Testing Equivariant Dynamics in a Network of Reaction-Diffusion Oscillators

Ian Hunter, Chris Simonetti, Maria Eleni Moustaka, and Seth Fraden
Brandeis University Physics, Waltham MA, 02453 USA

Michael M. Norton
Center for Neural Engineering, Department of Engineering Science and Mechanics, The Pennsylvania State University, University Park, PA 16802 USA

Bolun Chen
Brandeis University Volen National Center for Complex Systems, Waltham MA, 02453 USA and Department of Physics Boston University, Boston MA, 02215 USA

Jonathan Touboul
Brandeis University Volen National Center for Complex Systems, Waltham MA, 02453 USA and Brandeis University Mathematics Department

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The theory of equivariant dynamics predicts symmetry-required spatiotemporal patterns in complex networks, yet its robustness to symmetry-disrupting imperfections in natural systems is unresolved. Here, we develop a model experimental reaction-diffusion network of chemical oscillators to test practical applications of this theory. The network is a symmetric ring of 4 microreactors containing the oscillatory Belousov-Zhabotinsky reaction coupled to nearest neighbors via diffusion. Assuming perfect symmetry, theory predicts 4 categories of stable spatiotemporal phase-locked periodic states and 4 categories of invariant manifolds that guide and structure transitions between phase-locked states. In our experiments, we observed the predicted symmetry-derived synchronous clustered transients that occur when the dynamical trajectories coincide with invariant manifolds. However, we observe only 3 of the 4 phase-locked states that are predicted for the idealized homogeneous system. Quantitative agreement between experiment and numerical simulations is found by accounting for the small amount of experimentally determined heterogeneity. This work demonstrates that a surprising degree of the natural network’s dynamics are constrained by equivariant dynamics in spite of the breakdown of the assumptions of perfect symmetry and raises the question of why heterogeneity destabilizes some symmetry predicted states, but not others.

INTRODUCTION

Network science elucidates how dynamical systems interact. An idealized model considers network nodes to represent dynamical entities and connections between nodes to represent coupling [1]. This simple framework provides profound insights into the behavior of disparate systems ranging from electrical power grids to biological neural networks known as central pattern generators (CPG) responsible for autonomous movement such as animal locomotion [2,3].

Symmetries place hard constraints on networks of self-driven oscillators by dictating that certain dynamical features and steady state patterns must exist. Such universal organizing principles for far-from-equilibrium systems are exceedingly rare. An elegant method to predict the patterns formed in arbitrary networks of oscillators uses the theory of equivariant dynamics to show how the form, or permutation symmetry, of a network and the temporal symmetry of the oscillators combine to require the existence of specific periodic spatiotemporal patterns. Golubitsky, Stewart and colleagues used group theory to derive the H/K theorem, discussed more fully below, which enumerates all symmetry derived patterns in which phase-locked nodes co-evolve because they receive the same input from their neighbors [3,7,10]. Remarkably, some of the predicted patterns are far from obvious and bear little resemblance to the geometric symmetry of the network. Significantly, these patterns are universal. They depend only on the coupling topology and are independent of all system specific details regarding the nature of the non-linear oscillators themselves and even whether or not the coupling is non-linear. However, these striking results derive from the strong assumption that classes of nodes in the network and their interconnections are strictly identical [10].

In biological systems, the theory of equivariant dynamics has been applied to predict the symmetry of the smallest CPG needed to produce the observed gaits of quadrupeds leading to the hypothesis that form follows function in neuronal networks [3]. In the case of mammals, the existence of such a CPG is controversial. However, in electromechanical systems this theory has been used to design network topologies to generate desired states in populations of electronic oscillators [5,6]. A well-established model of the system was used to predict the stability of the theoretical periodic states, accurately predicting those observed in experiment. The correspon-
dence between theory and experiment was ascribed to the precision of the fabrication process of these electromechanical devices, ensuring the equivalence of each network node and connection.

We wish to determine the degree to which these symmetry based network theories are relevant to natural autonomous systems. By natural, we mean networks for which the dynamical entities and coupling are self-organized, as in biological [3, 11, 12] and chemical systems [13], in contrast to engineered networks comprising mechanical [6] and electronic components [14, 15]. There is support for aspects of the H/K theory to explain periodic states formed by living slime mold placed in deliberately designed networks of known symmetry [4]. However, because the underlying chemical dynamics of slime mold are not fully understood and the total number of oscillations are small, it is impossible to address questions of stability of the observed spatiotemporal patterns, to describe transient dynamics and to assess the impact of heterogeneity.

To test the H/K theory applied to natural systems, we develop a model experimental system consisting of a ring of 4 identical, nanoliter sized, chemical reactors containing the Belousov-Zhabotinsky (BZ) oscillating reaction and coupled to nearest neighbors by diffusion. This experimental system oscillates stably for about 70 periods [16], which is an order of magnitude longer than reported in previous studies of natural networks [4, 11, 12]. We model this reaction-diffusion network at two levels of description. The most detailed is a mathematical model of the system explicitly describing the BZ reaction chemistry, which we assume occurs only in the reactors, with coupling between nearest neighbors caused by diffusion of a subset of the BZ chemicals through the intervening PDMS. We theoretically reduce this reaction-diffusion network into a simpler phase model to analyze the predictions of the theory of equivariant dynamics. These models contain far fewer free parameters than independent measurements. This, and the longevity of the experiments, allows quantitative comparisons between theory and experiment leading to firm conclusions regarding the applicability of idealized network dynamics to model the steady-state and transient dynamics of this natural system in which both the oscillators and coupling are fully chemical.

In particular, our experiments reveal a bewildering array of transient and phase-locked spatiotemporal chemical dynamics. However, when we reduce these complex non-stationary solutions into the state-space of phase relationships, the H/K theorem allows us to represent complex chemical dynamics in terms of simple, model-independent geometric objects in the form of planes, lines, and points that are readily visualized. This geometric perspective leads to an appreciation of aspects of the experimental behaviors that are directly imposed by symmetries, thereby providing qualitative understanding of the complex dynamics, which complements and enriches the quantitative comparison between theory and experiment.

RESULTS AND DISCUSSION

Experimental Reaction-Diffusion Network

We designed a reaction-diffusion network consisting of a ring of four diffusively coupled nanoliter volume batch reactors laid out in a square 2x2 lattice with nearest neighbor coupling (see Fig. 1). Previously, we employed emulsions containing the BZ oscillating reaction to study reaction-diffusion networks [17-24]. But the diffusive coupling between surfactant stabilized emulsion drops was difficult to characterize and manufacturing of the networks was challenging, which contributed to a large degree of variability between experiments. Here, to improve reproducibility we manufactured these reactors to high precision from elastomeric PDMS using soft lithography techniques and filled the reactors with the oscillatory BZ reaction as described previously [13, 16], illustrated in Fig. 1 and in Appendix A. To obtain a large statistical sample of trajectories we made devices that combined 9 or 16 copies of the 2x2 network. To optimize homogeneity in the chemical concentrations of each of the reactors, we simultaneously filled the entire set of networks by piping a drop of BZ that floods all the reactors before seal-

![FIG. 1.](image)

(a) Schematic of a network of a ring of 4 inhibitory coupled oscillators. Indexing of nodes is indicated as either a number (1,2,3,4), or leg of a quadruped (LF, RF, RH, LH) with L left, R right, F front and H hind. (b) Schematic of the experimental system. The reactors are divots in the PDMS, filled with BZ and sealed between 2 glass plates. (c) Photograph of BZ filled 4-ring network. Actinic light illuminates BZ in a channel surrounding the network and provides a constant chemical boundary condition. (d) Two adjacent reactors (red and blue traces) in the network oscillating 180° out-of-phase with each other. Top: Measured transmitted intensity versus time. Bottom: Simulated oxidized catalyst concentration [mM] versus time. In both, time is rescaled by oscillation period $T_0$, indicated by the two arrows.
ing the sets of reactors by clamping the PDMS between two glass plates [Supplementary Material 25 Fig. 1-2, SI videos in [13].

The chemical coupling between adjacent reactors arises from the permeation of chemical species through the intervening PDMS wall and mainly consists of bromine-induced inhibition, with a weaker activator coupling, perhaps by bromous acid and the bromine dioxide radical [13, 17, 20, 22, 24, 26, 30]. After mixing the BZ reagents, pipetting them onto the PDMS networks, sealing the networks, and placing the sample in the dark for an induction period of 20 minutes, it was observed that all reactors began to oscillate and collectively form spatiotemporal patterns [Fig. 1(d)] [13].

The reactors form a closed system and consequently the oscillators have a finite lifetime as the reactants are consumed and waste products accumulate. However, although the amplitude of the chemical oscillations decreases over time, the oscillators maintain a nearly constant period for a duration of order 70 oscillations[16]. Based on this long term stability, we assume that the underlying phase dynamics of the individual BZ oscillators remains constant during the duration of the experiment, thus allowing us to study phase relationships between reactors as they evolve over time [Supplementary Material 25 Fig. 4, Movies S1-4]. Each 4-ring network is isolated from the environment because the reactors are surrounded by a zone of photosensitive BZ that is held at constant chemical conditions by the application of actinic light[13]. We also assume that each chemical reaction is well mixed, ignoring any spatial variation of chemical concentrations, because the size of the reactor is small compared with the length scale of diffusion, e.g. \( w < \sqrt{D\tau} \) with \( w \) the width of each square reactor (\( w = 62 \mu m \), \( D \), the diffusion constant of each BZ chemical (\( D \sim 10^{-9} m^2s^{-1} \) and \( \tau \), the duration of a BZ oscillation (\( \tau \sim 300s \)).

Theory and the Role of Symmetry

The fullest description of the dynamics of the 4-ring network that we consider is a reaction-diffusion network model. It focuses on the time dependent concentrations of the well mixed chemicals in each reactor, denoted as \( \bar{c}_1(t), \bar{c}_2(t), \bar{c}_3(t), \bar{c}_4(t) \), where \( \bar{c}_j(t) \) is a vector of concentrations in the \( j \)th reactor with indices as in Fig. 1A. Assuming that the reactors are identical, the behaviors are expected to have the same symmetries as a square, e.g. 3 rotations and 4 reflections. Associated with this symmetry group, the H/K theorem predicts invariant manifolds, subspaces in which the dynamics remains confined, that are universal to any ring of 4 oscillators, enumerated in Table 1. Although the theory is more general, we restrict ourselves to the case in which all the nodes are on the same limit cycle, as this corresponds to experiment. With this assumption the H/K theorem guarantees any system of 4 oscillators with square symmetry possesses 8 categories of invariant manifolds, including 4 categories of phase-locked periodic states. These states are therefore efficiently described by considering the phase relationship between pairs of reactors, defined as the fraction of period they are shifted from each other on their common limit cycle.

Invariant manifolds are denoted by a pair of symmetry operations, (H,K). The first symmetry, H, represents an exchange of nodes that results in the same state subject to one or more phase-shifts. The second symmetry, K, indicates symmetries under which the system is unchanged. Depending on the constraints imposed by H and K, these solutions may either maintain fixed phase relationships among all four nodes resulting in phase-locked solutions, or leave 1- or 2-dimensional freedom on these relationships, as enumerated in Table 1. The 4 categories of phase-locked periodic states are spatiotemporal periodic patterns that correspond to 6 point invariant manifolds in the phase difference space that can be identified with gaits of quadrupeds enumerated in Table 1 and visualized in Fig. 2(b). The first two categories are Pronk in which all the legs advance simultaneously and Trot for which diagonal legs are in phase, and the two diagonal pairs of legs are half a period out of phase. Pace and Bound form one category and we refer to them interchangeably in the remainder of the text. In Pace, legs on each side are in phase and opposite sides out-of-phase, while for Bound, legs on opposite sides are in phase and the front legs out-of-phase with the hind legs. Clockwise (counter clockwise) Rotary Gallop is another category in which the legs advance in a clockwise (counter clockwise) manner with each leg advancing a quarter of a period later than the preceding leg.

The remaining 4 categories correspond to higher dimensional invariant manifolds (lines or planes) that contain trajectories maintaining partial symmetries. Along 1-dimensional linear invariant manifolds, the network can be split into two pairs of reactors, such that within pairs the reactors are in phase or antiphase, while between pairs reactors have an arbitrary phase-shift. Along 2-dimensional manifolds, two nodes oscillate in phase and the other two nodes are at arbitrary phase-shifts. In fact, the 2-dimensional manifolds intersect the 1-dimensional manifolds, and the 1D manifolds intersect the phase-locked 0-dimensional manifolds [Fig. 2(a)]. Heuristically, these higher dimensional manifolds often act as privileged pathways that both guide and structure transient transitions between the phase-locked states. Beyond predicting the existence of these invariants, the H/K theorem neither prescribes their stability nor precludes the existence of others. To address questions of stability and existence of additional manifolds requires a specific model of the oscillators and their connections.
Chemical Kinetic and Phase Models

To model the reaction-diffusion dynamics of our experiments we use the Vanag-Epstein model of the BZ reaction, which treats the chemical kinetics of 4 BZ chemicals, Br₂, HBrO₂, Ferroin, and Br₂, combined with a diffusive coupling term between chemical species in which the coupling strength is fitted from the data. Noting that \( c_i \in \mathbb{R}^4 \) are the concentrations of these 4 chemicals in reactor \( i \in \{1, 2, 3, 4\} \) and \( R_0 : \mathbb{R}^4 \rightarrow \mathbb{R}^4 \) denotes the Vanag-Epstein BZ model vector field \([13, 17–20, 22–24, 26–30]\), we obtain the equation:

\[
\frac{d}{dt} c_i = \dot{R}_0(c_i) + \sum_{j=1}^{4} A_{ij} \mu(c_j - c_i)
\]

where \( \mu \in \mathbb{R}^{4 \times 4} \) accounts for the chemical coupling matrix between two adjacent cells, and depends on the permeability of the PDMS for each chemical species and the geometry of the reactors, while \( A \in \mathbb{R}^{4 \times 4} \) denotes the adjacency matrix between two reactors that is determined by the network topology \([Appendix C]\) for details on the model, choice of parameters and fits of free parameters). This model ignores spatial concentration gradients inside the reactors, effectively treating reactors as points corresponding to nodes of the network. The model also neglects the occurrence of chemical reactions within the PDMS, which acts as a connector that couples adjacent nodes.

Under the assumption that all reactors are oscillating on the same limit cycle, we can parameterize the time dependent concentrations through the phase of that cycle, as proposed by Winfree \([31]\) and widely used in various applications \([24, 32, 33]\). In this abstraction, the phase variable naturally progresses linearly from 0 to \( 2\pi \) at a frequency \( \omega_0 = 2\pi/T_0 \). Perturbing the chemical concentration of an individual reactor will lead to a modification of the phase that depends on the chemical species that is perturbed and phase of the reactor; this function is called the phase response curve (PRC). The impact on the phase of one reactor due to diffusive coupling from a neighbor can be summarized through the interaction function, \( H \), derived from convolving the PRC with the diffusive coupling between reactors and averaging over a period \([33]\) \( [Appendix C] \). Notably, this reduction of the chemical model of Eq. 1 to a phase model introduces no new parameters. Best fits between experiment and model are obtained with the interaction function \( H \) that arises from a combination of Br₂ and HBrO₂, as shown in Fig. 9(a). This leads to the phase equation:

\[
\frac{d}{dt} \phi_i = \omega_0 + k \sum_{j=1}^{4} A_{ij} H(\phi_j - \phi_i)
\]

where \( k \) the diffusive coupling rate.

Table I. Symmetry required invariant manifolds for an oscillator network possessing square or Dihedral 4 (\( D_4 \)) symmetry. \( D_4 \) all symmetries of a square; \( D_4^c \), reflection across \( n \) diagonals; \( D_4^r \), reflection across \( n \), vertical or horizontal, axes; \( Z_4 \), 90° rotation; \( Z_2 \), 180° rotation; 1, no operation. The first 4 classes of manifolds are phase-locked states. The column marked “Phase” graphically indicates the spatiotemporal pattern with symbols representing the phase in percentage of the period \( T_0 \), white circle - 0%; white/black - 25%; black circle - 50%; black/white - 75%. \( T_0 \) denotes the period of each oscillator in a given invariant manifold and can vary from manifold to manifold. The second 4 classes of manifolds are symmetrically clustered states, related by arbitrary phase shifts \( f_1, f_2 \), which vary from 0 to 1 as fraction of a period. The graphical representation of nodes in the column “Phase” have solid, striped, or dot motifs. Different motifs are related by an arbitrary phase shift. Similar motifs with opposite background colors are antiphase with each other.

| Name          | Phase  | \( \bar{c}_1 \) | \( \bar{c}_2 \) | \( \bar{c}_3 \) | \( \bar{c}_4 \) |
|---------------|--------|-----------------|-----------------|-----------------|-----------------|
| \((H,K)\)     |        |                 |                 |                 |                 |
| \((D_4, D_4)\) | \( \bar{c}(t) \) | \( \bar{c}(t) \) | \( \bar{c}(t) \) | \( \bar{c}(t) \)          |
| \((D_4, D_4^c)\) | \( \bar{c}(t) \) | \( \bar{c}(t + \frac{T_0}{4}) \) | \( \bar{c}(t) \) | \( \bar{c}(t + \frac{T_0}{4}) \) |
| \((D_4, D_4^r)\) | \( \bar{c}(t) \) | \( \bar{c}(t) \) | \( \bar{c}(t + \frac{T_0}{2}) \) | \( \bar{c}(t) \)          |
| \((D_2, D_2)\) | \( \bar{c}(t) \) | \( \bar{c}(t - \frac{T_0}{4}) \) | \( \bar{c}(t + \frac{T_0}{4}) \) | \( \bar{c}(t) \)          |
| \((D_2, D_2^c)\) | \( \bar{c}(t) \) | \( \bar{c}(t) \) | \( \bar{c}(t + \frac{T_0}{4}) \) | \( \bar{c}(t) \)          |
| \((D_2, D_2^r)\) | \( \bar{c}(t) \) | \( \bar{c}(t + \frac{T_0}{4}) \) | \( \bar{c}(t) \) | \( \bar{c}(t + \frac{T_0}{4}) \) |
| \((Z_4, 1)_A\) | \( \bar{c}(t) \) | \( \bar{c}(t + f_1 T_0) \) | \( \bar{c}(t + f_1 T_0) \) | \( \bar{c}(t) \)          |
| \((Z_4, 1)_B\) | \( \bar{c}(t) \) | \( \bar{c}(t + f_1 T_0) \) | \( \bar{c}(t + f_1 T_0) \) | \( \bar{c}(t) \)          |

Linear invariant manifolds:

\[
\begin{align*}
(D_4^c, D_4^c)_A & : \bar{c}(t) \bar{c}(t + f_1 T_0) \bar{c}(t + f_1 T_0) \\
(D_4^c, D_4^c)_B & : \bar{c}(t) \bar{c}(t + f_1 T_0) \bar{c}(t + f_1 T_0) \\
(D_4^r, D_4^r)_A & : \bar{c}(t) \bar{c}(t + f_1 T_0) \bar{c}(t + f_1 T_0) \\
(D_4^r, D_4^r)_B & : \bar{c}(t) \bar{c}(t + f_1 T_0) \bar{c}(t + f_1 T_0) \\
(Z_4, 1)_A & : \bar{c}(t) \bar{c}(t + f_1 T_0) \bar{c}(t + f_1 T_0) \\
(Z_4, 1)_B & : \bar{c}(t) \bar{c}(t + f_1 T_0) \bar{c}(t + f_1 T_0) \\
\end{align*}
\]

Planar invariant manifolds:

\[
\begin{align*}
(D_4^c, D_4^c)_A & : \bar{c}(t) \bar{c}(t + f_1 T_0) \bar{c}(t + f_1 T_0) \\
(D_4^c, D_4^c)_B & : \bar{c}(t) \bar{c}(t + f_1 T_0) \bar{c}(t + f_1 T_0) \\
(D_4^r, D_4^r)_A & : \bar{c}(t) \bar{c}(t + f_1 T_0) \bar{c}(t + f_1 T_0) \\
(D_4^r, D_4^r)_B & : \bar{c}(t) \bar{c}(t + f_1 T_0) \bar{c}(t + f_1 T_0) \\
\end{align*}
\]
Accordingly,
\[
\frac{d}{dt} \tilde{\theta} = \Psi(\tilde{\theta})
\] (3)

with \(\Psi(\tilde{\theta})\) following directly from Eq. 2. As each of the phase differences is periodic on \((0, 2\pi)\), the state-space is a 3-torus. Although the 3-torus cannot be drawn in three dimensions, it is equivalent to a Cartesian cube with periodic boundaries, allowing visualization of the full dynamics.

### Dynamics in the State-space of Phase Differences

This new coordinate system transforms the invariant manifolds identified by the H/K theorem in Table I to simple, geometric objects: points, lines, and planes, enumerated in Table II. This transformation enables the consequences of the H/K theorem on the dynamics in state-space to be visualized in a way that would be impossible in the full chemical model, Eq. 1. The point invariant manifolds Pronk, Bound, Trot, Rotary Gallop become steady-states in this new frame, rather than high-dimensional limit cycles. We are able to readily classify them as either attractors, repellers or saddles, according to whether the velocity vectors surrounding the steady state point inward, outward or change sign depending on orientation, respectively. Beyond the steady-states in the form of points, Fig. 2A shows a state-space structured by additional invariant manifolds in the form of lines and planes, all required by the spatiotemporal symmetries of the oscillator network.

The dynamical system of Equation 3 predicts that the network is multistable, with the point H/K manifolds forming competing attractors. We simulated exhaustively the model and observed that each initial condition flows to one of the four categories of phase-locked attractor states; (1) Pronk, (2) Pace/Bound, (3) Trot, and (4) CW/CCW Gallop [Fig. 3(a)(b)]. Furthermore, we show in the Supplementary Material [25] Sec. IIB that the system predicts the six phase-locked states are linearly stable, and thus attractors.

We found that the theoretical model also possesses many unstable, saddle phase-locked steady-states in addition to the six H/K derived attractors. In fact, topology predicts the existence of unstable steady-states. The topological index of both attractors and saddles with one attracting direction is +1, while the index of both repellors and saddles with two attracting directions is -1. Topology requires that the sum of the topological indices of all the steady-states must equal 0, the Euler characteristic of a 3-torus, as shown in the Supplementary Material [25] Sec. IV. Given the six H/K point invariant manifolds are attractors, we conclude there must be at least six unstable steady-states located in the 3-torus to satisfy the required charge neutrality. Moreover, unstable states organize the separatrices between invariant manifolds containing more than one attractor. We numerically searched for the required unstable states and found 158 saddle and 4 unstable steady-states dispersed throughout the state-space shown in Supplementary Material [25] Fig. 7. A notable and unexplained fact is that of the 168 numerically identified phase-locked steady-states, the sole attractors are the six invariant point manifolds required by the H/K theorem.

### Table II. Symmetry required invariant manifolds parameterized by relative phase. \(f_1, f_2\), which vary from 0 to \(2\pi\). All representations, modulo \(2\pi\), are shown.

| Name       | Phases | Hyperplane |
|------------|--------|------------|
| Pronk      | \(\theta_{21} = \theta_{32} = \theta_{43} = 0\) |            |
| Trot       | \(\theta_{21} = \theta_{32} = \theta_{43} = \pi\) |            |
| Pace       | \(\theta_{21} = -\theta_{43} = \pi, \theta_{32} = 0\) |            |
| Bound      | \(\theta_{21} = \theta_{32} = 0, \theta_{32} = \pi\) |            |
| CW Gallop  | \(\theta_{21} = \theta_{32} = \theta_{43} = +\frac{\pi}{2}\) |            |
| CCW Gallop | \(\theta_{21} = \theta_{32} = \theta_{43} = -\frac{\pi}{2}\) |            |

#### Linear invariant manifolds:

| Expression   | Phases | Hyperplane |
|--------------|--------|------------|
| \((D_1^1, D_1^0)\)_A | \(\theta_{21} = -\theta_{43} = f_1, \theta_{32} = 0\) |            |
| \((D_1^0, D_1^1)\)_B | \(\theta_{21} = \theta_{43} = 0, \theta_{32} = f_1\) |            |
| \((D_1^1, 1)\)_A | \(\theta_{21} = \pi, \theta_{32} = f_1, \theta_{43} = -\theta_{32}\) |            |
| \((D_1^1, 1)\)_B | \(\theta_{21} = f_1, \theta_{32} = \pi, \theta_{43} = \pi\) |            |
| \((Z_{2,1})\) | \(\theta_{21} = f_1, \theta_{32} = \pi - f_1, \theta_{43} = f_1\) |            |

#### Planar invariant manifolds:

| Expression   | Phases | Hyperplane |
|--------------|--------|------------|
| \((D_1^1, D_1^0)\)_A | \(\theta_{21} = -\theta_{32}, \theta_{32} = f_1, \theta_{43} = f_2\) |            |
| \((D_1^0, D_1^1)\)_B | \(\theta_{21} = f_1, \theta_{32} = f_2, \theta_{43} = -\theta_{32}\) |            |

We numerically determined the basins of attraction of each attractor by dividing the 3-torus into a fine grid and identifying each initial point with the attractor to which it flowed, as shown in Fig. 3A-B [37]. The Pronk, Bound and Rotary Gallop basins are smooth, closed volumes while the Trot basin fills the rest of the state-space [Fig. 3(b)]. The state with largest basin of attraction is Trot, followed by Rotary Gallop, Bound and Pronk. The attraction basin of the Bound state is anisotropic and aligned with the \((D_1^0, D_1^1)\) invariant manifolds [Fig. 3(a) 3(a)]. Fig. 3(a) and 3(b) reveal that trajectories remain near the \((D_1^0, D_1^1)\) invariant manifolds as they flow to Trot. Theory predicts that the network’s trajectories flowing towards its attractors are constrained and shaped by H/K linear and planar invariant manifolds.
To further elucidate how symmetric invariant manifolds guide and structure dynamics, we focus on the transverse dynamics, namely flows perpendicular to the invariant manifolds. We combined the unique system dynamics, Eqns. 2 and 3, and the universal structure of the plane and invariant manifolds to semi-analytically compute the manifolds’ transverse Lyapunov exponents, which measure the local attraction or repulsion rate of trajectories to or from them [38–40], in terms of the interaction function, $H$ [Appendix E]. The majority of the domains of the $D_s^1, D_s^3$ and $D_p^1, D_p^3$ manifolds are covered with negative exponents [Fig. 4(c)]. This causes trajectories to collapse and remain on these invariant manifolds [Fig. 4(a), (b)] [40]. While the regions with negative exponents organize the flows along the invariant manifolds, the small regions of positive exponents contain the separatrices of attractors on the same invariant manifolds, shown as saddles in the Supplementary Material [25] Fig. 7. In this way, the theory combines the restrictions of symmetry and the unique system dynamics to predict both the basins of attraction of the attractors and the symmetric, clustered transient transitions along the linear and planar invariant manifolds that connect the attractors.

The higher order H/K invariant manifolds are not the only invariant manifolds controlling transient flows. Additional invariant manifolds arise in the vicinity of steady-states because linear stability analysis permits an eigenvector decomposition of the dynamics. We see such an invariant manifold exists about the Rotary Gallop attractor as all the surrounding trajectories coalesce into a plane [Fig. 3(a)]. This invariant manifold is not aligned with any H/K invariant manifold and arises from the unique system dynamics rather than the H/K theorem or symmetry.

**Experimental Observations of Dynamics**

To compare the geometric framework provided by the theory of equivariant dynamics with experiment, we defined a reactor’s phase in reference to the moments of maximum oxidation, corresponding to a maximum in transmitted light intensity [Fig. 1(d)]. These moments were attributed phase $2\pi$, and phase was defined as the fraction of time spent between two peaks. This allows us to directly compare theory with experiment by measuring the experimental phase differences between 3 sequential, adjacent pairs of reactors ($\theta_{21}, \theta_{32}, \theta_{43}$), and to characterize the dynamics relative to invariant manifolds and their stability derived from the model.

We conducted 318 experiments of which 186, or 58%,
FIG. 3. Basins of attraction. States are labeled as in Fig. 2. (a) Simulations of eqn 3 show that all trajectories converge to the H/K point invariant manifolds, Pronk, Bound, Rotary Gallop or Trot, depending on initial condition. Video of different perspectives in 3D are shown in movie S5. The corresponding plot of all experiment is shown in movie S6. (b) Basin of attraction for experiments and theory. The theoretical basins of attraction are colormaps computed from 5399 simulations, including those in (a). For example, if an initial state is colored red, then it will flow to the Trot attractor. The experimental basins of attraction are partially reconstructed by disks located at their initial condition and colored by the attractor to which they converge, with the color code indicated in (c). We artificially shift slightly the experimental points with nearby initial conditions so that they are revealed. Video of different perspectives in 3D are shown in movie S7. (c) The probability, \( P(A_F|A_I) \), that an experiment which started at a set of phase differences in a given theoretical basin, \( A_I \), converges to each of the 4 experimental attractors, \( A_F \). The number of observations is listed in the row labeled “N”. For example, of the 2 initial conditions corresponding to Rotary Gallop, one ended up in the Trot basin and one in the Other basin, but neither went to the predicted basin. In contrast, of the 148 states initially in Trot, 48.7% went to Other, 2.0% to Pronk, 1.3% to Bound and 48.0% to Trot.

phase-locked as defined in Appendix B. During the interval of time soon after the first oscillation and before phase-locking, the oscillation periods of all of the reactors remained similar, ±10%. Because the periods of the oscillators are similar, we make the assumption that these reactors are on the same limit cycle. Experiments were stopped either when the system phase-locked or when 70 oscillations occurred, after which the amount of reactants consumed led to the oscillation periods becoming highly variable. We monitored the initial condition, as well as the full transient trajectory for each of the 186 trajectories on their path to phase locking. This allowed the assessment of whether the trajectories were constrained by the invariant manifolds and were affected by the transversal stability, as predicted by theory.

To classify experimental phase-locked states we measure the distance between the observed state and each of the theoretical attractors using a metric appropriate for a 3-torus [Appendix D]. Each phase-locked state is classified as the nearest attractor, or as Other if they are more than 1.0[rad] from each of the H/K attractors. Of the observed steady-states, a majority of 59% correspond to the predicted Pronk, Bound and Trot point invariant manifolds [Fig. 2(c)]. We were initially baffled by the remaining 41% of the observed phase-locked states as they are located a distance from each of the 4 classes of attractors that exceeds the aforementioned threshold radius [Fig. 2(c)], raising the question of their origin as they were not predicted by theory.

Strikingly, Fig. 4(a)(b) shows that experimental trajectories starting near invariant manifolds \((D^*_1, D^*_p)\) and \((D^*_p, D^*_T)\) closely follow the dynamics predicted by the theory. Such a consistency between experimental observations and clustered transient states predicted on the basis of network symmetry alone is quite remarkable. This suggests that the universal properties dictated solely by the symmetry of the system not only predict stationary behaviors of an experimental system, but also constrain transient dynamics from an initial condition to a stationary state.

There are three other noteworthy comparisons to make between theory and experiment. Firstly, we find experiments and theory have similar shaped Pronk, Bound and Trot basins of attraction, as illustrated in Fig. 3(b)(c). Secondly, the theoretically predicted Trot attractor is symmetrically surrounded by an extended cloud of phase-
FIG. 4. Transient dynamics along higher order H/K invariant manifolds in experiment and simulation. (a) Space-time plots from an experiment and simulation with a near-Pronk initial state transitioning to Pace. States form 2 symmetric clusters corresponding to the \((D_s^1, D_s^1)\) invariant manifold. In the lower panel the experimental trajectory is shown as an arrow traveling through a 2D slice of state-space superimposed over the theoretical velocity field. Video of experiment synchronized to progression along space-time plot and trajectory in state-space shown in movie S8. (b) Space-time plots from an experiment and simulation with a near-Pronk initial state transitioning to Trot. The transition corresponds to the \((D_p^1, D_p^1)\) invariant manifold. Video of experiment synchronized to progression along space-time plot and trajectory in state-space shown in movie S9. (c) The invariant manifold surfaces attract or repulse in a state-dependent manner. The analytically computed transverse Lyapunov exponents [Appendix E] are shown via heatmaps. When positive it indicates nearby trajectories are repulsed from the invariant manifold. When negative it indicates attraction. Both the 2D \((D_p^1, D_p^1)\) and 1D \((D_s^1, D_s^1)\) invariant manifolds are largely attracting. Video of 3D perspective of plot in movie S10.

locked states, denoted Other, which are significantly far from Trot, yet within the predicted Trot basin of attraction. These observations suggest that the experimental Other states are associated with the predicted Trot state, as shown in Fig. 3(b)(c) and Fig. 5(a). Thirdly, the Rotary Gallop states were absent in all our experiments. This is particularly surprising because the theory attributes to that state a large basin of attraction.

Inclusion of Slight Heterogeneity in Theory

A hypothesis to account for these discrepancies between theory and experiment is to consider heterogeneities. Indeed, natural systems differ from theoretical models in that they are bound to be heterogeneous, and in particular imperfectly symmetrical \([1, 33]\). For instance, modeling BZ micro-oscillators with small degrees of heterogeneity in reactor chemistry (in turn associated with heterogeneous frequencies), or in reactor volume, led in various situations to better match experimental results \([20, 22, 24]\). We thus tested whether small degrees of heterogeneity between reactors could indeed explain part of the discrepancy between theory and experiments. To this purpose, we defined a variation of our network model including heterogeneities between reactors, which, using phase reduction [see detail in Appendix C] led us to analyze a phase model with heterogeneous frequency of type\([34]\):

\[
\frac{d}{dt} \phi_i = \omega_i + k \sum_{j=1}^{4} A_{ij} H(\phi_j - \phi_i)
\]

(4)

To fit equation 4 to a trajectory of phase differences measured during an experiment requires a specific set of non-zero unperturbed frequency differences \(\omega_i - \omega_j\) [Appendix C]. Although the best fit unperturbed frequencies are different for each experiment, their statistical distribution fits a Laplacian probability distribution function corresponding to unperturbed frequencies \(\omega_i\) having a percent coefficient of variation of \(\pm 3\%\) [Supplementary Material \([25]\) Sec. II]. Multiple simulations from each initial condition are run using a new sampling from the best fit unperturbed frequency differences probability density function. The steady-state phase differences for phase-locking trajectories observed experimentally and in simulations with heterogeneity are shown in Fig. 5.

With the introduction of heterogeneity in the model using probability distributions fitted to the experiments, we observed that the Rotary Gallop state disappears, just as in experiment [Fig. 5]. The percent of phase-locked states which were Rotary Gallop was high in sym-
The absence of heterogeneity, the Rotary Gallop steady-states is significantly larger than in experiments. This 23-fold decrease in percentage of Rotary Gallop steady-states compared to the homogeneous simulations in Fig. 3(a)(b). Videos of 3D perspectives of plots shown in movies S11 and S12, respectively.

The higher dimensional manifolds consist of lines and planes that guide the transient dynamics from one point manifold to another. Additionally, network sub-clusters are sequentially synchronized when convergence to a final spatiotemporal pattern occurs along these manifolds.

CONCLUSION

Understanding how network structure controls spatiotemporal pattern formation remains a central problem in network science. Analysis of spatial network symmetries has led to great progress by illuminating mechanisms behind the emergence of clustered, dynamical states. Specifically, tools for identifying group orbits and equitable partitions have been particularly fruitful in systematizing the identification of topology-required clustered states. Here, the low-dimensionality of the representation of a 4-ring network by phase differences allows us to concretely illustrate the complex dynamical landscape underpinning the emergence of clusters. In particular, we studied the network dynamics through the prism of the theory of equivariant dynamical systems. In this theory, the H/K theorem is an important result because it allows prediction of a system’s universal dynamical features from the characterization of its spatial and temporal symmetries.

We designed an experiment to explore the H/K theory in a natural system in which the oscillators were reactors containing the Belousov-Zhabotinsky chemical reaction and the coupling was physical diffusion. The significance of studying a natural self-contained reaction-diffusion system lies in the potential for fabrication of autonomous devices, which would be impractical in devices based on systems that mediate the coupling between microscale oscillators through computer-controlled optoelectronics. In our integrated reaction-diffusion system, the adjustable parameters were few and the number of oscillations was large, thereby facilitating a detailed comparison between theory and experiment. To compare the high-dimensional chemical model with experiment, we mapped both to a 3D state-space of phase differences.

Through this transformation, we showed that the symmetry required invariant manifolds take on simple forms. Point manifolds are phase-locked states with spatiotemporal patterns corresponding to the gaits of quadrupeds. The higher dimensional manifolds consist of lines and planes that guide the transient dynamics from one point manifold to another. Additionally, network sub-clusters are sequentially synchronized when convergence to a final spatiotemporal pattern occurs along these manifolds. Thus the H/K theorem imposes a great deal of structure on the phase-locked and transient dynamics of the system that is dependent only on the network’s topology and independent of any of the specifics of the oscillators and their coupling.

Our experiments showed both consistencies and dis-
crepancies with the symmetry-based theory. In particular, most phase-locked states were recovered, and tracking trajectories from an initial condition to a phase-locked state showed that the theory not only predicted the steady-states, but also their basins of attraction and, more surprisingly, transient dynamics and transversal stability along invariant manifolds.

An important aspect of this study is its exhaustiveness: analyzing a small network allowed a complete application of the H/K theorem. Having shown the successes and limitations of the theorem using the general methods of phase-reduction, it provides a framework for analyzing other networks. Most readily comparable will be other networks with polygonal geometry. For larger-scale networks, it remains in principle possible to numerically employ a similar methodology to predict spatiotemporal patterns by applying the H/K framework in complex networks, for example by using computer-assisted calculations [10]. However, for large numbers of nodes and symmetries, it may become more practical and meaningful to approximate the network by a continuum and use continuous symmetry groups (e.g., dense lattices could be approximated by planes, or polygons with a large number of nodes by circles, with continuous rotations or translations as symmetries) [13–40]. Moreover, extensions of the theory will allow prediction of further invariant manifolds, which do not arise directly from the symmetry group of the network [8] [17] [48].

One key consequence of this work is the validation of a longstanding theoretical conjecture that symmetries in a natural system constrain their function. Indeed, while contemporary theory [3–49] proves that networks with the same symmetry as the 4-ring we studied are required to share a universal list of possible spatiotemporal patterns, it had remained unclear whether these were observable and played a role in the emergent dynamics of natural systems. Our model experimental system demonstrated that this is the case to a greater extent than what was expected from theory, since not only spatiotemporal stationary dynamics, but also transient dynamics are constrained by mathematical invariants induced by the network symmetry. These results therefore provide a strong support to many theoretical studies proposing that symmetries in chemical or biological neural networks could explain function, e.g., locomotion patterns [9] [49].

These experiments raise the deep theoretical question of how, in spite of this general consistency between symmetry based theories and experiment, that even small levels of heterogeneity have the potential of crucially modifying the dynamics. Two examples are that heterogeneity renders some symmetry-derived states no longer observable and the surprising phenomenon whereby the sensitivity of states to heterogeneous perturbations does not correlate with the strength and size of the basin of attraction of the state in the ideally symmetric system. These results emphasize the importance of assessing the robustness of symmetry-predicted results in the face of heterogeneity. This assessment is essential to validate the application of the symmetry-based theory to biological systems, as well as to guide the design of chemical reaction-diffusion networks to be used in engineered applications, such as soft robotics.

To date, we know of no theoretical framework addressing the structural stability of H/K’s predictions to heterogeneity that can explain our experimental and numerical observations. Thus this work encourages more theoretical and experimental studies such as systematically introducing symmetry breaking by controlling the degree to which nodes and connections are distinct, so as to finely characterize the origin of heterogeneity-induced destabilization or vanishing of steady-states [21]. Our experimental system, used here for the first time to test symmetry based theories in reaction-diffusion networks, is ideally suited for such studies [13]. Our results partially reveal the complex role of network structure on dynamics, but to articulate fully the engineering principles of network dynamics it remains to elucidate how heterogeneity impacts performance. We hypothesize that similarly to the phase-locked and transient dynamics studied here, the impact of network heterogeneity is partially symmetry generic and partially model specific.

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IH performed all experiments, data analysis, and simulations. MN guided all of the work. Experimental design by IH, MN, and SF. BC, CS, MN, JT, and IH contributed to understanding theoretical role of symmetry in system. MM helped fabricate microfluidic chips. IH, MN, JT, and SF wrote the manuscript.

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APPENDIX A: EXPERIMENTAL METHODS

Network Fabrication

The microfluidic reaction-diffusion network was made out of four adjacent reactors embedded in polydimethylsiloxane (PDMS). The reactors are formed out of divots in PDMS, forming effective buckets, which can be filled and then sealed all together by a piece of glass, forming a common lid. We manufactured these divots using a soft lithographic process in which PDMS is cured while pressed against an inverse (positive) of the divots made out of a photosresist deposited onto a silicon wafer. This was performed as previously published [13], with the exception of one adaptation described below. This generates a glass microscope slide coated with many reactors organized into networks of four reactors, shown in Fig. 1(b)(c) and Supplementary Material [25] Fig. 1 and 2(a).

The dimensions chosen for the network allow for robust coupling of four nodes in ring topology. By adjusting the sizes and distances between reactors we found that rectangular reactor dimensions 62µm x 62µm x 30µm (L x W x H) with side-to-side distance 26 µm resulted in strong coupling. The network reactors are organized in a 2 by 2 grid [Fig. 1(b)(c)] in such a way that nearest neighbor reactors possess much more shared surface area relative next-nearest neighbors across the diagonal. This results in a ring-like connectivity, where coupling between nearest neighbors is stronger than across the diagonal. The rectangle of BZ surrounding the network [Fig. 1(c)] is forced into a steady-state, setting the concentration of chemicals surrounding the network. During each experiment we observe nine or sixteen strongly coupled, individual networks, separated from one another by controlled barriers [Supplementary Material [25] Fig. 1(b)(c)].

The only alteration of the procedure in fabricating the PDMS networks published [13] was to change the way in which the PDMS was pressed and cured – instead of a 15kg lead brick applied for 12 hours – instead of a 15kg lead brick applied for 12 hours the layer of PDMS underneath sample less than 2 µm resulted in strong coupling. The network reactors are organized in a 2 by 2 grid [Fig. 1(b)(c)] in such a way that nearest neighbor reactors possess much more shared surface area relative next-nearest neighbors across the diagonal. This results in a ring-like connectivity, where coupling between nearest neighbors is stronger than across the diagonal. The rectangle of BZ surrounding the network [Fig. 1(c)] is forced into a steady-state, setting the concentration of chemicals surrounding the network. During each experiment we observe nine or sixteen strongly coupled, individual networks, separated from one another by controlled barriers [Supplementary Material [25] Fig. 1(b)(c)].

Sample Holders

In a previous work the PDMS reactors had BZ sealed inside of them and were loaded into a microscope using an acrylic plastic clamp [13]. This clamp did not control the temperature of the BZ. However, the frequency of BZ oscillations depends on temperature [50].

To maximize experimental reproducibility, we created a clamp that controlled sample temperatures to within .1°C. The clamp’s temperature is controlled through a thermistor that measures the temperature of the clamp nearby the sample [Supplementary Material [25] Fig. 2], 2 Peltier (TEC) devices [Supplementary Material [25] Fig. 2], and PID feedback between them mediated by an Arduino. The sample is robustly driven to the clamp’s temperature because the clamp possesses a large thermal mass relative the sample and large thermal contact area with the sample [Supplementary Material [25] Fig. 2]. During all trials samples were kept at 22.0°C.

We seal samples in the temperature-controlled clamp exactly the same way as with the previous, plastic clamp [13], described in Appendix A Protocol.

BZ Chemical Preparation

The BZ loaded into the microfluidic network is first mixed outside the microfluidic device. A .24mL volume of photo-sensitive BZ is prepared by sequentially adding equal 60µL volumes of Sulfuric acid, Sodium Bromide, Malonic acid, Sodium Bromate, Ferroin then Tris(2,2’-bipyridyl)diclororuthenium(II)hexahydrate to an Eppendorf tube, then mixing it with a Vortex mixer. Note that during the sequential pipetting of the chemicals, upon adding the Sodium Bromate, the solution converts from colorless to a vivid, transparent yellow for 15 seconds before returning to a colorless state. The volumes output by the pipette used had a measured percent coefficient of variance of 1.2%. The concentrations of the reagents in the final .24mL mixture, and ultimately in the individual BZ microreactors, are in Table III.

| Chemical                  | Molecular Formula | Concentration (mM) |
|---------------------------|-------------------|--------------------|
| Sulfuric Acid             | H₂SO₄             | 80                 |
| Sodium Bromide           | NaBr              | 25                 |
| Malonic Acid             | C₃H₄O₄            | 400                |
| Sodium Bromate           | NaBrO₃            | 288                |
| Ferroin                  | C₃₆H₂₄FeN₆O₄S    | 3                  |
| Tris(2,2’-bipyridyl)diclororuthenium(II)hexahydrate | | 1.2 |

TABLE III. Final experimental chemical conditions in reactors:

Optics

We measured the chemical state of the reactors through measuring their absorbance of green light. Ferroin’s absorbance of green light changes drastically be-
between its oxidized and reduced state. The green light is filtered to 515 ± 10 nm, to avoid exciting the photocatalyst, Ru(bipy)$_3$.

Light perturbation, used to set boundary conditions and initial conditions were set by projection of patterned blue light onto the sample, selectively exciting the photocatalyst. As in previous works [13] [18] [20], the patterned blue light was periodically turned off and on at a high frequency to allow accurate measurement of absorbance of Ferroin, with period 2 seconds and duty cycle of 50%. During some of the experiments the blue light was homogenized by directly replacing the sample with a CCD and using feedback between projected signals and the measured values to minimize measured variability, as previous published [10].

Boundary conditions were applied by shining light on the rectangle surrounding the network at an intensity that completely inhibit oscillations in it.

Initial conditions were set by applying light to the reactors by inhibiting all reactors with light for 300-600 seconds. Then, the light was turned off at different times from each of the reactors, thus causing them to resume oscillating at different times. The success rate of hitting target initial conditions far from Trot or Pronk was low.

The light intensity of sample illumination was measured by placing a power meter in the sample plane, the results are similar to in previous [18] work: Intensity of blue light applied to boundaries: 1 ± .04 mW cm$^{-2}$, Intensity of blue light applied to reactors during initial condition setting: 1 ± .2 mW cm$^{-2}$, Intensity of blue light when projector blank/black: .09 ± .009 mW cm$^{-2}$, Intensity of 515 nm green sample illumination: ~1 mW cm$^{-2}$. Errors, in standard deviations, express variance in average illumination across the whole sample field of view across all experiments, not the variance across the field of view in individual experiments.

### Protocol

The protocol for an experiment is as follows:

1. PDMS chip, reentrant window, and O-ring [Supplementary Material [25] Fig. 2(a)] are cleaned with isopropyl alcohol, deionized water, and dried with compressed air. They are left under petri dishes to prevent dust accumulation.

2. A small batch of BZ solution is prepared as detailed earlier in Appendix A. Solution is left in a dark chamber.

3. The PDMS chip is plasma treated for 3 minutes at 400 mbar in ambient atmosphere.

4. The BZ solution is then pipetted into the networks of interest in the PDMS chip as shown in depth in supplementary movie S7 of [13].

5. Now, with the reentrant window placed approximately above a feature of networks covered by BZ, the reentrant window must be secured more firmly and precisely. While viewing the sample using a stereomicroscope with green filtered transmission illumination, the thumbscrews [Supplementary Material [25] Fig. 2] are slowly turned, clamping the device. We alternated tightening them in a zig-zag pattern, with each tightening of a screw being roughly a 1/8 or less rotation. During this process any bubbles which are present in the reactors should decrease in size until they are invisible. Once all reactors are surrounded by dark outlines Supplementary Material [25] Fig. 1(a), there are no shearing distortions to the network, and there are no bubbles, this process is halted.

6. The clamp and the network with BZ sealed into it are then left in a dark, room temperature chamber until it has been 40 minute since the BZ was initially mixed in step 2, typically 20 minutes.

7. The clamp is then loaded into the projection illumination microscope Supplementary Material [25] Fig. 3(c). Then, a MATLAB code with GUI is used to align a projected pattern onto the sample Supplementary Material [25] Fig. 3(b) and initiate temperature control.

8. Light is projected onto boundaries and sets initial conditions of networks as described earlier in Appendix A. Data is gathered for between 3000 and 24000s, ∼ 10 and 81 periods of oscillation of each reactor.

9. In a few experiments a second attempt at setting initial conditions was made.

### APPENDIX B: PHASE-LOCKED CRITERIA

To identify phase-locked states in experiments we require that $\frac{d}{dt}(\phi_i - \phi_j)$ is almost zero and is not accelerating, $\frac{d^2}{dt^2}(\phi_i - \phi_j)$ is also small. The algorithm used:

1. Calculate the three phase differences versus time: $(\theta_{21}, \theta_{32}, \theta_{43})$

2. Lowpass them to form: $(\bar{\theta}_{21}, \bar{\theta}_{32}, \bar{\theta}_{43})$

3. Find the longest region in the $(\bar{\theta}_{21}, \bar{\theta}_{32}, \bar{\theta}_{43})$ time series when their velocities at below as threshold:

$$|\frac{d}{dt}\bar{\theta}_{21}|, |\frac{d}{dt}\bar{\theta}_{32}|, |\frac{d}{dt}\bar{\theta}_{43}| < 2.5 \times 10^{-4} \left[\text{rad s}^{-1}\right]$$
and the average acceleration is also below a threshold:

\[
\frac{d}{dt} \left( \frac{d}{dt} \theta_{21} \right) + \frac{d}{dt} \theta_{32} + \frac{d}{dt} \theta_{45} < 9 \times 10^{-8} \text{rad/s}^2
\]

4. If the longest region is 5 or more periods of oscillation of all oscillators (1500 seconds), we consider the experiment to be phase-locked.

**APPENDIX C: BEST FIT MODEL**

**Physical Models of BZ Microoscillators**

The chemical concentration oscillations of an isolated BZ microreactor are accurately modeled by the reaction kinetics derived for macroscopic reactors \[16\ 26\]. Denoting concentrations, \( \vec{c} = (x, y, z, u) \) where \( x = [\text{HBrO}_2] \), \( y = [\text{Br}^-] \), \( z = [\text{Oxidized catalyst}] \), \( u = [\text{Br}_2] \):

\[
\frac{d}{dt} \vec{c} = \vec{R}(\vec{c})
\]  

\[
\vec{R}(x, y, z, u) = \begin{bmatrix} R_x(x, y, z) \\ R_y(x, y, z, u) \\ R_z(x, z) \\ R_u(x, y, u) \end{bmatrix}
\]  

\[
R_x(x, y, z) = k_2 y - k_1 xy - 2k_3 x^2 + \frac{k_4 y (c_o - z)}{(c_o - z + c_{min})} + \frac{k_4 y (c_o - z)}{(b o + 1)}
\]

\[
R_y(x, y, z, u) = -2k_2 y + k_7 u + k_9 z - 3k_1 xy - k_3 x^2 + \frac{k_4 y (c_o - z)}{(c_o - z + c_{min})} + \frac{k_4 y (c_o - z)}{(b o + 1)}
\]

\[
R_z(x, z) = -(k_9 + k_10) z + 2 \frac{k_4 x (c_o - z)}{(c_o - z + c_{min})} + \frac{k_4 (c_o - z)}{(b o + 1)}
\]

\[
R_u(x, y, u) = k_2 y - k_7 u + 2k_1 xy + k_3 x^2
\]

The exchange of chemicals between adjacent BZ microreactors is limited because the PDMS between them is apolar. \( \text{Br}_2 \) is the only apolar intermediate of the BZ reaction which is certainly soluble in and diffusing through the PDMS between reactors. \( \text{HBrO}_2 \) may also be soluble to a lesser degree \[19\ 20\ 27\]. Because of the short separations between reactors \( \mathcal{O}(10\mu m) \), the diffusion of these chemicals between reactors is assumed to be quasi-static \[17\ 24\]. This results in a simple form of linear difference coupling between a pair of BZ microreactors, where \( k \) is the diffusive coupling rate of \( \text{Br}_2 \) and \( k_e \) is the ratio of the diffusive coupling rate of \( \text{HBrO}_2 \) relative \( \text{Br}_2 \):

\[
\frac{d}{dt} \vec{c}_1 = \vec{R}(\vec{c}_1) + \mu (\vec{c}_2 - \vec{c}_1)
\]

\[
\frac{d}{dt} \vec{c}_2 = \vec{R}(\vec{c}_2) + \mu (\vec{c}_1 - \vec{c}_2)
\]

\[
\mu = \begin{bmatrix} k_e k 0 0 \\ 0 0 0 0 \\ 0 0 0 \\ 0 0 k \end{bmatrix}
\]

To simulate our results, we adapt the above, established model. Firstly, we model the ring-like topology by adding strong diffusive coupling between nearest neighbors and weaker coupling coupling across the diagonal. Secondly, we also permit a small degree of heterogeneity in reaction rates within the reactors, representing: i) differences in reagent concentrations, ii) differences in powers of light hitting photo-sensitive reactors, and iii) slightly different boundary conditions. The model is then a function of: a) \( k \), the diffusive coupling rate of \( \text{Br}_2 \), b) \( k_e \), the ratio of the coupling rate of \( \text{HBrO}_2 \) relative \( \text{Br}_2 \), c) \( f \), the ratio of diagonal to nearest neighbor coupling, d) differences in local reactor reaction rates.

**TABLE IV. Simulation parameters known:**

| Description      | Value | Unit   |
|------------------|-------|--------|
| Total protons     | 160   | mM     |
| Bromomalonate     | 1.2×10^{-3} | M     |
| Total metal ion catalyst | 4.2 | mM     |
| a) Bromate       | 288   | mM     |
| b) Malonic acid  | 400   | mM     |
| c) Protons       | 160   | mM     |
| d) Acid          | 160   | mM     |

**Reagent rates and relevant constants:**

| Reagent rate    | Value    | Unit   |
|-----------------|----------|--------|
| \( k_1 \)       | 2×10^{7}h | m^{-1}s^{-1} |
| \( k_2 \)       | 2h^{2}a  | s^{-1}   |
| \( k_3 \)       | 3×10^{4} | M^{-1}s^{-1} |
| \( k_4 \)       | 42ha     | s^{-1}   |
| \( k_5 \)       | 5×10^{4} | M^{-1}s^{-1} |
| \( k_6 \)       | 10       | s^{-1}   |
| \( k_7 \)       | 29m      | s^{-1}   |
| \( k_8 \)       | 9.3m     | s^{-1}   |
| \( k_9 \)       | b        | s^{-1}   |
| \( k_{10} \)    | 0.05m    | s^{-1}   |
| \( k_{ed} \)    | 2×10^{4} | M^{-1}s^{-1} |
| \( k_{red} \)   | 5×10^{4} | M^{-1}s^{-1} |
| \( k_{f} \)     | 0        | s^{-1}   |
| \( b_{o} \)     | 0.05     | M       |
| \( c_{min} \)   | √(2k_{r}(k_{9} + k_{10})c_{o}/k_{r_{ed}}) | M       |
\[
\frac{d}{dt} \ddot{c}_i = \bar{R}_c(\ddot{c}_i) + e \dddot{c}_i + \sum_{j \neq i}^4 A_{ij} \mu (\ddot{c}_j - \ddot{c}_i) \tag{6}
\]

\[
A_{ij} = \begin{bmatrix}
0 & 1 & 1 & 1 \\
1 & 0 & 1 & 1 \\
1 & 1 & 0 & 1 \\
1 & 1 & 1 & 0
\end{bmatrix}; \mu = \begin{bmatrix}
k_e k & 0 & 0 & 0 \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & k
\end{bmatrix}
\]

To ease comparison to experiments and qualitatively understand the role of free parameters, we use established methods [32, 34, 35], described later in this section, to reduce the model above Eqn. 6 to the phase model Eqn. 4. The reduced model Eqn. 4 predicts the phase dynamics of the reactors relative one another as a function of the parameters: a) \(k\) which scales the interaction function \(H\), b) \(k_e\) which determines the shape of the \(H\) function Fig. 5(a), c) \(f\) which changes the adjacency matrix, d) differences in local reactors which change intrinsic frequencies \(\omega_i\).

We then construct a 3D model of the evolution of phase-differences between adjacent nodes in the network. Letting \(\theta_{ij} = \phi_i - \phi_j\) and \(\Delta \omega_{ij} = \omega_i - \omega_j\)

\[
\frac{d}{dt} \theta_{ij} = \Delta \omega_{ij} + k \left[ \sum_{k \neq j}^4 A_{ik} H(\phi_k - \phi_i) - \sum_{k \neq j}^4 A_{jk} H(\phi_k - \phi_j) \right] \tag{7}
\]

\[
\frac{d}{dt} \dot{\phi} = \begin{bmatrix}
\frac{d}{dt} \theta_{21} \\
\frac{d}{dt} \theta_{31} \\
\frac{d}{dt} \theta_{41}
\end{bmatrix} = \dot{\Psi}(\dot{\theta}) \tag{8}
\]

This gives us a model which is expected to qualitatively capture the dynamics of the system and allow us to better understand it. Since the parameters of the model, \(f\), \(k\) and so on, cannot be independently measured, the model must be empirically fit to experimental data. However, the best fit model reveals important, nontrivial insights into our particular symmetric 4 node network and BZ microoscillator networks in general.

The \(H\) function is shown in Fig. 6(a). We ran simulations with the \(H\) function saved as a Chebychev function 61 using MATLAB’s ODE45 with relative and absolute tolerances of \(1 \times 10^{-10}\).

**Fitting to Experiments**

The model Eqn. 4 was fitted to each experimental time series of phase differences versus time [Fig. 6(b)] using nonlinear regression. The nonlinear regression was performed on each individual experiment by constraining a simulation to start from an experimental initial condition, then optimizing the simulation’s parameters to reduce the squared error between its trajectory and the experiment’s trajectory using matlab 2019b’s surrogate optimization.

| Parameter | Fit values | Values used in theory |
|-----------|------------|-----------------------|
| \(k\)     | \(G(1.8 \times 10^{-2}, 2.7 \times 10^{-2})\) | \(2 \times 10^{-2}\) |
| \(k_e\)   | .05        | .05                   |
| \(f\)     | 0          | 0                     |

**Best Fit Simulations with Heterogeneity**

To determine the impact of experimentally realistic heterogeneity on the model, we ran simulations of Eqn. 4 with the experimental best fit parameters in Table V. Specifically, heterogeneity in intrinsic frequencies in simulations \(\Delta \omega_{ij}\) were drawn from the distribution which fits
Computing Phase Model Reduction

We use established methods to reduce the reaction-diffusion model of our 4 reactor network Eqn. to the phase model Eqn. In this framework, we first determine the phase-dependent phase shift of an uncoupled BZ reactor induced by sudden, small additions of its chemical species. We then compute the fluxes of chemical species between a pair of diffusively coupled reactors as a function of their relative phases. By combining these, we determine the rate of phase shift of a reactor as a function of its phase difference with a neighbor.

If chemicals are added to a BZ reactor on its limit cycle, the time until it next spikes will be changed. These time shifts, or phase shifts, depend on amount of chemicals added as well as the time along a period of oscillation, or phase, they are added at. We quantify the phase shifts of an unperturbed reactor to a perturbation at a given phase in terms of phase response curves (PRC). The PRC, $Q$, is a set of curves of phase shift, $\Delta \phi$, as a function of a chemical perturbation’s chemical concentration, $\Delta c$, and the phase, $\phi$, at which it is added at. Specifically, it allows calculation of $\Delta \phi = Q(\phi) \Delta c$, the case of the 4D model of a BZ reaction $Q : \mathbb{R}^4 \rightarrow S^1$ is a set of 4 curves with units of phase per chemical concentrations [rad m$^{-1}$]. We compute $Q$ in the limit of infinitesimal perturbations $|\Delta c| \rightarrow 0$ by the adjoint method. This allows us to interpret $Q$ as the total derivative $Q(\phi) = \nabla c \phi$.

Noting that rate of change of phase of a reactor is $\frac{d}{dt} \phi_i$ and is a sum of constant term, its intrinsic frequency $\omega_i$, and a time-varying term due to its coupling with its neighbors depending on their relative phases:

$$\frac{d}{dt} \phi_i = \omega_i + \sum_j A_{ij} F(\phi_i, \phi_j)$$

Using the PRC we can then compute the rate of change of phase of a reactor $F$ [rad s$^{-1}$] with respect to an incident, relative phase dependent flux due to coupling $\bar{g}(\phi_i, \phi_j)$ [M s$^{-1}$] using the PRC and the chain rule:

$$F(\phi_i, \phi_j) = Q(\phi) \bar{g}(\phi_i, \phi_j) \approx \nabla c \phi \bar{g}(\phi_i, \phi_j)$$ (10)

Letting the unperturbed limit cycle of a BZ reactor be parametrized $\bar{c}_{LC}(\phi)$ and denoting the neighboring reactor $j$, we see from our diffusive coupling Eqn. that
the specific form of phase dependent flux neighbors experience $\bar{g}(\phi_i, \phi_j) = \mu [\bar{c}_{LC}(\phi_j) - \bar{c}_{LC}(\phi_i)]$ and it follows that:

$$F(\phi_i, \phi_j) = Q(\phi)\mu [\bar{c}_{LC}(\phi_j) - \bar{c}_{LC}(\phi_i)] \quad (11)$$

Note that $F$ is a linear combination of flux due to $\text{Br}_2$, $u$, and $\text{HBrO}_2$, $x$:

$$F(\phi_i, \phi_j) = k [Q_u(u_{LC}(\phi_j) - u_{LC}(\phi_i))] + k_e Q_x(x_{LC}(\phi_j) - x_{LC}(\phi_i))]$$

(12)

Since the change of relative phase differences is small during a period of reactor oscillation, we compute $F(\phi_j, \phi_i)$ averaged over a cycle $[32, 34, 35]$. Doing so transforms it into a function of relative phase difference $H(\phi_j - \phi_i)$. Since $F$ is scaled by $k$, we define $H$ such that it must be used by explicit scaling by $k$, the diffusive coupling rate of $\text{Br}_2$ $[\text{s}^{-1}]$ in eqn [3]

$$H(\phi_j - \phi_i) \equiv k^{-1}(2\pi)^{-1} \int_0^{2\pi} F(\alpha, \alpha + \phi_j - \phi_i) d\alpha \quad (13)$$

We express the interaction function $H$ as the sum of two distinct, separately calculable terms, because $F$ is a linear combination of two functions, one for $\text{Br}_2$ and one for $\text{HBrO}_2$:

$$H(\phi_j - \phi_i) = H_{\text{Br}_2}(\phi_j - \phi_i) + k_e H_{\text{HBrO}_2}(\phi_j - \phi_i) \quad (14)$$

**APPENDIX D: METRIC OF DISTANCE**

To measure distances between two points in the state-space of the 3D phase difference dynamics, both experimentally and in simulations, we found a surprising function $d(\hat{\theta}, \hat{\theta}')$ was required. For a given pair of points $\hat{\theta}$ and $\hat{\theta}'$ it is calculated by the following algorithm:

1. Consider two points in the state-space: $\hat{\theta}' = (\theta_{21}', \theta_{32}', \theta_{43}')$ and $\hat{\theta} = (\theta_{21}, \theta_{32}, \theta_{43})$

2. Compute phase difference of fourth edge, which is completely determined by the other three $\hat{\theta}'_f = (\theta_{21}', \theta_{32}', \theta_{43}', \theta_{41}')$ and $\hat{\theta}_f = (\theta_{21}, \theta_{32}, \theta_{43}, \theta_{41})$

3. Define a vector of phase difference between states with $\angle$ being complex, or phasor, angle $\theta_{diff} = \angle \exp(i*(\theta_{diff}' - \theta_{diff}))$

4. Let the distance between $\hat{\theta}'$ and $\hat{\theta}$ be the Euclidean norm of the 4D phase difference vector $\hat{d}(\hat{\theta}, \hat{\theta}') = |\theta_{diff}'|/2$

**APPENDIX E: COMPUTING TRANSVERSE LYAPUNOV EXPONENTS OF INVARIANT MANIFOLDS**

The maximum transverse Lyapunov exponent (MTLE) of the higher order invariant manifolds describe whether trajectories collapse or diverge from them. If a higher order invariant manifold has a negative MTLE, trajectories will converge towards it $[38]$. In our particular system, we found the MTLE were often easy to calculate and easy to qualitatively understand.

The MTLE of the invariant manifolds can be computed at the phase model level using the well known method of linearizing the dynamics Eqn. [9] about the invariant manifolds $[38, 10, 52, 53]$. We explicitly list how we performed this procedure in our case in which the invariant manifolds are linear hyperplanes.

We begin by considering whether a point $\hat{\theta}'$ perturbed off an invariant manifold, displaced by $\epsilon \delta$ from point $\hat{\theta}'$,
converges back to or diverges from the manifold [Fig. 7]. The dynamics of the perturbed point take on a simple form:

\[
\frac{d}{dt} \tilde{\theta} = \tilde{\Psi}(\tilde{\theta}) = \tilde{\Psi}(\tilde{\theta}^\prime + \epsilon \tilde{\delta}) = \tilde{\Psi}(\tilde{\theta}^\prime) + \epsilon \nabla_{\bar{x}} \tilde{\Psi}(\bar{x})|_{\bar{x}=\bar{y}} \tilde{\delta} + O(\epsilon^2)
\]

It is convenient to consider the displacement between the perturbed solution and the solution on the invariant manifold:

\[
\frac{d}{dt} \tilde{\delta} = \frac{d}{dt} - \frac{d}{dt} \tilde{\delta}^\prime = \tilde{\Psi}(\tilde{\theta}) - \tilde{\Psi}(\tilde{\theta}^\prime) = \epsilon \nabla_{\bar{x}} \tilde{\Psi}(\bar{x})|_{\bar{x}=\bar{y}} \tilde{\delta} + O(\epsilon^2)
\]

(15)

We can determine if the component of the perturbation along a given direction normal to the invariant manifold, \( \bar{n}_i \), grows or decays of the displacement off of the invariant manifold. Letting \( J(\bar{x}^\prime) \equiv \nabla_{\bar{x}} \tilde{\Psi}(\bar{x})|_{\bar{x}=\bar{y}} \), the rate of change of the normal distance, \( \bar{n}^T \tilde{\delta} \) is given by:

\[
\frac{d}{dt} (\bar{n}^T \tilde{\delta}) \approx \bar{n}^T \epsilon J(\tilde{\theta}^\prime) \tilde{\delta}
\]

(17)

To precisely determine the exponential timescale with which the normal components of the perturbed trajectory grows or shrinks, we use a unitary transformation matrix \( P \) to projects a vector of phase differences from the canonical basis into a basis aligned with a given invariant manifold: Letting \( t_i \) be tangent the invariant manifold and \( \bar{n}_i \) be perpendicular, \( P = [\bar{t}_1...\bar{n}_1...]^T \) s.t. if \( \bar{\theta} = c_{t1}\bar{t}_1 + c_{n1}\bar{n}_1 + ... \) then \( PJ(\bar{\theta}^\prime) = (c_{t1}, c_{t2}, ...c_{n1}...) \).

Crucially, points on the invariant manifold have no normal components \( \forall j c_{nj} = 0 \) thus \( P.J^\prime = (c_{t1}, c_{t2}, ...0,...) \). Similarly, on the invariant manifold the velocity field \( \bar{P}.\tilde{\Psi}(\tilde{\theta}^\prime) = \frac{d}{dt}(c_{t1}, c_{t2}, ...c_{nj},...) \) must have all its normal component be 0, \( \forall j \frac{d}{dt}c_{nj} = 0 \), as by definition trajectories cannot flow out of, or transverse, an invariant manifold Fig. 7.

We can now consider the growth or decay of perturbations in or out of a manifold. Let \( \xi = \bar{P}\tilde{\delta} \):

\[
\frac{d}{dt} \xi = \frac{d}{dt}(P.J^\prime) = PJ^\prime = PJ^\prime P^{-1} \xi
\]

(18)

Letting \( J^\prime = PJ^\prime P^{-1} : \frac{d}{dt} \xi = J^\prime \xi \) - a linear time-varying equation. Since the dynamics of the system \( \xi \) normal to the invariant manifold are all 0, independent on the location along the manifold spanned by the tangent, it follows that the block dynamics in \( J^\prime \) corresponding to normal components will be independent of those for tangent components [38]. The maximum real eigenvalue of this block of normal dynamics gives an approximate bound on the exponential growth or decay of the trajectory’s distance normal an invariant manifold and is called the maximum transverse Lyapunov exponent.

Algorithm

The algorithm, detailed at length above, is as follows:

1. Choose an invariant manifold \( M \), of dimension \( k \), in an \( n \) node network.
2. Determine \( k \) orthonormal vectors which span \( M \) and label them the tangent vectors \( T \). Determine a set \( N \) of \( n - 1 - k \) vectors orthonormal one another and \( T \). We use the Gramm-Schmitt procedure.
3. Compute a unitary transformation matrix \( P \), with the first columns composed of invariant manifold tangents, then followed by normals.
4. Compute the Jacobian of your nonlinear flow at points on the invariant manifold \( J(\tilde{\theta}^\prime) \), written explicitly as a function of location on the invariant manifold \( \tilde{\theta}^\prime \).
5. Transform the Jacobian into its tangent and normal components using \( P \) via \( P.J(\tilde{\theta}^\prime).P^{-1} = J^\prime(\tilde{\theta}^\prime) \).
6. Extract the block of \( J^\prime \) that contains the decoupled transverse dynamics - the columns and rows corresponding to normal components.
7. Compute the maximum real eigenvalue of the normal block \( \lambda(J^\prime) \), which is the max Transverse Lyapunov Exponent.

An example of executing this algorithm for the \((D^t_1,D^t_3)\) invariant manifold of the 4 ring is in Supplementary Material [25] Sec. IIIA. Generic expressions of block of \( J^\prime \) for all invariant manifolds of a broad class of 4 ring networks are computed in terms of first derivatives of \( H \) in Supplementary Material [25] Table I. A comparison of the MTLE of a ring of 4 Kuramoto oscillators to our system is presented in Supplementary Material [25] Fig. 8.
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