H.; Sakaue, T.; Wakou, J. Hamilton–Jacobi Method for Molecular Distribution Function in a Chemical Oscillator. *J. Chem. Phys.* **2013**, *139*, 214105.
- (39) Baras, F. In *Stochastic Dynamics*; Lecture Notes in Physics 484; Schimansky-Geier, L., Poeschel, T., Eds.; Springer: Berlin, Germany, 1997; pp 167–178.
- (40) McEwen, J.-S.; Gaspard, P.; De Decker, Y.; Barroo, C.; Visart de Bocarmé, T.; Kruse, N. Catalytic Reduction of NO₂ with Hydrogen on Pt Field Emitter Tips: Kinetic Instabilities on the Nanoscale. *Langmuir* **2010**, *26*, 16381–16391.