Supplementary Materials for *Understanding Types of Transitions in Clinical Change: An Introduction from the Complex Dynamic Systems Perspective*

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Supplementary Materials A: Simulation Specifications

In the main text, we presented various simulations to illustrate different types of transitions. We used stochastic differential equations (SDEs) to specify the models and conducted those simulations with the sde package (Iacus, 2022) for univariate cases and the yuima package (Brouste et al., 2014) for multivariate cases. The R code to replicate all the simulations is available at

Examples of various types of transitions

We run each situation from $T = 0$ to $T = 100$, with a time step of 0.01, except for the R-tipping case for which we run the simulation from $T = 0$ to $T = 10$.

The landscape function of the B-tipping (fold bifurcation) example shown in the main text is specified as follows (adapted from Shi et al., 2016),

$$U = 0.5\left(\frac{1}{4}x^4 - \frac{3}{2}x^2 + \lambda x\right),$$

where λ is the control parameter that slowly changes following

$$\lambda = 3 - 0.06t.$$

The dynamics of the variable x is specified with the following SDE,

$$\mathrm{d}x = -\frac{\partial U}{\partial x}\mathrm{d}t + \sigma \mathrm{d}W,$$

where σ represents the strength of noise and takes 0.3 in this example.

For Hopf bifurcation, an additional variable is required to make the vibration behavior possible. Hence, we use the following SDEs,

$$\mathrm{d}x = \left((\lambda + x^2 + y^2 - (x^2 + y^2)^2)x - \left(\omega + b(x^2 + y^2)\right)y\right)\mathrm{d}t + \sigma \mathrm{d}W_1,$$

$$\mathrm{d}y = \left((\lambda + x^2 + y^2 - (x^2 + y^2)^2)y + \left(\omega + b(x^2 + y^2)\right)x\right)\mathrm{d}t + \sigma \mathrm{d}W_2,$$

for which the drift function is transformed from the polar coordinates’ representation,

$$U = \frac{1}{6}r^6 - \frac{1}{4}r^4 + \frac{1}{2}\lambda r^2,$$

$$\frac{\mathrm{d}r}{\mathrm{d}t} = -\frac{\partial U}{\partial r},$$

$$\frac{\mathrm{d}\theta}{\mathrm{d}t} = \omega + br^2.$$

We use the parameter setting $\omega = 0.5, b = 0.1, \sigma = 0.1$ in our simulation. Additionally, for the reversed direction, we use $\lambda = -3 + 0.06t$.

For the N-tipping example, we use the same potential function form as the B-tipping example but hold $\lambda = 0$, and we use a stronger noise of $\sigma = 0.65$.

For the R-tipping example, we use the following potential function,

$$U = 0.5\left(\frac{1}{4}(x-\lambda)^4 - \frac{3}{2}(x-\lambda)^2\right),$$

and we set $\lambda = -5 + 1.1t$.

For the N-diffusion example, we use the same potential function form as the B-tipping example but hold $\lambda = 0$, and we use a stronger noise of $\sigma = 2$.

The key parameters of those examples are summarized in Table A1

Table A1. Simulation settings in the examples. The parameters corresponding to the main cause of the transitions are marked bold.

Type of transition	Stability change (shape)	Stability change (position)	Variable change	Noise strength
B-tipping	**0.06**	0.00	0.50	0.30
N-tipping	0.00	0.00	0.50	**0.65**
R-tipping	0.00	**1.20**	0.50	0.30
N-diffusion	0.00	0.00	0.50	**2.00**

Examples of clinical scenarios

For the first scenario, we use the following potential function,

$$U = 0.5\left(\left(\frac{1}{4}x^4 - \frac{3}{2}x^2 + \lambda x\right) + 0.1\left(\frac{1}{4}y^4 - \frac{1}{2}y^2 - xy\right)\right),$$

the following for the control parameter,

$$\lambda = 1 - 0.06t,$$

and the noise strength is set as $\sigma_x = 0.3, \sigma_y = 0.5$.

For the second scenario, we use the same setting as the N-tipping example for x, the following potential function for λ,

$$U = \ln(1 + (1.5\mathrm{x} - \lambda)^2) + \ln(1 + x^2) - 0.18\lambda.$$

For y, we use the same setting as the R-tipping example.

Supplementary Materials B: Illustrations of Other Types of Bifurcations

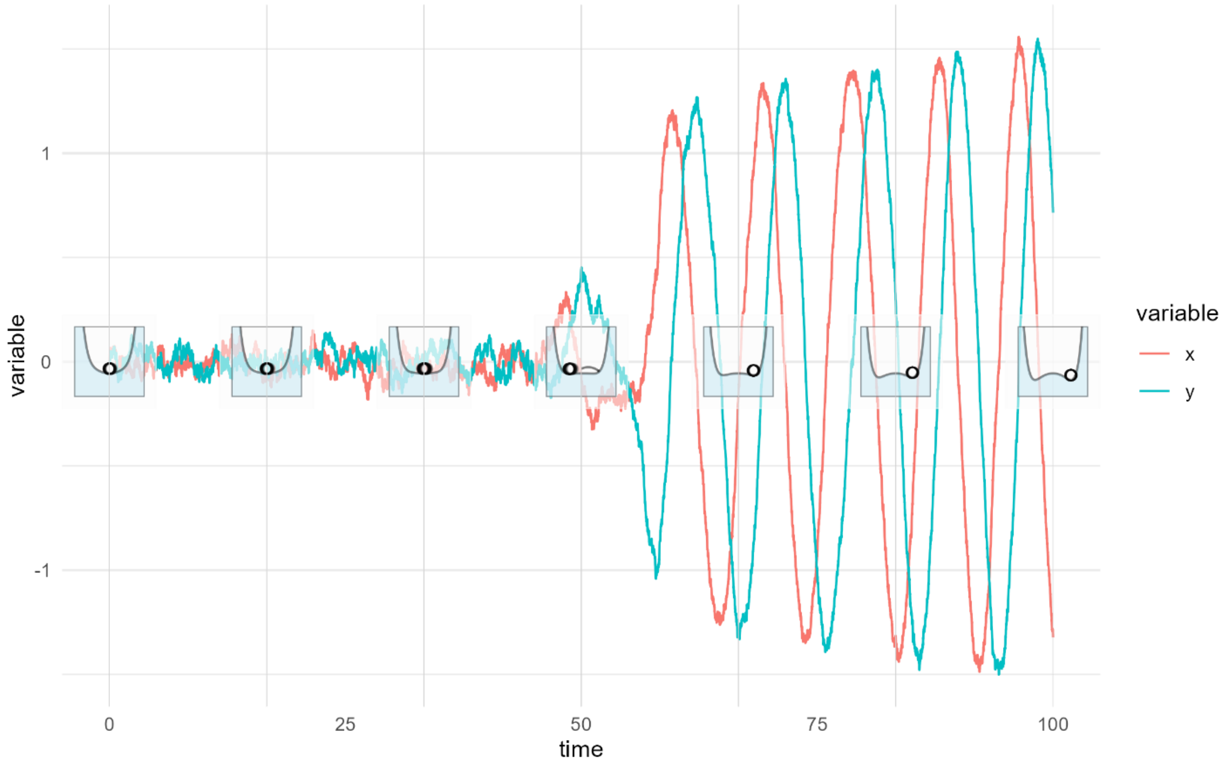

Figure B1. A simulated time series and ball-and-landscape illustrations for Hopf bifurcation.

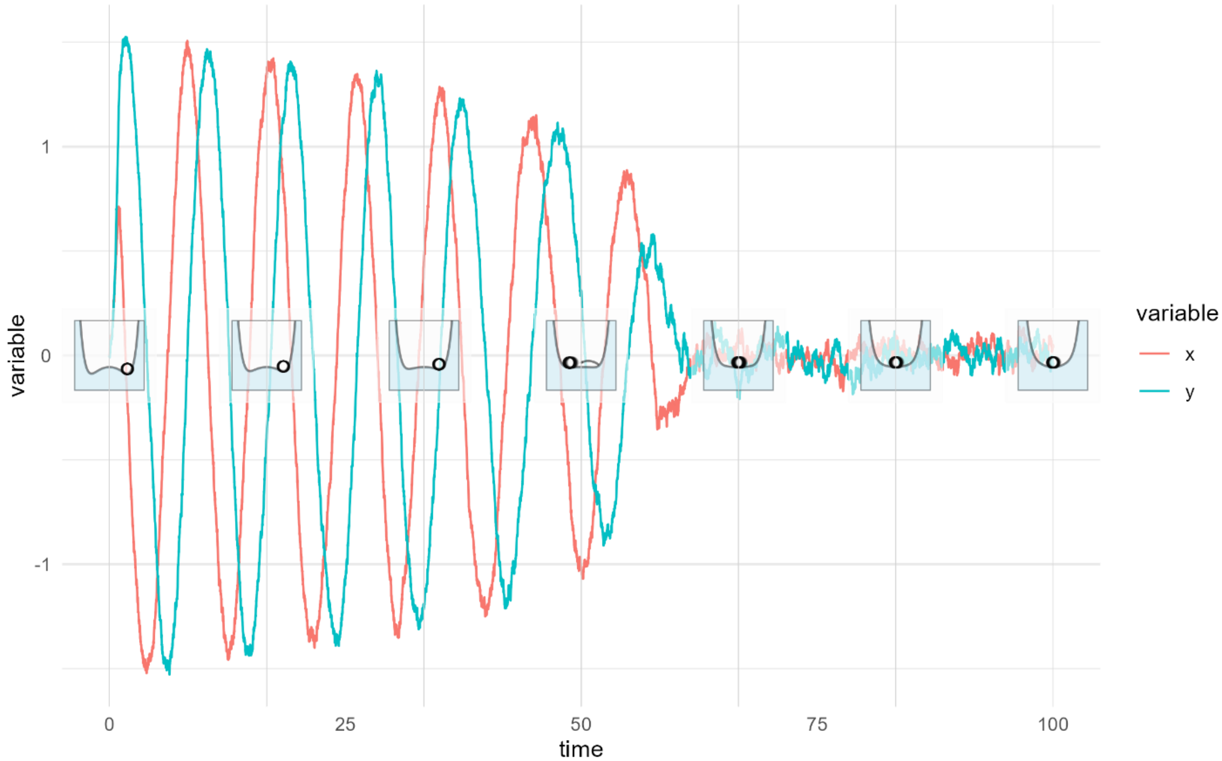

Figure B2. A simulated time series and ball-and-landscape illustrations for Hopf bifurcation (reversed direction).

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