Text S1. Supporting Methods and Results.

“A Design Principle of Group-level Decision Making in Cell Populations”
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1. Derivation of mathematical models
   1.1 Autoinduction circuit with direct import
   1.2 Dual positive-feedback circuit
   1.3 Positive-and-negative-feedback circuit
   1.4 Autoinduction circuit with trans-membrane receptor
   1.5 Effect of intracellular degradation
   1.6 Effect of diffusion

2. Conditions for group-level / autonomous bistability
   2.1 Group-level bistability in the autoinduction circuit
   2.2 Autonomous bistability in the autoinduction circuit
   2.3 Phase boundary in the dual positive-feedback circuit
   2.4 Cell-autonomous excitability in the positive-and-negative-feedback circuit

3. Parameter estimation for bacterial quorum sensing
   3.1 Normalized threshold $\bar{k}$
      3.1.1 Estimation of $\bar{k}$ from extracellular signal concentration
      3.1.2 Estimation of $\bar{k}$ from gene expression level
   3.2 The order parameter $\epsilon$
      3.2.1 rhl system
      3.2.2 las system
      3.2.3 car system
      3.2.4 lux system

Supporting Table S1 – S6
Supporting Figure S1 – S8
References
1. Derivation of mathematical models

1.1 Autoinduction circuit with direct import

Let us first describe a model that we have employed to study cell-state transition mediated by autoinducing signal synthesis in a population consisted of \( N \) number of cells. The model assumes that each cell synthesizes autoinducer molecules that are passively transported in and out of cells and degraded in the extracellular space. The molecule is assumed to diffuse fast so that spatial heterogeneity such as concentration gradient is not taken into account (See Text S1 1.6 for the spatio-temporal scale where such “well-mixed” approximation is valid). The synthesis rate of autoinducer in the \( i \)-th cell (\( i = 1, 2, \ldots, N \)) rapidly increases above a certain autoinducer concentration \( K_i \). Kinetics of autoinducer synthesis, transport and degradation in extra-cellular space (See Text S1 1.5 for effect of intra-cellular degradation) \([1-3]\) are given by

\[
\begin{align*}
\frac{dS_e}{d\tau} &= \rho_v c_{sec} (\bar{S} - S_e) - \gamma_e S_e \\
\frac{dS_i}{d\tau} &= c_{sec} (S_e - S_i) + A_{syn} X_i \\
\frac{dX_i}{d\tau} &= (V_{max} - V_{min}) \frac{S_i^2}{S_i^2 + K_i^2} + V_{min} - \gamma_X X_i + \eta_{X,i}
\end{align*}
\]

where \( S_e, S_i, \) and \( X_i \) are concentrations of extracellular and intracellular autoinducer and its synthetase in the \( i \)-th cell. \( \bar{S} = \frac{1}{N_{cell}} \sum_{j=1}^{N_{cell}} S_j \). \( V_{max} \) and \( V_{min} \) \((V_{min} < V_{max})\) denote the rate of enzyme synthesis at high and low concentration of intracellular autoinducer, respectively. According to change from \( V_{max} \) to \( V_{min} \), the amount of autoinducer synthesized increases \( \lambda \) times, where

\[
\lambda \equiv \frac{V_{max}}{V_{min}}
\]

represents the strength of autoinduction. Experimentally, the magnitude of \( \lambda \) has been measured (Table S1) and manipulated by an inducible promoter \([4,5]\).
We incorporated cell-cell variation in the value of $K_i$ and temporal fluctuation in the synthetase concentration $X_i$ ($\eta_{X,i}$ in Eq. S1-3), to account for the heterogeneous response to exogenously applied autoinducer as observed for isolated *V. fischeri* cells [6]. Full definition of variables and parameters are listed in Table S2. The model is almost identical to those studied earlier [7] and accounts for the kinetics of bacterial autoinducers such as AHLs (N-Acyl homoserine lactones) that is passively transported into the cells (Fig. 1C). A slightly modified version of the model for a case where signal molecules bind to trans-membrane receptors will be derived in Text S1 1.4.

The sensitivity or the threshold concentration $K_i$ for the switch response in Eq. S1-3 has been experimentally measured in isolated cells [6]. The Hill coefficient in Eq. S1-3 is higher than unity due to cooperative binding of signaling molecule to a transcriptional activator and DNA [7,8] as described in Test S1 1.2. To account for both group-level and autonomous bistability, the coefficient should be higher than unity [7]. Here we assume the Hill coefficient of 2. When the Hill coefficient is one, group-level bistability does not exist (Text S1 2.1) therefore the all-or-none transition cannot occur (Fig. S2C, grey points). On the other hand, when we take larger values of Hill coefficient, the order parameter $\varepsilon$ at the boundary between autonomous bistability and monostability (Eq. S2-15) becomes larger, while the boundary between the group-level and autonomous bistability (Eq. S2-15) remains almost unchanged (data not shown). The increase of $\varepsilon$ at the boundary between autonomous bistability and monostability with the Hill coefficient are also observed in the dual positive-feedback circuit (Eq. S2-23; Figs. 1D and 3B).

To clarify the relationship between the three variables $S_e$, $S_i$ and $X_i$, we transformed Eqs. S1-1, S1-2 and S1-3 into a single equality. When we assume that intra-cellular and extra-cellular kinetics (Eqs. S1-1 and S1-2) equilibrate to a steady state rapidly compared to enzyme synthesis and
degradation (Eq. S1-3). Eqs. S1-1 and S1-2 become

\[ S_e = \frac{\rho_v}{\rho_v + \frac{\gamma_{ex}}{c_{sec}}} \bar{S} \]  
(S1-5),

\[ S_i = S_e + \frac{A_{syn}}{c_{sec}} X_i \]  
(S1-6).

The first and second terms in the right-hand side of Eq. S1-6 represent autoinducer molecules imported from extracellular environment plus those that are synthesized and accumulated within the cell. By taking the ensemble average, Eq. S1-6 becomes

\[ \frac{\gamma_{ex}}{c_{sec}} \bar{S} = A_{syn} \bar{X} \]  
(S1-7).

By substituting Eqs. S1-5 and S1-7 into Eq. S1-6, we obtain

\[ S_i = A_{syn} \left( \frac{\rho_v \bar{X}}{\gamma_{ex}} + \frac{\gamma_{ex} X_i}{c_{sec}} \right) \]  
(S1-8).

where the first term is equal to \( S_e \). The earlier model [7] studied a case \( S_e = S_i \), i.e., \( \gamma_{ex}/c_{sec} = 0 \) which is oversimplification for the present purpose. For example, in \( P. aeruginosa \), \( S_i \) is more than three times larger than \( S_e \) [9]. Thus in this study, the intracellular autoinducer concentration is represented by Eq. S1-8 for a more general case \( S_e \leq S_i \). 

† The large difference between \( S_e \) and \( S_i \) can be confirmed by the coefficients in the second and the first term of Eq. S1-8, i.e., \( (S_i - S_e)/S_e = \gamma_{ex}/c_{sec}/\rho_v \), when \( X_i = \bar{X} \). \( \rho_v \) near the threshold can be estimated from OD in bulk experiments (Eq. S3-4; Table S6). As will be shown in Text S1 2.2, our model predicts that the autonomous bistability occurs when \( \gamma_{ex}/c_{sec}/\rho_v \) is smaller than 1 but non-zero. For the operons in Table S6, \( \gamma_{ex}/c_{sec}/\rho_v \) is 0.02 to 0.26 which is indeed small but not zero meaning that the autonomous bistability can occur.
Finally, based on the expression of \( S_i \) (Eq. S1-8), we derive a single variable differential equation Eq. 1 and a unique parameter \( \varepsilon \) that determines the nature of the switch. By substituting Eq. S1-8 into Eq. S1-3, the model (Eqs. S1-1 to S1-3) is reduced to a single variable

\[
\frac{dX_i}{d\tau} = \left( V_{\text{max}} - V_{\text{min}} \right) \frac{A_{\text{syn}}}{\gamma_{\text{ex}}} \left( \frac{\rho_v \bar{R} + \gamma_{\text{ex}} X_i}{c_{\text{sec}}} \right)^2 + V_{\text{min}} - \gamma X_i + \eta X_i.
\]

By rescaling variables \( X_i, S_i, \eta X_i \) and \( \tau \) by

\[
\begin{align*}
X_i &= \frac{\gamma X}{V_{\text{max}}} X_i, \\
S_i &= \frac{\gamma_{\text{ex}}}{A_{\text{syn}} V_{\text{max}}} \gamma X S_i, \\
\eta_i &= \frac{\eta X_i}{V_{\text{max}}}, \\
t &= \gamma X \tau
\end{align*}
\]

and by using normalized parameter

\[
k_i = \frac{\gamma_{\text{ex}} \gamma X}{A_{\text{syn}} V_{\text{max}}} K_i
\]

we obtain Eq. 1 in the main text

\[
\begin{align*}
\frac{dx_i}{dt} &= \left( 1 - \lambda^{-1} \right) \frac{s_i^2}{s_i^2 + K_i^2} + \lambda^{-1} - x_i + \eta_i \\
\frac{s_i}{dt} &= \rho_v \bar{R} + \gamma_{\text{ex}} x_i
\end{align*}
\]

where \( \eta_i \) is white Gaussian noise in the chemical Langevin equation \([10]\). At the steady state, the variance of the noise is given by \([11,12]\)
\[ |\eta_i|^2 = \left( 1 - \lambda^{-1} \right) \frac{s_i^2}{s_i^2 + k_i} + \lambda^{-1} + x_i \cdot \frac{1}{\gamma_x N_{ON}} \]

\[ = \frac{2x_i}{\gamma_x N_{ON}} \]  

(S1.11),

where \( N_{on} \) denotes the number of synthetase molecules in the ON-state cell (Eq. S1.3) given by

\[ N_{ON} = X_{ON} V_{cell}, \quad X_{ON} = \frac{V_{max}}{\gamma_x} \]  

(S1.12).

Using the original parameters, the order parameter \( \varepsilon \) (Eq. 2; Fig. 3) is given by

\[ \varepsilon \equiv \frac{\gamma_{ec}}{c_{sec} k} = \frac{A_{syn} V_{max}}{\gamma_x c_{sec} K} \]  

(S1.13).

where \( A_{syn} \) and \( \gamma_x \) are synthesis rate of autoinducer \( S_i \) and degradation rate of synthetase \( X_i \) respectively, and \( k \equiv \frac{1}{N_{cell}} \sum_i k_i \) and \( K \equiv \frac{1}{N_{cell}} \sum_i K_i \). By substituting \( X_{ON} \) (Eq. S1.12) into Eq. S1.13, we obtain Eq. 2 by

\[ \varepsilon = \frac{A_{syn} X_{ON}}{c_{sec} K} \]  

(S1.14)

where \( A_{syn} X_{on}/c_{sec} \) denotes the autoinducer concentration at the maximum synthesis activity (Eqs. S1.6 and S1.8). The concentration is equal to the threshold \( K \) when \( \varepsilon = 1 \), which roughly corresponds to the boundary between the graded and all-or-none transitions (Text S1.2.2).

1.2 Dual positive-feedback circuit

Recent experiments have shown that when an additional positive feedback loop is introduced into the autoinduction circuit (Fig. 1C and Eq. 1; Fig. 1D), autonomous bistability becomes more robust to parameter variation [13].
To analyze such a circuit, we extend the simple autoinduction circuit (Eqs. S1-1 to S1-3), and derive the order parameter $\varepsilon$ and show that this is identical with the that obtained for the simple autoinduction circuit (Eq. S1-13).

An additional feedback loop is typically found in bacterial quorum sensing systems such as complex formation of a transcriptional activator molecule LuxR with autoinducer molecules in V. fischeri [14] (Table 1). The promoter-complex formation induces expression of genes that encode the activator itself and the autoinducer synthase. To describe this, Eq. S1-3 is extended as follows:

\[
\begin{align*}
\frac{dX_i}{d\tau} &= \left( V_{\text{max}} - V_{\text{min}} \right) \frac{\left( Z_i S_i^m \right)^n}{\left( Z_i S_i^m \right)^n + \left( K_i^m \right)^n} + V_{\text{min}} - \gamma X_i + \eta X_i \\
\frac{dZ_i}{d\tau} &= v_Z \left( \frac{V_{\text{max}} - V_{\text{min}}}{Z_i S_i^m} \right) - \gamma Z_i
\end{align*}
\]

(S1-15),

where $Z$, $m$ and $n$ denote concentration of the activator, cooperativity of $S$-$Z$ and $Z$-promoter binding, respectively. The model closely follows that proposed recently by Thattai and his colleagues [7], with exception of a minor change in the expression of $S_i$ (Eq. S1-8). The parameter values were determined from earlier experimental studies ($m = 2$ and $n = 1.45$ in the luxI and luxR circuit [7,15]) (Table S3). $v_Z$ represents relative difference of synthesis rate between $Z$ and $X$. In addition to normalization of $X$, $S$, $\tau$ as in the simple autoinduction circuit (Eq. S1-9), the variable $Z$ and parameter $K_i$ are normalized as
We obtain expression for Eq. 3,

\[
\begin{align*}
\frac{d x_i}{dt} &= (1 - \lambda^{-1}) \frac{z_i^n \cdot s_i^{m\nu} + \lambda^{-1} - x_i + \eta_i}{z_i^n \cdot s_i^{m\nu} + k_i^{m\nu}} \\
\frac{d z_i}{dt} &= (1 - \lambda^{-1}) \frac{z_i^n \cdot s_i^{m\nu} + \lambda^{-1} - z_i}{z_i^n \cdot s_i^{m\nu} + k_i^{m\nu}} \\
s_i &= \rho_x \bar{X} + \frac{\gamma_{ex}}{c_{sec}} x_i
\end{align*}
\]

At a steady state, we see that

\[
\begin{align*}
z_i &= x_i, \\
Z_i &= a_z X_i
\end{align*}
\]  
\text{(S1·17)}

The order parameter \( \varepsilon \) (Eq. 2; Fig. 3B) is given by

\[
\varepsilon \equiv \frac{\gamma_{ex}}{c_{sec} \bar{k}} = \frac{A_{syn} V_{max}}{\gamma_X} \frac{1}{c_{sec} \bar{K}}
\]  
\text{(S1·18)}

where bars indicate population mean. By assuming \( a_z = 1 \), i.e., \( Z_i = X_i \) at the steady state (Eq. S1·17), one can see that Eq. S1·18 reduced to Eq. S1·13. Notations for the model parameters are summarized and listed in Table S3.
1.3 Positive-and-negative-feedback circuit

As a natural extension of quorum sensing, we introduced a negative feedback loop into the simple autoinducing gene circuit (Fig. 1C and Eq. 1; Fig. 1E; Table 2) to study the so-called dynamical quorum sensing transition [16-21]. We adopt a model recently proposed by Danino and colleague to describe the synthetic oscillatory circuit [18]. Here, autoinducer AHL directly activates expression of aiiA as well as its own synthetase luxI. Gene aiiA encodes lactonase AiiA that degrades AHL. Following the notation in ref.[18], the kinetics are given by

\[
\begin{align*}
\frac{dX_i}{d\tau} &= C_i \frac{\delta + \alpha S_i^2}{1 + k_i S_i^2} - \gamma_i X_i + \eta X_i \\
\frac{dY_i}{d\tau} &= C_A \frac{\delta + \alpha S_i^2}{1 + k_i S_i^2} - \gamma_A Y_i \\
\frac{dS_i}{d\tau} &= bX_i - \gamma_h Y_i S_i + D(S_e - S_i) \\
\frac{dS_e}{d\tau} &= D\rho_e (S_e - S_i) - \mu S_e
\end{align*}
\]  

(S1-19),

where \( X_i \) and \( Y_i \) denote LuxI and AiiA concentration, respectively. For simplicity, the time delay from gene regulation to luxI and aiiA were assumed to be negligible, and Michaelis-Menten kinetics of degradation and synthesis of autoinducer was approximated by first-order kinetics.

To clarify the relationship between Eq. S1-19 and the simple autoinduction circuit (Eq. 1), we normalize the variable \( X_i, Y_i, \) and \( S_i \) as in Eq. S1-9, and derive the parameter \( \varepsilon \) and show that this again yields identical formula to that we obtained for the simple autoinduction circuit (Eq. S1-13). First, by assuming quasi-steady state of extracellular AHL kinetics and by replacing the parameter notation in line with the present autoinduction model (Eqs. S1-1 to S1-3), Eq. S1-19 become
\[
\begin{aligned}
\frac{dX_i}{d\tau} &= \left( V_{\text{max}} - V_{\text{min}} \right) \frac{S_i^2}{S_i^2 + K_i^2} + V_{\text{min}} - \gamma_i X_i + \eta_{x,i} \\
\frac{dY_i}{d\tau} &= \frac{C_A}{C_I} \left( \frac{V_{\text{max}} - V_{\text{min}}}{S_i^2 + K_i^2} \right) - \gamma_A Y_i \\
\frac{dS_i}{d\tau} &= A_{\text{syn}} X_i - \gamma_B Y_i S_i + c_{\text{sec}} \left( \rho S - S_i \right)
\end{aligned}
\]

(S1-20),

where
\[
\begin{aligned}
V_{\text{min}} &= C_A \delta \\
V_{\text{max}} &= C_A \alpha \\
K_i &= \frac{1}{\sqrt{k_1}} \\
\rho &= \frac{\rho_v}{\rho_v + \frac{\gamma_{ex}}{c_{\text{sec}}}} = \frac{\rho_v}{\rho_v + \frac{\mu}{D}}
\end{aligned}
\]

(S1-21),

As in the simple autoinduction circuit (Eq. S1-9), by normalizing the variables as
\[
\begin{aligned}
x_i &= \frac{\gamma_I}{V_{\text{max}}} X_i \\
y_i &= \frac{C_I}{C_A} \frac{\gamma_A}{V_{\text{max}}} Y_i \\
s_i &= \frac{c_{\text{sec}} \gamma_I}{A_{\text{syn}} V_{\text{max}}} S_i \\
t &= \gamma_I \tau
\end{aligned}
\]

(S1-22),

we arrive at Eq. 4 in the main text,
\[
\begin{align*}
\frac{dx_i}{dt} &= (1 - \lambda^{-1}) \frac{s_i^2}{s_i^2 + k_i^2} + \lambda^{-1} x_i + \eta_i \\
\frac{dy_j}{dt} &= (1 - \lambda^{-1}) \frac{s_i^2}{s_i^2 + k_i^2} + \lambda^{-1} y_i \\
a_s \frac{ds_i}{dt} &= x_i - gy_i s_i + \rho s - s_i
\end{align*}
\]

where

\[
\begin{align*}
K_i &= \frac{c_{sec} \gamma_I}{A_{syn} V_{max}} ,
K_i &= \frac{\gamma_I D k_i}{C_A \alpha b} \\
g &= \frac{C_A V_{max}}{C_A c_{sec} \gamma_A} \gamma_H = \frac{C_A \alpha \gamma_H}{k_1 \gamma_A D} \\
a_s &= \frac{\gamma_I}{c_{sec}} \\
a_s &= \gamma_I \\
a_s &= \gamma_A
\end{align*}
\]

Comparison of Eq. S1·23 and Eq. S1·13 indicates that the mean threshold \( \bar{k} \) corresponds to inverse of the order parameter \( \epsilon \) in the simple autoinduction circuit

\[
\bar{k} = \frac{1}{N_{cell}} \sum_i k_i = \frac{c_{sec} \gamma_I}{A_{syn} V_{max}} \bar{K} = \epsilon^{-1}
\]

since \( \gamma_I \) corresponds to \( \gamma_X \) in Eq. S1·3. Table S4 shows comparison of these parameters to those in the earlier model (Eq. S1·19) [18].

Finally, to analytically study the group-level transition, we analyze the nullclines for an isolated cell and the population. First, we consider the isolated condition, \( \rho = 0 \). At the steady state, Eq. 4 becomes
\begin{align*}
\frac{dx_i}{dt} = (1 - \lambda^{-1}) \frac{s_i^2}{s_i^2 + \lambda^{-1}} + \lambda^{-1} - x_i = 0 \\
\frac{dy_i}{dt} = (1 - \lambda^{-1}) \frac{s_i^2}{s_i^2 + \lambda^{-1}} + \lambda^{-1} - y_i = 0 \\
\frac{ds_i}{dt} = s_i - g y_i \cdot s_i - s_i = 0
\end{align*} 
(S1.25).

By substituting the third equation into the first and second equations, we obtain nullclines for the isolated condition ($\rho = 0$ in Fig. S5C-D). They are

\begin{align*}
y_i &= \frac{1}{g} \left( -1 + \frac{x_i}{k} \sqrt{\frac{1 - x_i}{x_i - \lambda^{-1}}} \right) \\
x_i &= (g y_i + 1) k \sqrt{\frac{y_i - \lambda^{-1}}{1 - y_i}}
\end{align*} 
(S1.26).

Next, assuming that there is a group-level all-or-none response, we can take $x_i = \bar{x}$, $y_i = \bar{y}$, $s_i = \bar{s}$ for all $i$ at the steady state. Eq. 4 is rewritten as

\begin{align*}
\frac{d\bar{x}}{dt} = (1 - V_{\text{max/min}}^{-1}) \frac{\bar{x}^2}{\bar{x}^2 + \bar{k}^2} + \lambda^{-1} - \bar{x} = 0 \\
\frac{d\bar{y}}{dt} = (1 - V_{\text{max/min}}^{-1}) \frac{\bar{y}^2}{\bar{y}^2 + \bar{k}^2} + \lambda^{-1} - \bar{y} = 0 \\
\frac{d\bar{s}}{dt} = \bar{x} - g \bar{y} \cdot \bar{s} + \rho \bar{s} - \bar{s} = 0
\end{align*} 
(S1.27),

where bars indicate the population mean. By substituting the third equation and Eq S1.24 into the first and second equations, we obtain nullclines for the homogeneous population (e.g., $\rho = 1$ in Fig. S5C-D). They are
\[
\begin{align*}
\bar{y} &= \frac{1}{g} \left( \rho - 1 + \bar{x} \epsilon \sqrt{\frac{1 - \bar{x}}{x - \lambda^{-1}}} \right) \\
\bar{x} &= (g\bar{y} - \rho + 1) \epsilon^{-1} \sqrt{\frac{\bar{y} - \lambda^{-1}}{1 - \bar{y}}} 
\end{align*}
\]

(S1-28).

Autonomous oscillations (Figs. 4A and S5A) can be distinguished from the autonomous excitation [22,23] by looking at two properties of the nullclines in the isolated condition (Eq. S1-26). One is the slope of the nullclines at their intersection. The other is whether or not \( x \) at the intersection is larger than \( x \) at the local minimum and maximum of the nullcline \( dx_i/dt = 0 \). When the value of \( \epsilon \) is high, cells with \( k_i < \bar{k} = \epsilon^{-1} \) (Eq. S1-24) exhibit an oscillatory instability (Fig. S5C, \( \rho = 0 \), dotted lines). In the oscillatory cells, the instability is indicated by a fixed point, i.e., an intersection of the nullclines, where the gradient of \( dy_i/dt = 0 \) is steeper than that of \( dx_i/dt = 0 \) (Fig. S5C, \( \rho = 0 \), open circle at intersection of the dotted lines). Irrespective of the initial conditions and the magnitude of \( \eta_i \) (Eq. 4), the trajectory in the state space \((x_i, y_i)\) converges to a limit cycle, whose trajectory is roughly bounded by the local minimum and maximum of the nullcline \( dx_i/dt = 0 \). At the same time, the other cells having \( k_i > \bar{k} \) are excitable (Fig. S5C, \( \rho = 0 \), solid lines). In the excitable cells, a fixed point (closed circle in Fig. S5C, \( \rho = 0 \)) which is located on the left of local minimum of the nullcline \( dx_i/dt = 0 \) (at \( x_i \sim 0.001 \) in Fig. S5C, \( \rho = 0 \)) indicates stability. When intrinsic noise or extrinsic perturbation dislocates the state \((x_i, y_i)\) on right of the local minimum \((x_i > 0.01 \) in Fig. S5C, \( \rho = 0 \)), the state transiently escapes from the stable fixed point and reaches a local maximum of the nullcline \( dx_i/dt = 0 \) (Fig. S5C, at \( x_i \sim 0.5 \)), before returning to the stable fixed point. In contrast, at low \( \epsilon \), the system exhibits excitability irrespective of the magnitude of \( k_i \), since the stable fixed point is lower than the local minimum \( dx_i/dt = 0 \) (Fig. S5D, \( \rho = 0 \), solid and dashed lines), as seen for high \( \epsilon \).
Similarly, the nullclines obtained at the level of population description (Eq. S1-28) allow us to identify the type of bifurcation that takes place when the group of cells switches from excitation to oscillations above a certain cell density. A pair of stable and unstable fixed points (closed and left open circles in $\rho = 0$ in Fig. S5C) disappears so that a limit cycle around the other unstable fixed point (right open circle at $\rho = 0$ in Fig. S5C; $\rho = 1$ in Fig. S5C-D) emerges. The nullclines in the isolated cell and the cell population together capture the essence of the graded transition at high $\varepsilon$. At low density, there is a sub-population of cells that are autonomously oscillatory. As density is increased, the remaining population undergoes a saddle-node bifurcation so that resulting transition at the population-level appears to occur gradually.

1.4 Autoinduction circuit with transmembrane receptor

In many cases, especially in eukaryotic cells, the signaling molecules do not pass freely thoroughly the membrane nor act directly in the autoregulatory loop. The autoinducing molecule binds to a transmembrane receptor to invoke a series of second-messenger responses that lead to further synthesis and secretion of autoinducing molecules. After adiabatic elimination of the signal transduction kinetics which usually takes place at a much faster time scale compared to autoinducer synthesis, kinetics of autoinducer can be simplified so that they appear, at the level of mathematical description, to directly obey the extracellular signal concentration $S_e$. Instead of Eq. S1-3, the kinetics of synthetase concentration is represented by

$$\frac{dX_i}{d\tau} = (V_{\text{max}} - V_{\text{min}}) \frac{S_e^2}{S_e^2 + K_i^2} + V_{\text{min}} - \gamma X_i X_i$$

(S1-29).

From steady state approximation of Eqs. S1-1 and S1-2 and by rescaling Eq. S1-10, Eq. S1-29 becomes
\[
\frac{dx_i}{dt} = (1 - \lambda^{-1}) \frac{(\rho_v \bar{x})^2}{(\rho_v \bar{x})^2 + k_i^2} + \lambda^{-1} - x_i \tag{S1·30},
\]

where \(k_i\) is given by Eq. S1·10. Eq. S1·30 becomes Eq. 1 when \(\gamma_{ex}/c_{sec} \sim 0\), i.e., export rate \(c_{sec}\) is much larger than extracellular degradation rate \(\gamma_{ex}\). To account for autonomous bistability, an additional intracellular positive feedback such as one described in Eq. 3 is introduced into Eq. S1·30 so that

\[
\frac{dx_i}{dt} = (1 - \lambda^{-1}) \frac{x_i^2 (\rho_v \bar{x})^2}{x_i (\rho_v \bar{x})^2 + k_i^2} + \lambda^{-1} - x_i \tag{S1·31}.
\]

However, under the isolated condition \((\rho_v = 0)\) we obtain \(\frac{dx_i}{dt} = 0 + \lambda^{-1} - x_i\), so that the autonomous bistability cannot occur. In other words, cooperative regulation between extracellular and intracellular feedback, quite naturally, must form an OR gate instead of an AND gate [24]. We thus obtain

\[
\frac{dx_i}{dt} = (1 - \lambda^{-1}) \frac{(\rho_v \bar{x})^2 + \alpha^2 x_i^2}{(\rho_v \bar{x})^2 + \alpha^2 x_i^2 + k_i^2} + \lambda^{-1} - x_i + \eta_i \tag{S1·32},
\]

where \(\alpha\) represents strength of the intracellular feedback (Fig. S7A). Eq. S1·32 exhibits both cell and population bistability depending on \(\varepsilon\) which is

\[
\varepsilon \equiv \frac{\alpha}{k} = \frac{\alpha A_{\text{ext}} V_{\text{max}}}{\gamma_{ex} \gamma_x K} \tag{S1·33},
\]

where the second equality is derived from Eq. S1·13. The phase boundary of graded and all-or-none transitions underlying autonomous and group-level bistability, respectively, is identical with the simple autoinduction circuit Eq. S2·15 (Fig. S7B-F).
As with the direct import model, we extend our study on the role of parameter $\varepsilon$ to oscillatory transitions. By introducing a negative feedback into Eq. S1·32 (Fig. S8A), we obtain

$$
\begin{align*}
\frac{dx_i}{dt} &= (1 - \lambda^{-1}) \frac{\rho_v \bar{x} + \alpha^2 x_i^2}{\rho_v \bar{x} + \alpha^2 x_i^2 + \beta^2 y_i^2 + k_i^2} + \lambda^{-1} - x_i \\
\frac{dy_i}{dt} &= x_i - y_i
\end{align*}
$$

(S1·34).

where $a_y$ and $\beta$ denote time scale of $y$ and strength of the negative feedback, respectively. For simplicity, we assume synthesis of $y_i$ to follow first order kinetics. Following the same approach taken for the direct import model (Eq. 4; Eq. S1·25 to S1·28), we derive the nullclines for the isolated cells and for the population. When cells are isolated ($\rho_v = 0$) and at the steady state, Eq. S1·34 becomes

$$
\begin{align*}
\frac{dx_i}{dt} &= (1 - \lambda^{-1}) \frac{\alpha^2 x_i^2}{\alpha^2 x_i^2 + \beta^2 y_i^2 + k_i^2} + \lambda^{-1} - x_i = 0 \\
\frac{dy_i}{dt} &= x_i - y_i = 0
\end{align*}
$$

(S1·35).

By rewriting Eq. S1·35, we obtain nullclines for the isolated condition ($\rho_v = 0$ in Fig. S8B-C)

$$
\begin{align*}
y_i &= \frac{1}{\beta} \sqrt{\frac{1 - x_i}{x_i - \lambda^{-1} \alpha^2 x_i^2}} \\
y_i &= x_i
\end{align*}
$$

(S1·36).

At the population-level description, when the concentrations of all cells are identical, i.e., $x_i = \bar{x}$ and $y_i = \bar{y}$, we obtain nullclines

$$
\begin{align*}
\bar{y} &= \frac{1}{\beta} \sqrt{\frac{1 - \bar{x}}{\bar{x} - \lambda^{-1} (\rho_v \bar{x} + \alpha^2 \bar{x}^2)} - k^2} \\
\bar{y} &= \bar{x}
\end{align*}
$$

(S1·37).
The nullclines for the isolated condition (Eq. S1-36) and for the homogeneous population (Eq. S1-37) are shown in Fig. S8B-C. We see that, the slope and the shape of the nullclines that account for excitation and oscillations exhibit the same dependence on the order parameter $\varepsilon$ and the cell density $\rho_V$ as described above for the direct import model (Eq. 4; Fig. S5C-D). In the isolated condition ($\rho_V = 0$), at high $\varepsilon$, a fraction of the cells are oscillatory having an unstable fixed point but no stable fixed point (dotted line in Fig. S8B, $\rho_V = 0$). The remainder of the cells in a stable fixed point are however excitable; i.e. suprathreshold external perturbation or intrinsic noise would transiently evoke a trajectory of large excursion towards the local maximum of the nullcline $dx_i/dt = 0$ (at $x_i \sim 0.5$, $y_i \sim 0.1$ in Fig. S8B, $\rho_V = 0$) before returning to the stable fixed point (closed circle in Fig. S8B, $\rho_V = 0$). In high density populations, the stable fixed point and an unstable fixed point coalesce and disappear via saddle node bifurcation so that oscillatory state emerges around the other unstable fixed point (Fig. S8B, $\rho_V = 1$). Because this transition happens gradually as cell density increases, we have a graded transition at the population level. In contrast, at low $\varepsilon$, the individual cells are all excitable at first (dotted and solid lines in Fig. S8C, $\rho_V = 0$), before they bifurcate to the oscillatory state simultaneously at high density (Fig. S8C, $\rho_V = 1$). These properties of nullclines at high and low $\varepsilon$ are consistent with behaviors observed in numerical simulations (Fig. S8D-E).

1.5 Effect of intracellular degradation

When intracellular degradation of the autoinducer is incorporated into the basic model (Eq. S1-1 ~ S1-3; Fig. 1C), Eq. S1-2 is replaced by

$$\frac{dS_i}{d\tau} = c_{sec} (S_c - S_i) + A_{syn} X_i - \gamma_{in} S_i$$  \hspace{1cm} (S1-38),

where $\gamma_{in}$ denotes rate of the intracellular degradation. Accordingly, the
intracellular concentration of autoinducer $s_i$ (Eq. 1) and the order parameter $\varepsilon$ (Eq. 2) are rewritten as

$$
\begin{align*}
    s_i &= \frac{1}{1 + \frac{\gamma_{in}}{c_{sec}}} \left[ \frac{1}{1 + \frac{\gamma_{in}}{\rho_Y + \frac{\gamma_{ex}}{c_{sec}}} \left( 1 + \frac{\gamma_{ex}}{c_{sec}} \frac{\gamma_{in}}{x_i} \right)} \right], \\
    \varepsilon &= \frac{1}{1 + \frac{\gamma_{in}}{c_{sec}}} \frac{\gamma_{ex}}{c_{sec} k}
\end{align*}
$$

By comparing Eq. S1-39 with Eqs. 1 and 2, one sees that as long as $\gamma_{in}$ is much lower than $c_{sec}$ and $\gamma_{ex}$, the rate of intracellular degradation has little influence on the value of $\varepsilon$ nor does it change the steady state level of $s_i$. This is supported by estimating values of $\gamma_{in}$, $c_{sec}$ and $\gamma_{ex}$. $\gamma_{in}$ can be estimated from the effective dilution rate of intracellular molecules due to cell growth, e.g., order of $10^{-2}$ min$^{-1}$, which is much lower than $c_{sec} = 0.2 \sim 3.0$ min$^{-1}$ (estimated in Table S6). On the other hand, $\gamma_{in}$ is considerably higher than $\gamma_{ex} = 4.8 \times 10^{-4} \sim 1.8 \times 10^{-3}$ min$^{-1}$ (estimated in Table S6). Even so, one sees that the values of $\varepsilon$ and $s_i$ are not severely affected considering the following arguments. $\varepsilon$ is independent of the ratio by definition (Eq. S1-39), whereas $\rho_Y$ in the autoinducer concentration $s_i$ (Eq. 1) is multiplied by a factor of $(1 + (\rho_Y + \frac{\gamma_{ex}}{c_{sec}}) \frac{\gamma_{in}}{\gamma_{ex}})^{-1}$ (Eq. S1-39). When we substitute the values for these parameters from biochemical studies ($\gamma_{in} = 10^{-2}$ min$^{-1}$; $\gamma_{ex}$ and $c_{sec}$ from Table S6; $\rho_Y$ from OD at the threshold in Table S6 and Eq. S3-4), we see that this factor ranges between 0.58 to 0.92. Accordingly, the threshold cell density increases by approximately inverse of the factor, i.e., 72% to 9%. Such deviation is within experiment-to-experiment variation (the standard deviation of OD at the threshold normalized by its mean is 25% and 9% for las and rhl operons respectively in Table S6). Thus, our conclusions hold even when intracellular degradation is taken into account (Fig. 3; Text S1 2).
1.6 Effect of diffusion

In the models (Text S1 1.1 ~ 1.4), the autoinducer molecule is assumed to diffuse fast so that spatial heterogeneity is negligible. Here, we estimate the spatial scale where this assumption is valid. Based on dimensional analysis, characteristic length $L$ defined by diffusion coefficient $D$ of the autoinducer is roughly given by

$$L \sim \sqrt{DT}$$  \hspace{1cm} (S1-40),

where $T$ denotes the characteristic time scale which can be represented by the inverse of autoinducer degradation rate $\gamma_{ex}$ (Eq. S1-1) in case of autoinduction and dual positive-feedback circuits (Fig. 1C-D). In case of the positive-and-negative feedback circuit (Fig. 1E) that exhibits oscillatory dynamics (Fig. 4), the time scale can be represented by the period of the oscillations. By substituting experimentally measured values of $D$ and $T$ into Eq. S1-40, we obtain $L \sim 1$ mm (Table S5). Therefore, the assumption of well-mixing holds for group-level dynamics that emerges at a few hundred micrometer scale or smaller.

2. Conditions for group-level / autonomous bistability

2.1 Group-level bistability in the autoinduction circuit

Group-level bistability means that when the synthetase concentration of all cells is uniform, i.e. $x_i = \bar{x} = \frac{1}{N_{cell}} \sum_{j}^{N_{eq}} x_j$ the population can take two stable steady states depending on the initial concentration. To derive sufficient condition for the group-level bistability, we analyzed steady state of Eq. 1. When $x_i = \bar{x}$ is substituted into Eq. 1, the steady state is given by
\[
(1 - \lambda^{-1}) \left( \frac{\rho_v + \frac{\gamma_{ex}}{c_{sec}} \bar{x}}{\left( \rho_v + \frac{\gamma_{ex}}{c_{sec}} \right)} \right)^2 + \lambda^{-1} - \bar{x} = 0
\]  
(S2·1),

which can be rewritten as

\[
f(\bar{x}) = \bar{x}^3 - \bar{x}^2 + \left( \frac{\bar{k}}{\rho_v + \frac{\gamma_{ex}}{c_{sec}}} \right)^2 \bar{x} - \lambda^{-1} \left( \frac{\bar{k}}{\rho_v + \frac{\gamma_{ex}}{c_{sec}}} \right)^2 = 0
\]  
(S2·2).

Bistability occurs when the equation has two stable and an unstable solution. When the three states degenerate, bistability disappears via pitchfork bifurcation. At \( \bar{x} = x_0 \), Eq. S2·2 has a three-fold root \([7]\) thus takes the form

\[
f(\bar{x}) = (\bar{x} - x_0)^3 = 0
\]  
(S2·3).

Eq. S2·2 satisfies

\[
\begin{align*}
  f(x_0) &= 0, \\
  \frac{df}{dx} \bigg|_{x=x_0} &= 0, \\
  \frac{d^2f}{dx^2} \bigg|_{x=x_0} &= 0.
\end{align*}
\]  
(S2·4).

By substituting Eq. S2·2, we obtain
\[
\begin{align*}
\left( \frac{k}{\rho + \frac{\gamma_{cs}}{c_{sec}}} \right)^2 &= \frac{x_0^2(1-x_0)}{x_0 - \lambda^{-1}}, \\
\left( \frac{k}{\rho + \frac{\gamma_{cs}}{c_{sec}}} \right)^2 &= 2x_0 - 3x_0^2, \\
x_0 &= \frac{1}{3}.
\end{align*}
\]

which yields
\[
\begin{align*}
\left( \frac{k}{\rho + \frac{\gamma_{cs}}{c_{sec}}} \right)^2 &= \frac{1}{3}, \\
\lambda &= 9.
\end{align*}
\]

When \( \lambda > 9 \), there are two stable states and one unstable steady state in intermediate cell density (red and yellow lines in Fig. 2B; closed and open circles in Fig. S1D), whereas the system is monostable irrespective of cell density when \( \lambda < 9 \).

The stability of each stable fixed point can be analyzed by plotting the activity of synthetase \( \frac{d\bar{x}}{dt} \) as a function of \( \bar{x} \) (Fig. S1F). When a sub-population switches to the ON-state, the activity (Eq. 1) of remaining population is approximated by,
\[
\frac{dx}{dt} = (1 - \lambda^{-1}) \left( \frac{\rho_v ((1 - p)x + p \cdot 1) + \gamma_{ex} x / c_{sec}}{\rho_v ((1 - p)x + p \cdot 1) + \gamma_{ex} x / c_{sec}} \right)^2 + \lambda^{-1} - x \tag{S2·7},
\]
where \( p \) denotes fraction of cells in the ON-state \((x_i \sim 1)\). Above a certain fraction of the ON-state (e.g., \( p = 0.02 \), red line in Fig. S1F), the stable fixed point on the left (closed circle in Fig. S1F) corresponding to the OFF-state and the fixed point on the right (open circle in Fig. S1F) coalesce and disappears via saddle-node bifurcation so that the remaining population in the OFF-state inevitably switches to the ON-state.

2.2 Autonomous bistability in the autoinduction circuit

The autonomous bistability requires that there are two stable states in an isolated condition \((\rho_v = 0 \text{ for Eq. 1})\). To derive the phase boundary for the autonomous bistability, we analyze the steady state which is given by

\[
(1 - \lambda^{-1}) \left( \frac{\gamma_{ex} x_i}{c_{sec}} \right)^2 + \lambda^{-1} - x_i = 0 \tag{S2·8}.
\]

For simplicity, \( k_i \) can be replaced by the population mean \( k_i = \bar{k} \). Thus we obtain

\[
f(x_i) = x_i^3 - x_i^2 + \varepsilon^2 x_i - \lambda^{-1} \varepsilon^2 = 0
\tag{S2·9},
\]

where \( \varepsilon = \gamma_{ex} / c_{sec} \bar{k} \) (Eq. S1·13). When one of the stable fixed points, and the unstable fixed point are degenerate, bistability disappears through saddle-node bifurcation

\[
f(x_i) = (x_i - x_A)^2 (x_i - x_B) = 0 \tag{S2·10},
\]
where \( x_i = x_A \) and \( x_B \) denote the fixed points. At \( x_i = x_A \), Eq. S2-9 satisfies

\[
\begin{align*}
  f(x_A) &= 0, \\
  \left. \frac{df}{dx_i} \right|_{x_i=x_A} &= 0 \\
\end{align*}
\]  

(S2-11).

By substituting Eq. S2-9, we obtain

\[
\begin{align*}
  \varepsilon^{-2} &= \frac{x_A^2 (1-x_A)}{x_A - \lambda^{-1}} \\
  \varepsilon^{-2} &= 2x_A - 3x_A^2
\end{align*}
\]  

(S2-12).

By dividing the first equation by the second equation, a quadratic equation

\[
2x_A^2 - (3\lambda^{-1} + 1)x_A + 2\lambda^{-1} = 0
\]

(S2-13)

is derived. We obtain \( x_A \) and \( \varepsilon \) as a function of \( \lambda \)

\[
\begin{align*}
  x_A &= \frac{1 + 3\lambda^{-1} \pm \sqrt{1 - 10\lambda^{-1} + 9\lambda^{-2}}}{4} \\
  \varepsilon^{-2} &= \frac{1 + 18\lambda^{-1} + 27\lambda^{-2} \pm (1 - 9\lambda^{-1})\sqrt{1 - 10\lambda^{-1} + 9\lambda^{-2}}}{4}
\end{align*}
\]  

(S2-14).

When \( \lambda >> 1 \), Eq. S2-14 is approximated to be

\[
\begin{align*}
  x_A &\approx \frac{1 + 3\lambda^{-1} \pm (1 - 5\lambda^{-1})}{4} = \frac{1 - \lambda^{-1}}{2}, 2\lambda^{-1} \\
  \varepsilon &\approx 2(1 - \lambda^{-1}), \frac{\sqrt{\lambda}}{2}
\end{align*}
\]  

(S2-15).

The two solutions for \( \varepsilon \) define the phase boundaries between the group-level
bistability (GB) / autonomous bistability (AB) and AB / monostability (M) shown in Fig. 3A, respectively.

The stability of each stable fixed point can be analyzed also for the population ($\rho_V > 0$) by plotting the production rate of synthetase $dx_i / dt$ as a function of $x_i$ (Fig. S1E). When all cells are in the OFF-state, i.e., $x = V_{max/min}^{-1}$, the production rate is approximated by

$$\frac{dx_i}{dt} \approx (1 - \lambda^{-1}) \left( \frac{\rho_V V_{max/min}^{-1} + \gamma_{ec} x_i / c_{sec}}{\left( \frac{\rho_V V_{max/min}^{-1} + \gamma_{ex} x_i / c_{sec}}{2} \right)^2 + \kappa^2} + \lambda^{-1} - x_i \right)$$  \hspace{1cm} (S2·16).

As cell density is increased, the basin of attraction for the OFF-state (region between left closed circle and open circle in Fig. S1E) decreases so that probability to switch from the OFF- to ON-state increases.

### 2.3 Phase boundary in the dual positive-feedback circuit

To derive the equations for the phase boundary in the dual positive-feedback circuit (Eq. 3), the derivation described above for the simple autoninduction circuit (Text S1 2.2) is applied to the dual positive-feedback circuit. The steady state in the isolated condition ($\rho_V = 0$ for Eq. 3 and Eq. S1·17) is given by

$$\left( 1 - \lambda^{-1} \right) \frac{x_i^n \left( \gamma_{ex} / c_{sec} \right)^{m_n}}{x_i^n \left( \gamma_{ex} / c_{sec} \right)^{m_n} + \kappa_i^{m_n}} + \lambda^{-1} - x_i = 0 \hspace{1cm} (S2·17),$$

which rewrites to

$$f(x_i) = x_i^{m_n+1} - x_i^{m_n} + \varepsilon^{-m_n} x_i - \lambda^{-1} \varepsilon^{-m_n} = 0 \hspace{1cm} (S2·18),$$

where $\varepsilon = \gamma_{ec} / c_{sec} \kappa$ (Eq. S1·18). By applying Eq. S2·10 and S2·11 to Eq. S2·18,
we obtain
\[
\begin{align*}
\varepsilon^{m,n} &= \frac{x_A^{m,n+1}(1-x_A)}{x_A - \lambda^{-1}} \\
\varepsilon^{m,n} &= (m \cdot n + n)x_A^{m,n+1} - (m \cdot n + n + 1)x_A^{m,n+1}
\end{align*}
\] (S2·19).

By dividing the upper by the lower equation, a quadratic equation
\[
(m \cdot n + n)x^2 - (m \cdot n + n - 1 + \lambda^{-1}(m \cdot n + n + 1))x + (m \cdot n + n)\lambda^{-1} = 0
\] (S2·20)
is derived. Thus we obtain
\[
x_A = \frac{m \cdot n + n - 1 + \lambda^{-1}(m \cdot n + n + 1) \pm \sqrt{(m \cdot n + n - 1 + \lambda^{-1}(m \cdot n + n + 1))^2 - 4\lambda^{-1}(m \cdot n + n)^2}}{2(m \cdot n + n)}
\] (S2·21).

When \( \lambda >> 1 \), these solutions can be approximated by
\[
x_A \approx \frac{m \cdot n + n - 1 + \lambda^{-1}(m \cdot n + n + 1) \pm (m \cdot n + n - 1)\left(1 - \lambda^{-1}\frac{1 + (m \cdot n + n)^2}{(m \cdot n + n - 1)^2}\right)}{2(m \cdot n + n)}
\] (S2·22).

By substituting Eq. S2·22 into Eq. S2·19, the phase boundaries for the autonomous bistability are derived
\[
\varepsilon \approx \left\{ \begin{array}{ll}
(m \cdot n + n - 1)\frac{m+1}{m \cdot n} \left(1 - \frac{\lambda^{-1} m}{m \cdot n + n - 1}\right), \\
\lambda \frac{m+1}{m \cdot n} \left(1 - \lambda^{-1}\frac{m+1}{m \cdot n + n - 1}\right).
\end{array} \right. 
\] (S2·23).
The upper and the lower solutions define the GB/AB boundary (solid line; Figs. 3B and S3) and AB/M boundary (dashed lines; Figs. 3B and S3), respectively. The value of parameter \( \epsilon \) at the AB/M boundary increases steeply about 10 times when Hill coefficient is changed from \( m = 1 \) to \( m = 4 \) at \( n = 1 \) and \( \lambda = 100 \), whereas it increases twice to change from \( n = 1 \) to 4 at \( m = 2 \). \( \epsilon \) at the GB/AB boundary decreases by half, according to change in \( m = 1 \) to 4 at \( n = 1 \), or \( n = 1 \) to 6 at \( m = 2 \). In summary, the parameter region of AB, i.e., ratio of AB/M and GB/AB boundaries expands according to increase in \( m \) and \( n \) (See also Figs. 3B and S3). The analysis shows that the auto-induction circuit with dual positive-feedback loop is more robust to variation of parameter \( \epsilon \) than the simple autoinduction (Eq. 1).

2.4 Cell-autonomous excitability in the positive-and-negative-feedback circuit

To derive the necessary condition for the cell-autonomousous excitability, we analyze the nullclines of isolated condition (Eq. S1·26). By “cell-autonomous” excitability, we mean that a transient response can be evoked by suprathreshold intrinsic noise in individual cells without relying on the secreted signal (\( \rho \tilde{\tau} \) in Eq. 4). In the state space \( (x_i \geq 0, y_i \geq 0) \), the excitatory response appears as a large excursion from the stable fixed point (closed circle in Fig. S6A) towards a local maximum of the nullcline \( dx_i/dt = 0 \) (at \( x_i \sim 0.5 \) in Fig. S6A; Eq. S1·26) before returning back to the fixed point [22,25]. Thus the autonomous excitability requires the local maximum of \( y_i \) to be larger than 0 in the isolated condition (\( \rho = 0 \) for Eq. 4; \( \epsilon = 2 \) and 4 in Fig. S6A). Otherwise there is no local maximum of the nullclines in the state space \( (x_i \geq 0, y_i \geq 0) \) (\( \epsilon = 1 \) in Fig. S6A) meaning no threshold response. When \( y_i \) is equal to 0 at the local maximum, the upper equation of Eq. S1·26 should satisfy
\[
\begin{align*}
\begin{cases}
y_i = 0, \\
dy_i &= 0, \\
dx_i &= 0
\end{cases} \\
\text{(S2.24)}
\end{align*}
\]

From the upper equation of Eq. S1.26, Eq. S2.24 is rewritten as
\[
\begin{align*}
x_i^3 - x_i^2 + \epsilon x_i - \lambda^{-1} \epsilon^2 &= 0 \\
2x_i^2 - (3\lambda^{-1} + 1)x_i + 2\lambda^{-1} &= 0
\end{align*}
\]
\[
\text{(S2.25)}
\]

where \( k_i \) can be replaced by the population mean \( k_i = \bar{k} = \epsilon^{-1} \) (Eq. S1.24). Interestingly, the upper and lower equations of Eq. S2.25 are identical with Eqs. S2.9 and S2.13, respectively; the necessary conditions for autonomous bistability in the simple autoinduction circuit. Thus \( \epsilon \) can similarly be defined by Eq. S2.15, i.e.,
\[
\begin{align*}
\begin{cases}
x_i &\approx \frac{1 - \lambda^{-1}}{2}, \\
\epsilon &\approx 2(1 - \lambda^{-1})
\end{cases} \\
\text{(S2.26)}
\end{align*}
\]

Since \( x_i \approx (1 - \lambda^{-1})/2 \) and \( x_i \approx 2\lambda^{-1} \) correspond to the local maximum and minimum of the nullcline, respectively, we obtain
\[
\epsilon \approx 2(1 - \lambda^{-1})
\]
\[
\text{(S2.27)}
\]
The solution defines the necessary condition for the autonomous excitability, i.e., \( \epsilon > 2(1 - \lambda^{-1}) \) (on the right of solid black line in Figs. 5C and S6D-E).
3. Parameter estimation for bacterial quorum sensing

3.1 Normalized threshold $\bar{k}$

To calculate the order parameter $\varepsilon$ (Eq. 2 and Fig. 3), we estimated the population mean of normalized threshold $\bar{k}$ (Eq. S1-11) in the actual bacteria. To this end, we adopted the following two methods.

3.1.1 Estimation of $\bar{k}$ from extracellular signal concentration

From Eq. S1-18 and S1-12, the normalized threshold in dual positive-feedback circuit (Eq. 3) is given by

$$\bar{k} = \frac{\gamma_{x}}{A_{syn}} \frac{\gamma_{e} \bar{K}}{V_{max} a_{z}^{m} A_{syn} X_{ON} a_{z}^{m}}$$

(S3-1).

Although $A_{syn}$ can be estimated from the turnover rate of signal synthesis in vitro, concentration of the synthase $X_{ON}$ and $a_{z}$, i.e., the ratio of $Z$ and $X$ at the steady state (Eqs. S1-16 and S1-17) were not available from literatures. Here we assumed $a_{z} = 1$ for simplicity. In case $a_{z}$ is much lower than unity, i.e., concentration of LuxR ($Z$) is much lower than that of LuxI ($X$), the value of $\bar{k}$ must be $a_{z}^{-1/m}$ times larger than the estimated value in Text S1 3.2. For larger $m$, $a_{z}^{-1/m}$, i.e., the ratio between the real and the estimated value decreases to unity.

For $X_{ON}$, we tooled an alternative method based on the extracellular autoinducer concentration. From Eq. S1-5 and S1-7, we obtain

$$A_{syn} \bar{V} = \frac{\gamma_{ex}}{\rho_{v}} S_{e}$$

(S3-2).

After substituting Eq. S3-2 into $A_{syn}X_{ON}$, Eq. S3-1 becomes

$$\bar{k} = \bar{K} \frac{P_{v,ON}}{S_{e,ON}}$$

(S3-3).
$S_{v,ON}$ and $\rho_{V,ON}$ were estimated from the extracellular autoinducer concentration and the cell density at the time gene expression within the referencing operon, e.g., $luxI$ or $luxR$, is fully induced. The volume cell density $\rho_V$ is converted to the optical density (OD) reading using the proportional constant

$$\frac{\rho_v}{OD} = 3.6 \cdot 10^{-3} \quad \text{(S3-4)},$$

which depends little on growth medium and growth rate of population in two strains of $E. coli$ (Table 1 and Fig. 2A in ref. [26]; see also [27]). We estimated $K$ from threshold concentration of autoinducer where expression of genes within the operon takes the half maximum.

### 3.1.2 Estimation of $\tilde{k}$ from gene expression level

To estimate a set of parameters for both $luxI$ and $luxR$ feedback regulation, Thattai and colleagues examined engineered $E. coli$ strains, each with different parts of the dual positive-feedback gene circuit, so as to separately analyze the feedback components [7]. Following their study (Eq. S29 in ref. [7]), the normalized threshold of the dual positive-feedback circuit (Eq. 3) equates to

$$\tilde{k} = \frac{\rho_v}{OD} \frac{1}{(Q_R a_z)^m \tilde{\mu} Q_I} = 2.6 \cdot 10^{-5} \quad \text{(S3-5)},$$

where $m$, $Q_I$, $Q_R$ denote Hill coefficient of AHL-LuxR binding, protein production rates per transcript of $luxI$ and $luxR$ scaled by the protein decay rates (Eq. 4 in ref.[7]; Table S6), respectively. $\tilde{\mu}$ is ratio of autoinducer concentration and $luxI$ expression level (Eqs. 1 and S14 in ref.[7]). Value of the parameters were substituted from Table S3 in ref. [7]. $a_z$ denotes the concentration ratio of LuxR divided by LuxI (Eqs. S1-18 and S1-17), which was assumed to take between 1 and 0.01 [7] due to different translation rates. Here we assumed $a_z = 1$.  

29
3.2 The order parameter $\varepsilon$

Here we estimate the value of the order parameter $\varepsilon = \gamma_{ci} / c_{sec} \bar{k}$ (Eq. 2; Fig. 3B) in four well-studied autoinducer operons rhl, las, car and lux. To estimate $\bar{k}$, we applied Eq. S3-5 to one data set in lux system, and Eq. S3-3 to the other data sets, respectively. In Eq. S3-3, $\bar{k}$ can be estimated from the autoinducer concentration and cell density (Eq. S3-2) at the time when expression of genes within the quorum-sensing operon are fully induced. For the rates of secretion $c_{sec}$ and degradation $\gamma_{ex}$, we adopted export [9,28] and hydrolysis [28] rate constants of AHLs, respectively, following the earlier study [29]. We assumed the oxo- and hydroxyl- derivatives have an identical hydrolysis rate. Table S6 summarizes the set of parameters that are estimated in detail below. Moreover, the estimation applies to the positive-and-negative-feedback circuit (Fig. 1E), since the expression of $\varepsilon$ (Eq. S1-24) is identical with that of the autoinduction circuit $\varepsilon = \gamma_{ci} / c_{sec} \bar{k}$ (Eq. 2).

3.2.1 rhl system

In Pseudomonas aeruginosa, the autoinducer N-butryrly-L-Homoserine lactone (C4-HSL) is produced from S-adenosylmethionine by the synthetase RhlI. Michaelis-constant of the enzymatic reaction is much lower than the intracellular concentration of the substrate [30] indicating that substrates are not rate-limiting. Thus we can assume the synthesis rate depends mainly on the synthetase concentration. A transcriptional activator RhlR forms a complex with C4-HSL that binds to a promoter at the upstream of rhl operon. At high cell density, C4-HSL induces expression of genes within the operon: e.g., the synthetase gene rhlII, the transcriptional activator gene rhlR, and rhlA that encodes surfactant rhamnolipid which is a virulence factor [31] used for biofilm formation [32]. Therefore, concentrations of RhlII and RhlR play the role of $X$ and $Z$ in the dual positive-feedback circuit (Eq. S1-15).

To calculate $\bar{k}$ and $\varepsilon$ in Eq. S1-18 based on Eq. S3-3, we estimated the
extracellular C4-HSL concentration $S_{e,ON}$, the cell density $\rho_{V,ON}$ (Eqs. S3-3 and S3-4), the threshold of C4-HSL concentration $K$, the rates of secretion $c_{sec}$ and degradation $\gamma_{ex}$ of C4-HSL. The extracellular concentration of C4-HSL in a batch culture is $S_{e,ON} = 26 \, \mu M$ at cell density of $OD = 2.0$ where rhlR expression is induced (Figs. 4B and 3B in ref.[33]). Based on measurement of C4-HSL concentration at half-maximal induction of both rhlA-lacZ reporter activity and rhamnolipid synthesis ($0.5 \, \mu M$ from Fig. 4B in ref.[34] and $0.5 \, \mu M$ from Fig. 5B in ref.[35], respectively), the estimated threshold for the response by the cells to 3-oxo-C6-HSL was $\bar{K} = 0.5 \, \mu M$. We substituted $c_{sec} = 2 \, \text{min}^{-1}$ into the secretion rate, based on measurement of radioactive C4-HSL exported from P. aeruginosa cells [9]. The degradation rate of C4-HSL estimated from hydrolysis of 3-oxo-C4-HSL in vitro is $\gamma_{ex} = 4.8 \times 10^{-4} \, \text{min}^{-1}$ [28]. When these data are substituted into Eqs. S3-3, 2 and S3-4, we obtain

$$
\begin{align*}
\bar{k} &= \bar{K} \frac{\rho_{V,ON}}{S_{e,ON}} = 0.5 \frac{2.0}{26} 0.0036 = 1.4 \times 10^{-4}, \\
\varepsilon &= \frac{\gamma_{ex}}{c_{sec}} \frac{k}{\bar{k}} = 0.00048 \frac{2}{k} = 1.7.
\end{align*}
$$

To verify the above estimation, we compared it with an independent experimental report showing that rhlR expression becomes fully induced when the extracellular C4-HSL concentration reaches $5.8 \, \mu M$ at $OD = 2.4$ (Figs. 5B and 4B in ref.[36]). Thus we obtain

$$
\begin{align*}
\bar{k} &= \bar{K} \frac{\rho_{V,ON}}{S_{e,ON}} = 0.5 \frac{2.4}{5.8} 0.0036 = 7.4 \times 10^{-4}, \\
\varepsilon &= \frac{\gamma_{ex}}{c_{sec}} \frac{k}{\bar{k}} = 0.00048 \frac{2}{k} = 0.32.
\end{align*}
$$

The difference between the two estimation is within one order of magnitude. The results are plotted in Fig. 3B.

3.2.2 las system

In P. aeruginosa, synthesis of another AHL,
N-3-oxo-dodecanoyl-L-Homoserine lactone (3-oxo-C12-HSL), is catalyzed by the synthetase LasI. When a complex of AHL and transcriptional activator LasR binds to the promoter of the las operon, it induces expression of genes in the operon such as the synthetase gene lasI, the transcriptional activator gene lasR and a virulence gene lasB. Here we estimated a set of the parameters of 3-oxo-C12-HSL in Eqs. S3-3 and 2, following the same scheme described above for the rhl system. The extracellular concentration of 3-oxo-C12-HSL in a batch culture is 4.6 µM at cell density of OD = 2.5 at a time when lasI expression is fully induced (Figs. 2F and 2C in ref.[37]). According to a study based on lasB-lacZ reporter activity, the threshold of autoregulatory response by the cells to 3-oxo-C12-HSL was \( K = 1 \) µM (Fig. 1A in ref.[38]). The secretion rate of \( c_{sec} = 0.2 \) min\(^{-1}\) was estimated from measurement of tritium labeled 3-oxo-C12-HSL exported from \( P. \) aeruginosa [9]. We estimated the degradation rate as \( \gamma_{ex} = 2.9 \times 10^{-4} \) min\(^{-1}\) based on the rate of hydrolysis of 3-oxo-C12-HSL in vitro [28]. By substituting these parameters into Eqs. S3-3, 2 and, S3-4, we obtain
\[
\kappa = 2.0 \times 10^{-3}, \ \varepsilon = 0.74.
\]
As in the rhl systems, we compared the above estimation with another independent experimental result showing that lasR expression becomes fully induced when extracellular 3-oxo-C12-HSL concentration reaches 5.5 µM at OD = 1.5 (Figs. 4A and 2 in ref.[33]). By substituting these parameters into Eqs. S3-3, 2 and S3-4, we obtain
\[
\kappa = 9.8 \times 10^{-4}, \ \varepsilon = 1.5
\]
The difference of \( \kappa \) and \( \varepsilon \) between the two cases is below one order of the magnitude.

3.2.3 car system

In plant pathogen \( E. \) carotovora, production of an AHL N-3-oxo-hexanoyl-L-Homoserine lactone (3-oxo-C6-HSL), is catalyzed by the synthetase CarI to induce state of virulence at high cell density. The
autoinduction works through its binding to the transcriptional activator CarR. Here we estimate a set of parameters on 3-oxo-C6-HSL in car operon to calculate $\bar{k}$ in Eq. S3-3 and $\varepsilon$ in Eq. 2. The extracellular concentration of 3-oxo-C6-HSL in batch cultures is about 8 $\mu$M at cell density of OD = 3.4 which is just before the stationary phase (Fig. 5a in ref.[39]). Based on the measurements of 3-oxo-C6-HSL binding to CarR (1.5 $\mu$M, Table 3 in ref.[40]; 2.0 $\mu$M, Fig. 3 in ref.[41]), the estimated threshold for the autoregulatory response by the cells to 3-oxo-C6-HSL was $\bar{K} = 1.75$ $\mu$M. 3-oxo-C6-HSL freely diffuses out from V. fischeri cells at a rate $c_{sec} = 3$ min$^{-1}$ [42]. We assumed that E. carotovora also secrete at the identical rate. The degradation rate is estimated at $\gamma_{ex} = 1.8 \times 10^{-3}$ min$^{-1}$ based on the rate of hydrolysis of 3-oxo-C6-HSL in vitro [28]. Thus we obtain $\bar{k} = 2.7 \cdot 10^{-3}$, $\varepsilon = 0.22$.

3.2.4 lux system

In V. fischeri, synthetase LuxI catalyzes production of 3-oxo-C6-HSL. When a complex of 3-oxo-C6-HSL and transcriptional activator LuxR binds to the promoter of the lux operon, it induces expression of the synthetase gene luxI, the transcriptional activator gene luxR and genes luxAB that encode subunits of luciferase required for their luminescence at high cell density. The autoinduction works by its binding to the transcriptional activator LuxR. We estimated a set of parameters for the lux operon to obtain the values of $\bar{k}$ in Eq. S3-3 and $\varepsilon$ in Eq. 2. Extracellular concentration of 3-oxo-C6-HSL in a batch culture is 18 $\mu$M when the bioluminescence is fully induced at cell density of OD = 1.0 (Fig. 5c in ref.[39]). Based on the measurements of 3-oxo-C6-HSL concentration at half-maximum of LuxR binding to DNA (0.07 $\mu$M, Fig. 2A in ref.[15]) and bioluminescence ( < 0.12 $\mu$M, Table 1 in ref.[43]; < 0.2 $\mu$M, Fig. 2 in ref.[42]; 0.12 ~ 0.2 $\mu$M, Fig. 6B in ref.[6]; 0.12 ~ 0.18 $\mu$M, Table 1 in ref.[44]), the estimated threshold concentrations of 3-oxo-C6-HSL was $\bar{K} = 0.1$ $\mu$M. We substituted $c_{sec} = 3$ min$^{-1}$, based on the measurement of radioactive
3-oxo-C6-HSL exported from V. fischeri [42]. The degradation rate of 3-oxo-C6-HSL \( \gamma_{ex} = 1.8 \times 10^{-3} \text{ min}^{-1} \) was inferred from that of the car system. Thus we obtain

\[
\bar{k} = 2.0 \cdot 10^{-5}, \quad \epsilon = 30.
\]

When we compared this to another estimate based on independent experiment of lux system [7] using Eq. S3-5 instead of Eq. S3-3 and substituting \( a_z = 1 \) and the same estimated values of \( c_{sec} \) and \( \gamma_{ex} \) described above, we obtain

\[
\epsilon = \frac{\gamma_{ex}}{c_{sec} \bar{k}} = \frac{0.0018}{3.0} \sqrt{\frac{a_z}{2.6 \cdot 10^{-5}}} = 23 \sqrt{a_z} = 23.
\]

The difference of \( \bar{k} \) between the two cases is below one order of magnitude. \( \epsilon \) in the two cases are about 10 times larger than AB/GB boundary \( \epsilon \sim 2 \) (Eqs. S2-15 and S2-23; solid lines in Fig. 3B). These value might be an overestimate if \( a_z \ll 1 \). Because the expression of \( \epsilon \) is identical for the simple autoinduction circuit and the positive-and-negative feedback circuit (Eq. 2; Eq. S1-24), the above estimate is valid for the engineered E. coli that harbors a negative feedback of luxI gene downstream of lux promoter in E. coli [18]. As long as the value of \( \bar{k} \) is close to the above estimate, it is reasonable to expect \( \epsilon > 2 \) suggesting a graded transition for the oscillatory circuit.
Figure S1. Supporting figure for Figure 2.

(A)-(B) Heterogeneous response of isolated cells (N = 100) to exogenously applied autoinducer due to cell-cell heterogeneity in $k_i$. $\rho_s x_i$ in Eq. 1 is replaced by exogenous signal concentration $s_e$. (C)-(D) Nullclines of Eq. 1 in case of two cells, where the values of $\epsilon = \gamma_{\text{ex}/c_{ac}k}$ and $\lambda$ are identical with those used in Figs. 2A and 2B, respectively. Closed and open circles indicate stable and unstable fixed points, respectively. At the both stable fixed points, $x_1$ and $x_2$ are identical indicating group-level bistability. $(x_1, x_2) \sim (1, 0.01)$ and $(0.01, 1)$ are also allowed in (B) indicating coexistence of ON and OFF states. (E)-(F) Activity of synthetase $dx/dt$ plotted as a function of $x$; autonomous (E; Eq. S2-16) and group-level (F; Eq. S2-7) bistability. The values of $\epsilon$ in (E) and (F) are identical with Figs. 2A and 2B, respectively.
Figure S2. Supporting figure for Figure 3A.

(A) Phase boundaries AB/GB (solid line), AB/M (dashed line), and GB/M (dotted line) determined analytically (black, Eqs. S2-6 and S2-14) and numerically (grey). In numerical simulations of cell population (Eq. 1), the AB phase is assigned when the ON- and OFF-state cells coexisted at the steady state. The GB phase is assigned when the entire population uniformly takes either the ON- or the OFF state at all density. (B)-(C) $CV_\rho/CV_k$ plotted as a function of $\epsilon$ for $\lambda = 100$ and 1000 (B) and $\lambda$ for $\epsilon = 0.25$ (C), respectively, for the simple autoinduction circuit (Eq. 1). In case of group-level bistability ($\epsilon < 2$ in (B); red points in (C)), $CV_\rho/CV_k$ decreases with decreasing $\epsilon$ and increasing $\lambda$. On the other hand, $CV_\rho$ is approximately equal to the intrinsic variation $CV_k$, when the group-level bistability disappears ($\epsilon > 2$ in (B) for autonomous bistability; grey points in (C) represent simple autoinduction without cooperativity.

$$\frac{dx_i}{dt} = \left(1 - \lambda^{-1}\right) \frac{\rho \bar{x} + \gamma x_i / c_{sc} + \lambda^{-1} - x_i}{\rho \bar{x} + \gamma x_i / c_{sc} + k_i}.$$  

(D) The response of synthetase concentration $x_i$ to cell density $\rho$ is highly variable between the cells at $\lambda = 10$ compared to $\lambda = 100$ (Fig. 2B). The value of $\epsilon$ and standard deviation of $k_i$ are the same as Fig. 2B. Each point in indicates time average at the steady state.
Figure S3. Supporting figure for Figure 3B. (A)-(C) Phase diagram of $CV_r/CV_k$ in dual positive-feedback circuit (Eq. 3). $(m, n) = (1, 1)$ (A), (2, 1) (B), and (2, 2) (C), respectively. Solid, dashed and dotted black lines indicate analytically determined boundary $AB/GB$ (Eq. S2-23), $AB/M$ (Eq. S2-23), and $GB/M$, respectively. Yellow line is $\log_{10} CV_r/CV_k = 0$ determined numerically.

Figure S4. Growth rate dependence of the phase diagram. The boundary line between all-or-none and graded transition, i.e., $CV_r/CV_k = 1$ is plotted for three different increasing rate of cell density, i.e., growth rate (Models). The ratio of the increasing rate to the degradation rate of synthetase ($\gamma_X$ in Eq. S1-3) is set to 1/2 (red), 1/10 (blue) and 1/40 (yellow), respectively, for the simple autoinduction circuit (A; Fig. 1C) and the dual positive-feedback circuit (B-C; Fig. 1D). The yellow line was imported from Figs. 3A, S3A, and S3B to (A), (B) and (C), respectively. The boundary lines are almost independent of the growth rate.
(A)-(B) Heterogeneous response of synthetase concentration $x_i$ in isolated cells (blue line: time course of a representative cell; light blue point: pulsatile response of each cell indexed in Y-axis). $\rho \bar{x}$ in Eq. 4 is replaced by the extracellular autoinducer concentration $s_e$ that is applied exogenously as an exponentially increasing function (violet line). $\varepsilon = 16$ in (A) and 4 (B) as in Figs. 4A and 4B, respectively. $\lambda = 10^3$ and $g = 30$ in (A) and (B). At $s_e = 0$, a fraction of cells are already oscillatory in (A), whereas all cells are quiescent in (B). (C)-(D) Nullclines of isolated condition (Eq. S1-26) for $\rho = 0$ and population mean (Eq. S1-28) for $\rho = 1$. Value of the parameters in (C) and (D) are same with (A) and (B) respectively. At $\rho = 0$, the $i$-th cell is either excitatory or oscillatory depending on $k_i$ (C). In (D), cells are always excitatory regardless of $k_i$. At $\rho = 1$, all cells are oscillatory in both (C) and (D). Red and blue lines indicate $dx/dt = 0$ and $dy/dt = 0$, respectively. Solid and dotted lines at $\rho = 0$ indicate $k_i$ is 50% larger and smaller than $\bar{k} = \varepsilon^{-1}$ (Eq. S1-24).
Figure S6.
Supporting figure for Figure 5.
(A) The necessary condition for cell-autonomous excitability. \( \frac{dx_i}{dt} = 0 \) in isolated condition (Eq. S1-26) for \( \varepsilon = 1, 2 \) and 4 (1/\( k_i = \varepsilon \) in Eq. S1-24). For ease of view, \( \frac{dy_i}{dt} = 0 \) is plotted only for \( \varepsilon = 4 \) (light blue line). The local maximum (\( x_i \sim 0.5 \)) is positive at \( \varepsilon = 4 \), zero at \( \varepsilon = 2 \) and negative at \( \varepsilon = 1 \) indicating no excitability at \( \varepsilon = 1 \) and 2. Thus cell-autonomous excitability requires \( \varepsilon > 2 \), consistent with analytical derivation (Text S1 2.4). (B)–(C) Phase diagram of \( CV_{\rho_i}/CV_{k_i} \) for \( g = 3 \) (B) and 10 (C) in presence of intrinsic noise (\( \eta_i \) in Eq. 4; \( |\eta_i| = 0.1 \)). The other parameters are identical with Fig. 5. (D)–(E) \( \log_{10} CV_{\rho_i}/CV_{k_i} = 0 \) plotted for cases with noise (yellow dotted line) or without (green dotted line). Black solid line indicates the excitable/oscillatory boundary \( \varepsilon \sim 2 \) derived analytically (Eq. S2-27). The region surrounded by black dashed curves supports autonomous oscillations in isolated condition in numerical simulations. \( g = 3 \) (D) and 10 (E).
Figure S7.
Graded and all-or-none quorum sensing transitions in a trans-membrane receptor model.

(A) Schematics of an autoinduction circuit with transmembrane receptor model (Eq. S1-32) in operation.

(B)-(C) Heterogeneous response in isolated cells to exogenously applied autoinducer signal (Eq. S1-32; $k_i$ has intrinsic variability as in Eq. 1; $|\eta_i| = 0.1$). $\varepsilon = 2.5$ (B) and 0.25 (C). $\lambda = 100$. Bistability appears cell-autonomously in (B) but not in (C). (D) Autonomous bistability and (E) group-level bistability (red line, analytical solution for the population mean) underlie graded and all-or-none transitions, respectively. Parameters in (D) and (E) are identical with (B) and (C), respectively. (F) Phase diagram of $CV_\rho/CV_k$. Solid, dashed and dotted black lines indicate analytically determined boundary AB/GB, AB/M, and GB/M, respectively. Yellow line is $\log_{10} CV_\rho/CV_k = 0$ determined numerically. x and + correspond to (D) and (E), respectively.
Dynamic quorum sensing transitions in a negative-feedback mediated trans-membrane receptor model.

(A) Schematics of positive-and-negative feedback circuit with transmembrane receptor model (Eq. S1-34). (B)-(C) Nullclines for the isolated cell (Eq. S1-36; left panel) and the population (Eq. S1-37; right panel) predict transitions from quiescence to oscillations depending on cell density \( \rho \). Similar to the direct import model (Eq. 4; Fig. S5C-D), at \( \rho = 0 \), cells are either excitatory or oscillatory depending on \( k_i \) in case of \( \varepsilon = \alpha / \bar{k} = 5.6 \) (B). Cells are always excitatory irrespective of \( k_i \) in \( \varepsilon = \alpha / \bar{k} = 2.8 \) (C). Solid and dotted lines at \( \rho = 0 \) indicate \( k_i \) is 25% larger and smaller than \( \bar{k} = \varepsilon^{-1} \) (Eq. S1-24). \( \alpha = 2.4 \), \( \beta = 10 \), and \( \lambda = 100 \) in (B) and (C). (D)-(E) Simulations of communicating cell populations demonstrate graded (D) and all-or-none (E) transitions during exponential increase in cell density \( \rho \) (grey line). The randomized parameter \( k_i \) has a lognormal distribution with \( CV_k = 0.25 \). \( \varepsilon = \alpha / \bar{k} \) in (D) and (E) are the same with (B) and (C), respectively. \( \lambda \), \( \alpha \), and \( \beta \) in (D) and (E) are also identical with (B) and (C). \( a_y = 100 \). \( |\eta_i| = 0.0 \).
Supporting Tables

Table S1. Representative examples of autoinduction.

<table>
<thead>
<tr>
<th>Species</th>
<th>Signal</th>
<th>Autoinduction λ</th>
<th>Hill coefficient</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>AHL</td>
<td>36</td>
<td>2</td>
<td>[7]</td>
</tr>
<tr>
<td>P. putida</td>
<td>AHL</td>
<td>10</td>
<td>2.5</td>
<td>[3]</td>
</tr>
<tr>
<td>D. discoideum</td>
<td>cAMP</td>
<td>10~40</td>
<td>N/A</td>
<td>[20,45]</td>
</tr>
</tbody>
</table>
### Table S3. Parameter values chosen in dual positive-feedback circuit Eq. 3.

<table>
<thead>
<tr>
<th>Parameters in present model</th>
<th>Expression in earlier model [7]</th>
<th>Present model (Figs. 3B and S3)</th>
<th>Earlier model</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\bar{k}$</td>
<td>$\frac{\rho_v}{OD \left(Q_k A \right)^{m}} \tilde{\mu} Q_1$</td>
<td>6 x $10^{-6}$ ~ 6 x $10^{-3}$#</td>
<td>7 x $10^{-6}$ ~ 7 x $10^{-5}$*</td>
</tr>
<tr>
<td>$a_z$</td>
<td>$A$</td>
<td>1</td>
<td>0.01 ~ 1</td>
</tr>
<tr>
<td>$m$</td>
<td>$m$</td>
<td>1 ~ 2</td>
<td>2</td>
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<tr>
<td>$n$</td>
<td>$n$</td>
<td>1 ~ 2</td>
<td>1.45</td>
</tr>
</tbody>
</table>

*Range of $\varepsilon$ in Fig. 3B is calculated from Eq. 2 by substituting rates of degradation $\gamma_c = 1.8 \times 10^{-3}$ min$^{-1}$ and transport $c_{sec} = 3$ min$^{-1}$ which were estimated from literatures (Text S1 3.2.4).

* The parameters were referred to Table S3 in ref.[7], except for OD / $\rho_v$ from Eq. S3-4.

### Table S4. Parameter values chosen in positive-and-negative feedback circuit Eq. 4.

<table>
<thead>
<tr>
<th>Parameters in present model</th>
<th>Expression in earlier model [18]</th>
<th>Present model (Figs. 4, 5, S5 and S6)</th>
<th>Earlier model *</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\lambda$</td>
<td>$\frac{\alpha}{\delta k_i}$</td>
<td>$10^1$ ~ $3 \times 10^3$</td>
<td>$2.5 \times 10^7$</td>
</tr>
<tr>
<td>$G$</td>
<td>$\frac{C \alpha \gamma_h}{k_i \gamma_a D}$</td>
<td>3 ~ 30</td>
<td>26.7</td>
</tr>
<tr>
<td>$\bar{k}$</td>
<td>$\frac{\gamma_i D k_i}{C \alpha b}$</td>
<td>0.03 ~ 3</td>
<td>0.01</td>
</tr>
<tr>
<td>$a_y$</td>
<td>$\gamma / \gamma_h$</td>
<td>100</td>
<td>1.6</td>
</tr>
<tr>
<td>$a_s$</td>
<td>$\gamma / D$</td>
<td>1</td>
<td>9.6</td>
</tr>
</tbody>
</table>

* Calculated from Supplementary Information of ref. [18].
### Table S5. Dimensional analysis of spatial scale of extracellular environment.

<table>
<thead>
<tr>
<th>Autoinducer</th>
<th>Diffusion coefficient $D$</th>
<th>Time scale $T$</th>
<th>Spatial scale $L$</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>V. fischeri</em></td>
<td>AHL $550 \mu m^2/sec$ #1</td>
<td>560 min *1</td>
<td>4.3 mm</td>
</tr>
<tr>
<td>engineered <em>E. coli</em></td>
<td>AHL $550 \mu m^2/sec$</td>
<td>50~80 min *2</td>
<td>1.3~1.6 mm</td>
</tr>
<tr>
<td><em>D. discoideum</em></td>
<td>cAMP $250$~$1,000 \mu m^2/sec$ #2</td>
<td>300~600 sec *3</td>
<td>0.27~0.77 mm</td>
</tr>
</tbody>
</table>


### Table S6. Parameters estimated from literatures.

<table>
<thead>
<tr>
<th>System</th>
<th>$S_{e,ON}$ µM</th>
<th>OD µM</th>
<th>$K$ µM</th>
<th>$\gamma_{ex}$ min$^{-1}$</th>
<th>$c_{sec}$ min$^{-1}$</th>
<th>$\bar{k}$</th>
<th>$\varepsilon$</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>rhl</em></td>
<td>26</td>
<td>2.0</td>
<td>0.5</td>
<td>$4.8 \times 10^{-4}$</td>
<td>2.0</td>
<td>$1.4 \times 10^{-4}$</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>5.8</td>
<td>2.4</td>
<td></td>
<td></td>
<td></td>
<td>$7.4 \times 10^{-4}$</td>
<td>0.32</td>
</tr>
<tr>
<td><em>las</em></td>
<td>4.6</td>
<td>2.5</td>
<td>1.0</td>
<td>$2.9 \times 10^{-4}$</td>
<td>0.2</td>
<td>$1.9 \times 10^{-3}$</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>5.5</td>
<td>1.5</td>
<td></td>
<td></td>
<td></td>
<td>$9.8 \times 10^{-4}$</td>
<td>1.5</td>
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<tr>
<td><em>car</em></td>
<td>8</td>
<td>3.4</td>
<td>1.75</td>
<td>$1.8 \times 10^{-3}$</td>
<td>3.0</td>
<td>$3.7 \times 10^{-3}$</td>
<td>0.22</td>
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<tr>
<td><em>lux</em></td>
<td>40</td>
<td>2.0</td>
<td>0.1</td>
<td>$1.8 \times 10^{-3}$</td>
<td>3.0</td>
<td>$2.0 \times 10^{-5}$</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$2.6 \times 10^{-5}$</td>
<td>23</td>
</tr>
</tbody>
</table>
References

quorum-sensing systems ain and lux sequentially induce luminescence gene expression and are important for persistence in the squid host. Mol Microbiol 50: 319-331.


