Dynamical Quorum Sensing and Synchronization in Large Populations of Chemical Oscillators

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Populations of certain unicellular organisms, such as suspensions of yeast in nutrient solutions, undergo transitions to coordinated activity with increasing cell density. The collective behavior is believed to arise through communication by chemical signaling via the extracellular solution. We studied large, heterogeneous populations of discrete chemical oscillators (~100,000) with well-defined kinetics to characterize two different types of density-dependent transitions to synchronized oscillatory behavior. For different chemical exchange rates between the oscillators and the surrounding solution, increasing oscillator density led to (i) the gradual synchronization of oscillatory activity, or (ii) the sudden “switching on” of synchronized oscillatory activity. We analyze the roles of oscillator density and exchange rate of signaling species in these transitions with a mathematical model of the interacting chemical oscillators.

From the periodic firing of neurons to the flashing of fireflies, the synchronization of rhythmic activity plays a vital role in the functioning of biological systems (1–3). The mechanisms by which single cells or whole organisms coordinate their activity continue to inspire research over a range of disciplines (4–6). Synchronization may occur by global coupling, where each oscillator is connected to every other oscillator through a common (mean) field. With this mechanism, mathematically formalized by Kuramoto (7), oscillators are regulated by the average activity of the population (the mean field) and a collective rhythm emerges above a critical coupling strength. A number of oscillatory systems are thought to synchronize by this mechanism (8, 9), such as stirred suspensions of the cellular slime mold Dictyostelium discoideum (10), but it has been experimentally characterized only recently in a system of coupled electrochemical oscillators (11).

A distinctly different type of transition to synchronized oscillatory behavior has been observed in suspensions of yeast cells (12). The density-dependent transition, discovered by Aldridge and Pye (13) more than 30 years ago, recently has been studied in a stirred-flow reactor configuration (14). Relaxation experiments reveal that slightly below the critical cell density, the system is made up of a collection of quiescent cells rather than unsynchronized oscillatory cells, whereas slightly above the critical density, the cells oscillate in nearly complete synchrony (12). This type of transition is much like quorum-sensing transitions in bacteria populations, where each member of a population undergoes a sudden change in behavior with a supercritical increase in the concentration of a signaling molecule (autoinducer) in the extracellular solution (15). Many examples of quorum-sensing transitions have been found, such as the appearance of bioluminescence in populations of Vibrio fischeri (16–18) and biofilm formation in Pseudomonas aeruginosa (19).

We studied a population of chemical oscillators to characterize the transition to synchronization as a function of population density and transport rate of signaling species to the surrounding solution. We used porous catalytic particles (~100 μm in radius) that were suspended in a fixed volume of catalyst-free Belousov-Zhabotinsky (BZ) reaction mixture (20, 21). The catalyst for the reaction, Fe(phen)3 will, ferroin, is immobilized on the cation exchange particles (22, 23). Reagents in the solution react with the ferroin to produce an activator, HBrO2, which catalyzes its own production, and an inhibitor, Br−, which inhibits autocatalysis. A catalyst-loaded particle changes from red to blue as ferroin is oxidized and HBrO2 is produced. The oxidized metal catalyst reacts with solution reagents to regenerate the reduced form of the catalyst and Br−. The cycle repeats when the inhibitor level falls sufficiently. Each catalyst-loaded particle has its own oscillatory period, on the order of 1 min (45 ± 13 s), which depends on the catalyst loading and the particle size. The period distribution (fig. S1) is obtained by monitoring the color change associated with the oxidation of the ferroin catalyst on each particle in unstirred solutions (21, 24).

A sketch of the experimental setup is shown in Fig. 1. Both the activator HBrO2 and inhibitor Br− are exchanged between the catalyst particles and the surrounding solution, with the exchange rate depending on the stirring rate (21). The surrounding solution is monitored with a Pt electrode, where the potential increases with an increasing concentration of HBrO2 relative to Br−, the oxidation state of the particles is monitored by high-speed video (21). The first time series in Fig. 1 illustrates the change in amplitude of the potential as the oscillator density is increased. The second time series shows the corresponding average intensity obtained from the mean of the individual particle intensities in each image (scaled by the average intensity of fully oxidized particles). When all particles are simultaneously oxidized, the scaled average intensity increases from 0 (all particles red) to 1 (all particles blue), and the value is less than 1 when a fraction of the population is oxidized. The coherence of the population can be seen in images of the stirred particles (Fig. 1).

We observed two distinct types of transitions to synchronous activity, depending on the stirring rate. One type occurs at low stirring rates, as

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Fig. 1. Experimental setup (21). Catalytic microparticles are globally coupled by exchange of species with the surrounding catalyst-free BZ reaction solution. Electrochemical time series illustrates the change in oscillatory amplitude and period with increasing particle density (red line) for a stirring rate of 600 rpm. A typical series of images obtained during one oscillation is shown, from which the (normalized) average intensity of the particles is calculated as a function of time. The associated time series illustrates the change in oscillatory amplitude and period with increasing particle density (red line) for a stirring rate of 600 rpm. A density of 0.02 g cm−3 corresponds to ~1.3 × 1010 particles cm−3.
shown in Fig. 2A for 300 rpm. At low particle densities, the global electrochemical signal is noisy with no regular oscillations. There are also no oscillations in the average intensity of the particle images; however, an approximately constant fraction of oxidized catalyst particles is observed (~20%), representing the fraction of the oscillatory cycle in the oxidized state. As the density is increased, small-amplitude oscillations emerge, and there is a gradual growth in the amplitude of the global electrochemical signal. Corresponding oscillations are also observed in the average image intensity. With a density of 0.02 g cm\(^{-3}\), ~50% of the particles are simultaneously oxidized in an oscillation, and this approaches 100% for densities greater than 0.04 g cm\(^{-3}\), as shown by the maximum average intensity as a function of particle density. Also shown is the period of the oscillations decreasing slightly with increasing particle density.

The other type of transition to synchronous activity occurs at high stirring rates. At low particle density, there is no oscillatory signal in the electrochemical potential and there are no oxidized catalyst particles in the associated images, as shown in Fig. 2B for 600 rpm. As the density is increased beyond a threshold value, large-amplitude oscillations in the global signal suddenly appear, and analysis of the average image intensity shows that ~80% of the particles are simultaneously oxidized each oscillation. As the density is increased further, the maximum fraction of oxidized particles during an oscillation approaches a constant value. The period of oscillation, which is greater than in the low stirring rate case, decreases with increasing density.

Insights into these transitions to synchronized oscillatory behavior can be gained by examining a model of the oscillatory particle system (20, 21). A sketch of the exchange between the particles and the surrounding solution is shown in Fig. 3. The model is based on the three-variable ZBKE scheme (25) for the ferroin-catalyzed BZ reaction (26), with variables \( X \) for the autocatalyst, \( Y \) for the inhibitor, and \( Z \) for the oxidized form of the metal ion catalyst. The concentration of the autocatalyst for the \( i \)th particle \((i = 1, \ldots, N)\) is given by

\[
\frac{dX_i}{dt} = -k_\text{ex}(X_i - X_s) + f(X_i, Y_i, Z_i) \quad (1)
\]

and in the surrounding solution

\[
\frac{dX_s}{dt} = \frac{\mathcal{V}}{V_s} \sum_{i=1}^{N} k_\text{ex}(X_i - X_s) + g(X_s, Y_s) \quad (2)
\]

where \(f(X_i, Y_i, Z_i)\) represents the chemical reaction on the particle, and \(g(X_s, Y_s)\) represents the reaction in the surrounding solution (21). The exchange rate of the autocatalyst between the particle and the surrounding solution is given by the term \(-k_\text{ex}(X_i - X_s)\), where the value of the exchange rate constant \(k_\text{ex}\) increases with increasing stirring rate (21). The sum of the contributions from each particle gives the concentration in the surrounding solution, with the dilution factor \(\mathcal{V}/V_s\), where \(V_s\) is the total volume of solution and \(\mathcal{V}\) is the average volume of a particle. The particle dynamics is periodic for \(k_\text{ex} = 0\) and depends on the number density and the exchange rate for nonzero \(k_\text{ex}\).

There is no mechanism for oscillation in the surrounding solution in the absence of particles; however, in the presence of oscillatory particles, oscillations in \(X_s\) and \(Y_s\) arise from the exchange between the particles and the solution.

The coherence of the population of oscillators is determined for a sample of \(N = 1000\) using the order parameter \(K\) introduced by Shinomoto and Kuramoto (27):

\[
K = \left( \frac{1}{N} \sum_{j} \exp(i\theta_j) - \left( \frac{1}{N} \sum_{j} \exp(i\theta) \right)^N \right) \quad (3)
\]

where \(\theta_j\) is the phase of the \(j\)th oscillator and angle brackets indicate the time average. This coherence measure is 0 when all particles oscillate out of phase with each other (or when the particles are not oscillating) and 1 when all particles oscillate in perfect synchrony. For \(k_\text{ex} = 0\), the particles have a broad distribution of natural periods (38 ± 6 s).

The surface plot in Fig. 3A shows the amplitude of the activator species \(X_s\) in the surrounding solution as a function of the number density of particles \(n\), where \(n = N/V_s\), and the exchange rate constant \(k_\text{ex}\). The growth in the amplitude of \(X_s\) with increasing \(n\) depends on the value of \(k_\text{ex}\). For \(k_\text{ex} = 0.3\), there is a distribution in the natural period for low \(n\) (Fig. 3B).

There is a corresponding gradual increase in the coherence parameter \(K\) with increasing particle density as the individual oscillators gradually align their frequencies and phases. For \(k_\text{ex} = 3.0\), the catalyst particles are not oscillatory for low values of \(n\) (Fig. 3C); however, when \(n\) is increased beyond a threshold value, the particles suddenly begin to oscillate in perfect synchrony. The coherence parameter switches from 0 to 1. The gradual transition from unsynchronized to synchronized oscillations at low values of \(k_\text{ex}\), and the sharp switching transition from steady-state behavior to synchronized oscillations at high values of \(k_\text{ex}\) can be seen in the surface plot of the global signal \(X_s\) (Fig. 3A).

The gradual synchronization of particles for low \(k_\text{ex}\) can be understood within the framework of the Kuramoto model, where \(X_s\) playing the role of the mean-field coupling. The time variation of \(X_s, X_c\), and the exchange rate \(-k_\text{ex}(X_i - X_s)\) for a particle are shown in Fig. 4A for one cycle, with \(k_\text{ex} = 0.3\) and \(n = 4000\). The value of \(X_s\) increases when several of the oscillators fire together (Fig. 4A, top). This increase in turn influences the individual oscillators through the exchange rate, which becomes positive for a particle when the concentration is higher in the solution (Fig. 4A, middle), leading to an increase in \(X_s\). When \(X_s\) crosses a threshold value, the particle fires in synchrony with the others (Fig. 4A, bottom). For low \(n\), particles with frequencies that differ from that of the global oscillation are little affected by the weak signal in \(X_s\); however, as \(n\) is increased, the magnitude of
the $X_i$ signal increases, and more of the oscillators join the rhythm. In this way, the particles are synchronized by an internally generated signal.

The exchange rate for all particles averaged over one cycle is negative and therefore constitutes an overall loss rate in $X_i$, shown as a function of $k_{ex}$ in Fig. 4B. As $k_{ex}$ increases for fixed $n$, the average concentration of activator in the surrounding solution $X_i$ increases (blue line), but the loss rate also increases (red line), and hence the average concentration of $X_i$ on a particle decreases (black line). When it decreases below a threshold value, oscillations are no longer supported and a sudden transition to the steady state is observed. The $X_i$ loss rate increases slightly as $k_{ex}$ is further increased.

The model predicts that both a dynamical quorum-sensing transition and a desynchronization transition will be observed upon decreasing the stirring rate (Fig. 4C, upper panel). The oscillations suddenly appear and then decrease in amplitude with decreasing $k_{ex}$ because of the loss of synchronization until a noisy non-oscillatory signal corresponding to out-of-phase oscillators is observed. The transition to the desynchronized state is best observed at low particle densities, as can be seen in Fig. 3A for $n = 1.8 \times 10^4 \text{ cm}^{-3}$. The transition from steady-state to oscillatory behavior followed by a gradual desynchronization is also observed experimentally (Fig. 4C, lower panel).

For high $k_{ex}$ and low $n$, the catalyst particles are quiescent, as oscillations are not supported because of the high loss rate of $X_i$. As the number density is increased, the concentration both in the surrounding solution $X_i$ and on the individual particles $X_i$ increases, with a corresponding slight decrease in the average loss rate of $X_i$ on the particles (Fig. 4D). At a critical density $n$, the value of $X_i$ on the individual particles reaches the threshold for the transition from steady-state behavior to oscillatory behavior. Although there is a considerable spread in oscillator frequencies, the transition is sharp, with all particles oscillating synchronously, indicating cooperative behavior in the transition (21).

We have shown that there are two distinct types of transitions to synchronized oscillatory behavior with increasing oscillator density, where coupling occurs by exchange of signaling species through the surrounding solution. For low exchange rates, the oscillators gradually synchronize their rhythms via a weak coupling through the low solution concentration of activator. For high exchange rates, the oscillators are quiescent below a critical density, as the activator concentration on the particles is not sufficient to support oscillatory behavior. Higher exchange rates give rise to lower activator concentrations on individual particles, because only activator-consuming processes occur in the surrounding solution. As the density is increased, the activator concentration in the surrounding solution and on each particle increases until a threshold concentration is reached, and synchronous oscillations suddenly appear.

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**Fig. 3.** Behavior of BZ particle population model (20, 21) with oscillators coupled by exchange of species with the surrounding solution (see table S1 for parameter values). (A) The order parameter $K$ as a function of number density of oscillators and exchange rate constant. (B) The amplitude of the oscillations in autacatalyst in the surrounding solution as a function of number density of oscillators and exchange rate constant, as can be seen in Fig. 3A for $n = 1.8 \times 10^4 \text{ cm}^{-3}$. The transition from oscillatory to steady-state behavior with increasing oscillator density, where coupling occurs by exchange of signaling species through the surrounding solution. As the number density is increased, the concentration both in the surrounding solution $X_i$ and on the individual particles $X_i$ increases, with a corresponding slight decrease in the average loss rate of $X_i$ on the particles (Fig. 4D). At a critical density $n$, the value of $X_i$ on the individual particles reaches the threshold for the transition from steady-state to oscillatory behavior.

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**Fig. 4.** Influence of exchange rate $-k_{ex}(X_i - X_e)$ on model dynamics. (A) Variation of autacatalyst in solution (blue line), on a particle (black line), and the exchange rate (red line) during one oscillation, with $n = 1.8 \times 10^4 \text{ cm}^{-3}$ and $k_{ex} = 0.3 \text{ s}^{-1}$. (B) Transition from oscillations to steady state with increasing $k_{ex}$ ($n = 1.8 \times 10^4 \text{ cm}^{-3}$). Time-averaged autacatalyst on the particles (black line), in solution (blue line), and loss rate of autacatalyst from the particles (red line $= k_{ex}(X_i - X_e)$). (C) Appearance and desynchronization of oscillations in autacatalyst in solution (blue line) and electrode potential (black line) with decreasing $k_{ex}$ ($n = 1.8 \times 10^4 \text{ cm}^{-3}$) and stirring rate (density $= 0.0162 \text{ g cm}^{-3}$) shown as red lines. (D) Transition from steady state to oscillations with increasing $n$ ($k_{ex} = 3.0 \text{ s}^{-1}$). Color coding is same as in (A).
Single Nanocrystals of Platinum Prepared by Partial Dissolution of Au-Pt Nanoalloys

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Small metal nanoparticles that are also highly crystalline have the potential for showing enhanced catalytic activity. We describe the preparation of single nanocrystals of platinum that are 2 to 3 nanometers in diameter. These particles were generated and immobilized on spherical polyelectrolyte brushes consisting of a polystyrene core (diameter ~100 nanometers) onto which long chains of a cationic polyelectrolyte were affixed. In a first step, a nanoalloy of gold and platinum (a solid solution) was generated within the layer of cationic polyelectrolyte chains. In a second step, the gold was slowly and selectively dissolved by cyanide ions in the presence of oxygen. Cryogenic transmission electron microscopy, wide-angle x-ray scattering, and high-resolution transmission electron microscopy showed that the resulting platinum nanoparticles are faceted single crystals that remain embedded in the polyelectrolyte-chain layer. The composite systems of the core particles and the platinum single nanocrystals exhibit an excellent colloidal stability, as well as high catalytic activity in hydrogenation reactions in the aqueous phase.

References and Notes


Metallic nanoparticles (NPs) of controlled size and shape have been of great interest recently for a number of possible applications in electronic or optical materials, as well as in catalysis (1–8). Particle morphology can play a central role in catalysis. For example, faceted Pt crystals can exhibit higher catalytic activity than spherical particles (9, 10), and the activity of the exposed faces may vary considerably (11, 12). The reactivity and selectivity of NPs can be tuned by controlling their morphology; for example, amorphous Pt NPs have exhibited a much reduced catalytic activity (13).

However, faceted nanocrystals (NCs) with a well-developed shape and a narrow size distribution that have been reported generally were in the size range of 100 nm and more. For instance, Sun and Xia obtained well-defined Au and Ag crystals with sizes on the order of 100 nm (4). Nanoprisms of Ag with dimensions around 100 nm were prepared by Jin et al. by photochemical conversion of Ag spheres (3). Anisotropic Ag NPs of similar size were synthesized by Liz-Marzan and co-workers through careful choice of a suitable surfactant (14), and Pt NPs with high-index facets were obtained recently by Tian and co-workers (6). Again, the typical sizes ranged between 50 and 200 nm. The only reported route to faceted single crystals in the size range of a few nanometers was the synthesis of well-defined clusters, for example, Au935 cluster, and a subsequent heat treatment (15).

Platinum NPs have been of particular interest because of their role in many catalytic reactions and because the growth of specific surfaces can be controlled by amphiphilic polymers or suitable surfactants (9, 16–19). However, downsizing the Pt NPs to a few nanometers is often accompanied by a broadening of their size distribution and partial loss of the control of the particle shape (5). The reduction of the metal ions and the generation of the NPs seem to proceed very rapidly and leads to disordered structures and distorted crystal shapes.

We present a simple synthesis of faceted, well-defined Pt single NCs with a typical size of 2 to 3 nm. As shown in Fig. 1, the Pt NCs are obtained by partial dissolution of nanoalloys of Pt and Au. In case of larger nanoalloy particles, this procedure leads to spongelike or hollow structures (20, 21). We found that the dissolution of the Au component of the nanoalloy leads to reorganization of the Pt atoms and the formation of well-defined, faceted NCs. We started from a nanoalloy of Au and Pt generated on the surface of a spherical polyelectrolyte brush (SPB), as described recently (22). These particles consist of a solid polystyrene (PS) core with colloidal dimensions (diameter ~100 nm) onto which long charged polymer chains are grafted. Spherical polyelectrolyte brushes are well suited for the...