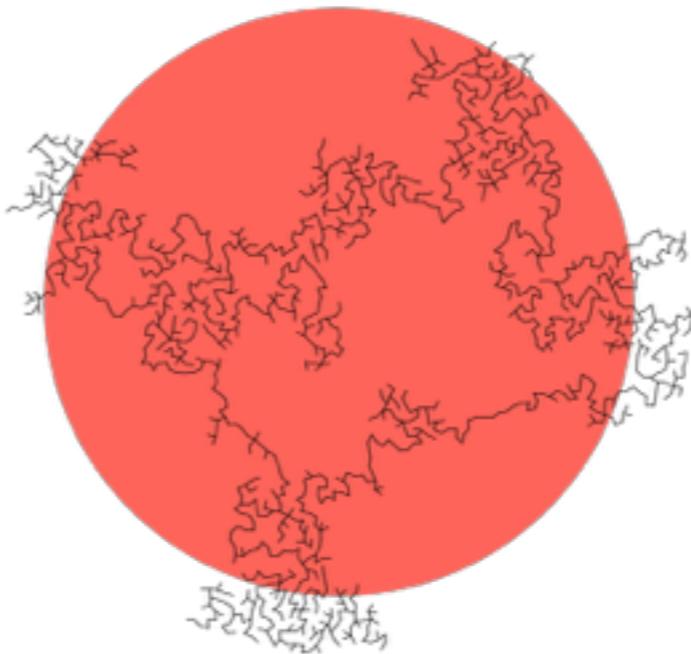


Dinámica de Plásmidos y Series Sintéticas Estocásticas



Automatas Celulares en Sistemas
Híbridos de BactoComputación

Carles Tardío Pi



Segundo Encuentro Biología Matemática
y Métodos No Arquimedianos

Sotuta de Peón, Yucatán, 21-24 Nov. 2022

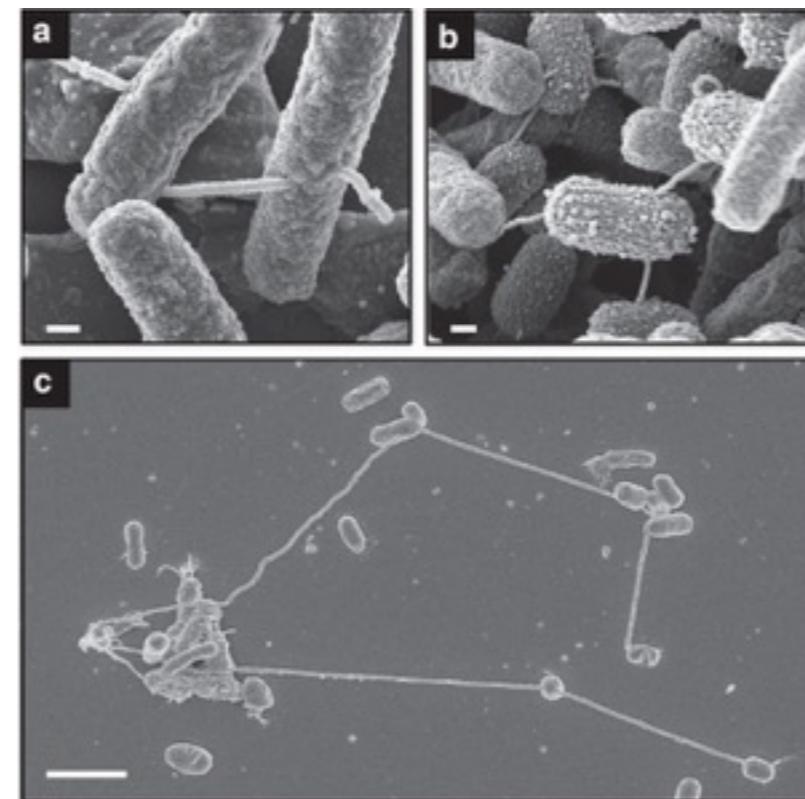


ESCUELA
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SUPERIORES
UNIDAD
MÉRIDA



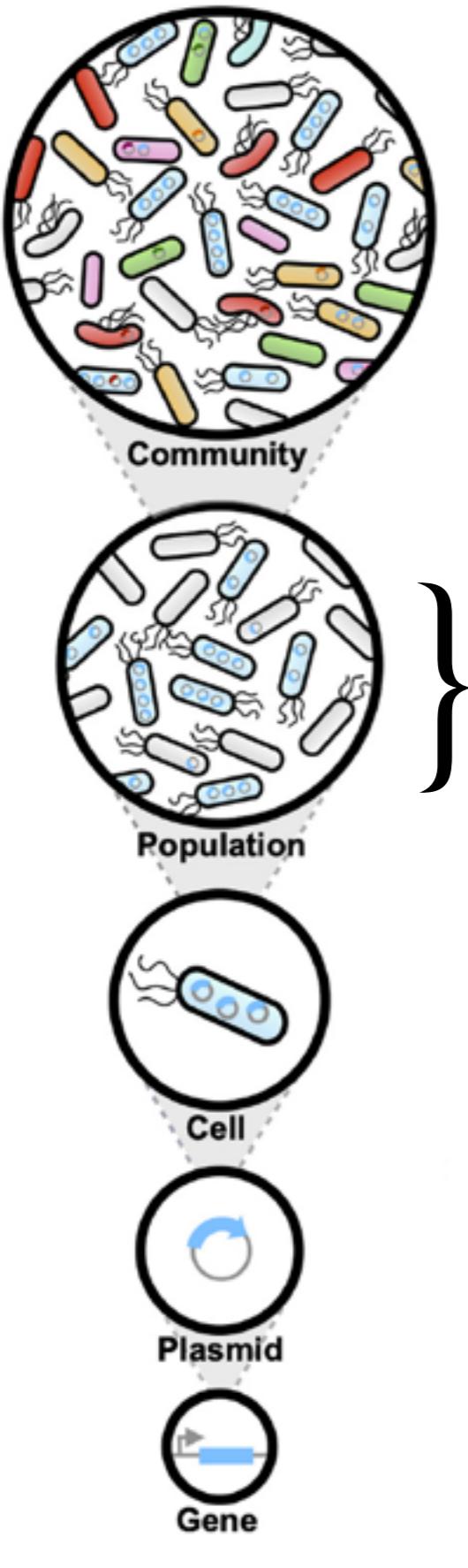
“Without a constant misuse of language there
cannot be any discovery, any progress”

Paul Karl Feyerabend, *Against Method*



Intercellular nanotubes among bacteria, Kost et. al. 2015

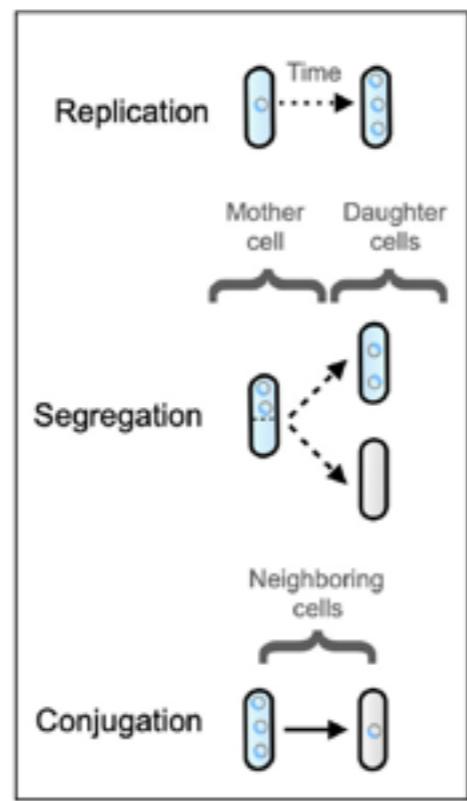
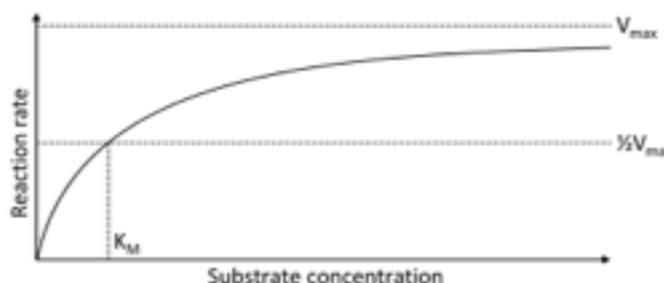
Ciclo de Vida en Plásmidos: dinámica de poblaciones



$$U(R) = \frac{V_{max} R}{R + K_m},$$

Monod term, $G(R) = \rho \cdot U(R)$

$$\psi = (\rho, V_{max}, K_m)$$



$$\frac{dR}{dt} = - U(R; \psi_p) \cdot B_p - U(R; \psi_0) \cdot B_0,$$

$$\frac{dA}{dt} = - \alpha A (B_p + B_0)$$

$$\frac{dB_p}{dt} = (G(R; \psi_p) - \kappa_p A - \sigma) \cdot B_p + \gamma B_p B_0,$$

$$\frac{dB_0}{dt} = (G(R; \psi_0) - \kappa_0 A) \cdot B_0 + \sigma G(R; \psi_p) \cdot B_p - \gamma B_p B_0,$$

$$\bar{x} = (R, A, B_p, B_0)$$

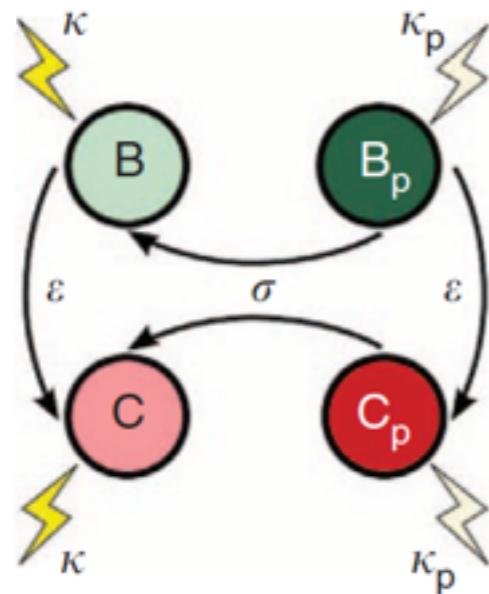
$$\frac{dR}{dt} = - U(R; \psi) \cdot B,$$

$$\frac{dA}{dt} = - \alpha A \cdot B,$$

$$\frac{dB}{dt} = (G(R; \psi) - \kappa A) \cdot B,$$

c.i. $x_0 = (R_0, A_0, B_0)$

Ciclo de Vida en Plásmidos: mutación compensatoria



ε : Mutation rate

σ : Segregation rate

κ : Killing rate (plasmid-free)

κ_p : Killing rate (plasmid-bearer)

$$x^i(0) = (A^i(0), R^i(0), B^i(0), B_p^i(0), C^i(0), C_p^i(0))$$

$$\mu_*(R(t)) = \frac{\bar{\mu}_* R(t)}{K_* + R(t)}$$

$$\frac{dA}{dt} = -\alpha A(B + C) - \alpha_p A(B_p + C_p),$$

$$\frac{dR}{dt} = -\mu_b(R)B - \mu_{bp}(R)B_p - \mu_c(R)C - \mu_{cp}(R)C_p,$$

$$\frac{dB}{dt} = ((1 - \varepsilon)G_b(R) - \kappa A)B + \sigma_b G_{bp}(R)B_p,$$

$$\frac{dB_p}{dt} = ((1 - \varepsilon - \sigma_b + \varepsilon\sigma_b)G_{bp}(R) - \kappa_p A)B_p,$$

$$\frac{dC}{dt} = (G_c(R) - \kappa A)C + \sigma_c G_{cp}(R)C_p + \varepsilon G_b(R)B,$$

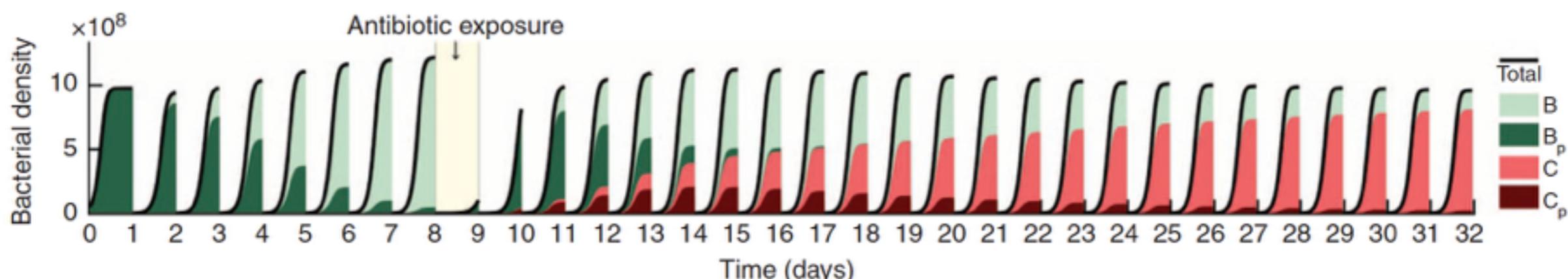
$$\frac{dC_p}{dt} = ((1 - \sigma_c)G_{cp}(R) - \kappa_p A)C_p + \varepsilon G_p(R)B_p,$$

Open Access | Published: 10 October 2014

Positive selection and compensatory adaptation interact to stabilize non-transmissible plasmids

A. San Milan , R. Peña-Miller, M. Toll-Riera, Z. V. Halbert, A. R. McLean, B. S. Cooper & R. C. MacLean

Nature Communications 5, Article number: 5208 (2014) | [Cite this article](#)



Ciclo de Vida en Plásmidos: modelos de comunidades

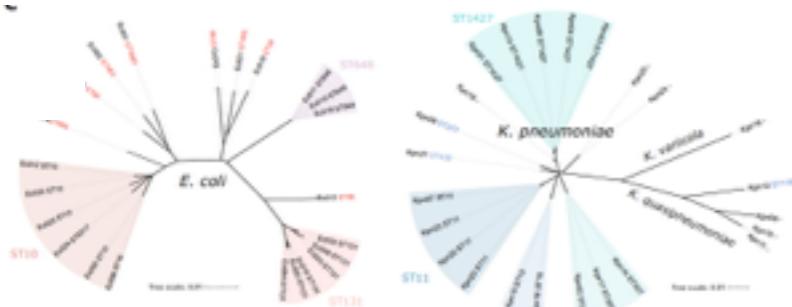
$$\bar{B} = (B_p^1, B_p^2, \dots, B_p^N, B_0^1, B_0^2, \dots, B_0^N)$$

$$\frac{dB_p^i}{dt} = (1 - \lambda)G_p^i(R)B_p^i + \gamma \sum_{j=1}^M B_p^j B_0^i - dB_p^i,$$

$$\frac{dB_0^i}{dt} = G_0^i(R)B_0^i + \lambda G_p^i(R)B_p^i - \gamma \sum_{j=1}^M B_p^j B_0^i - dB_0^i.$$

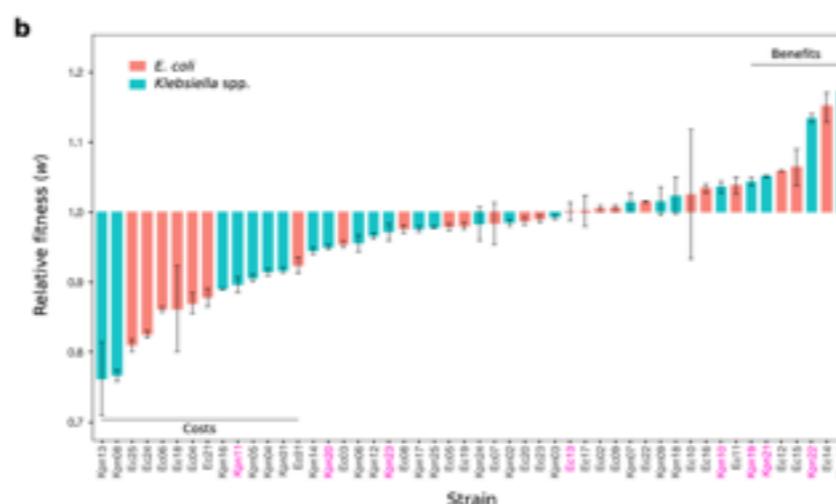
$$\frac{dR}{dt} = - \sum_{i=1}^M (u_p^i(R)B_p^i + u_0^i(R)B_0^i) - d(R - \hat{R})$$

Experimentos en Ambientes Clínicos: heterogeneidad de fitness

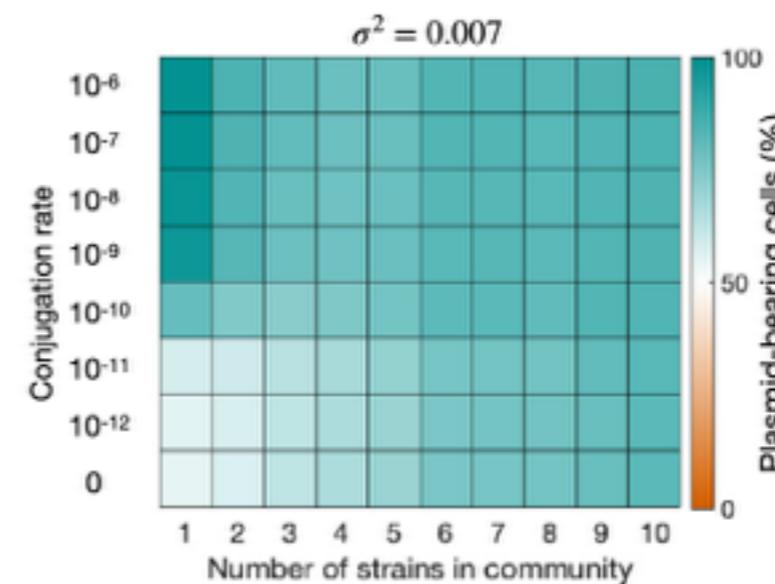
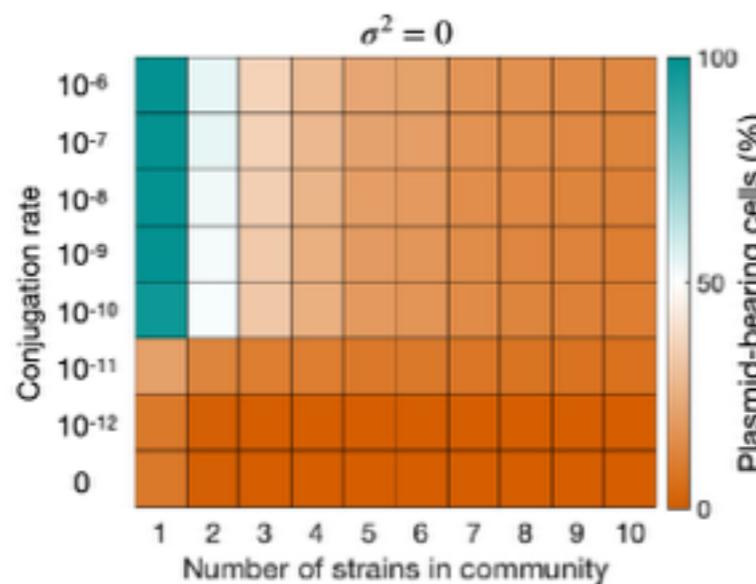
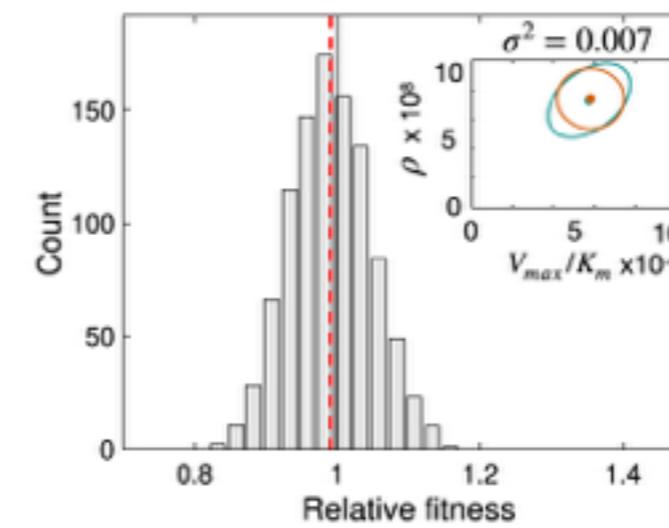
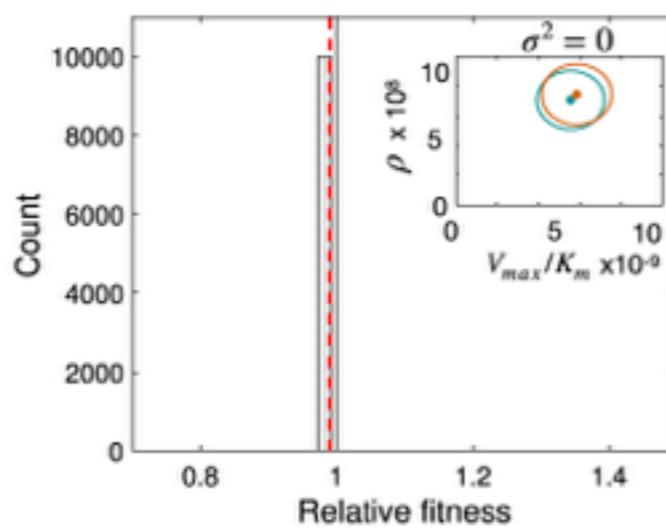
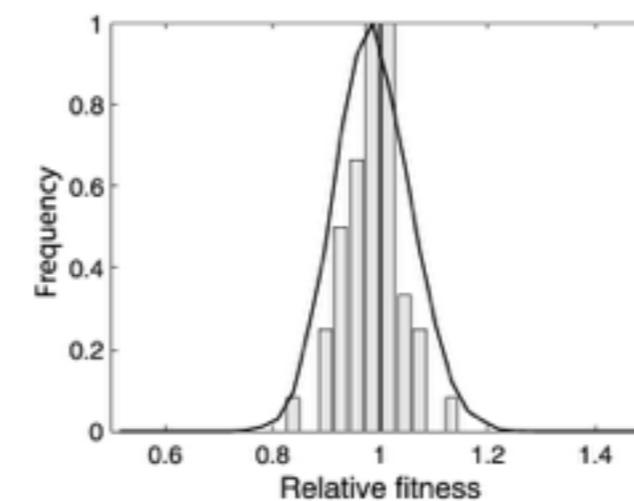
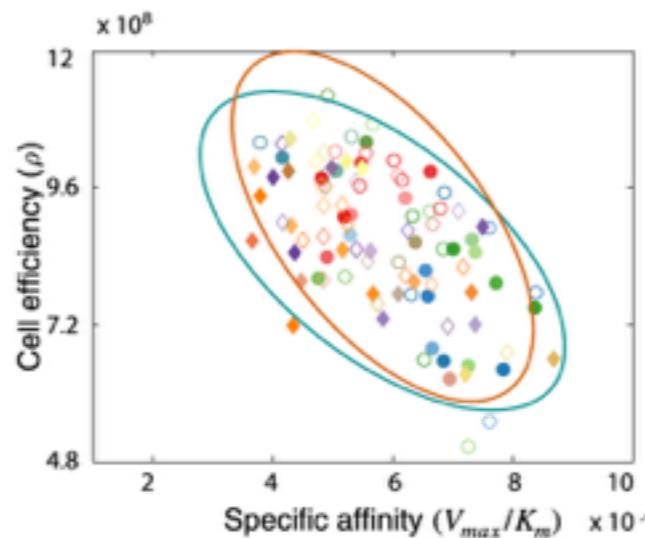


Variability of plasmid fitness effects contributes to plasmid persistence in bacterial communities

Aida Alonso-del Valle, Ricardo León-Sampedro, Jerónimo Rodríguez-Beltrán, Javier DelaFuente, Marta Hernández-García, Patricia Ruiz-Garbaosa, Rafael Cantón, Rafael Peña-Miller & Alvaro San Millán



Ciclo de Vida en Plásmidos: modelos de comunidades



Ciclo de Vida en Plásmidos: Ambientes Selección

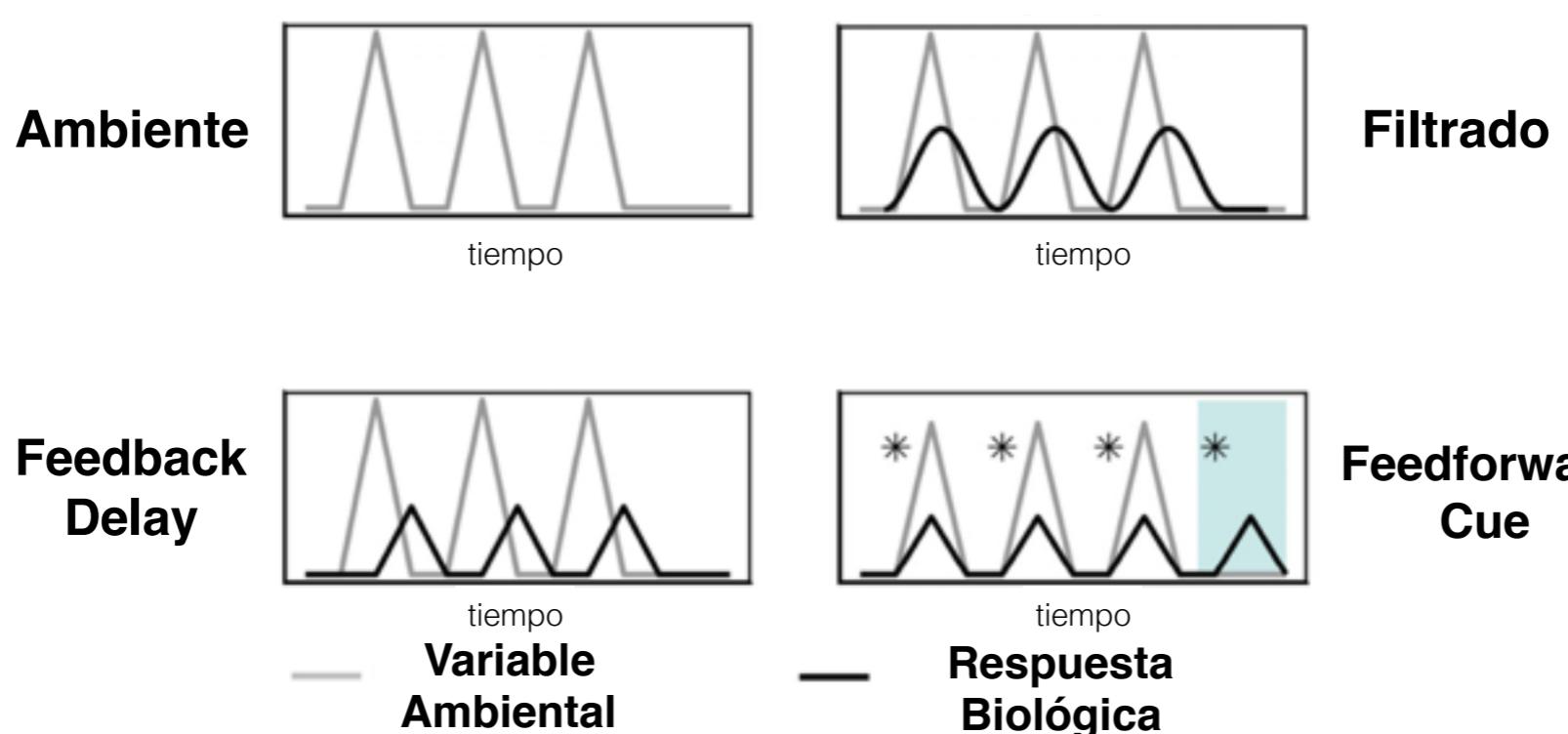
$$\bar{B} = (B_p^1, B_p^2, \dots, B_p^N, B_0^1, B_0^2, \dots, B_0^N)$$

$$\frac{dR}{dt} = - \sum_{j=1}^N \left(U(R(t); \psi_p^j) \cdot B_p^j(t) + U(R(t); \psi_0^j) \cdot B_0^j(t) \right)$$

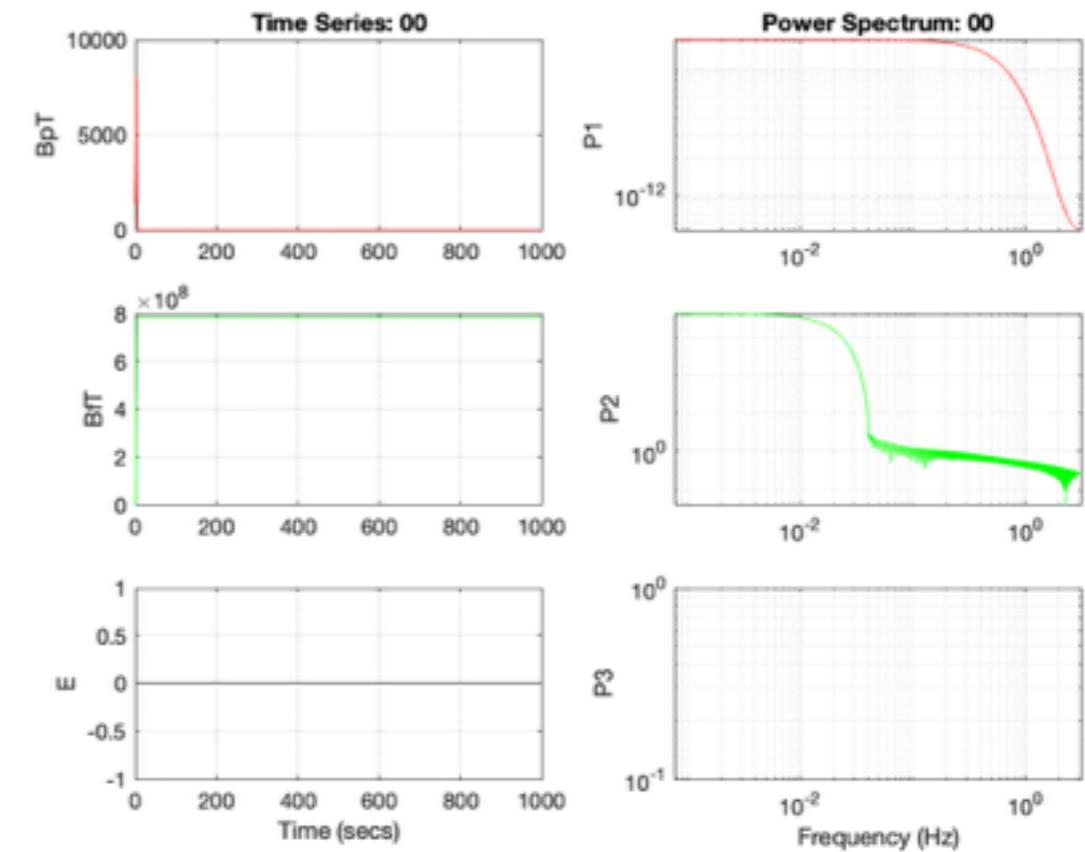
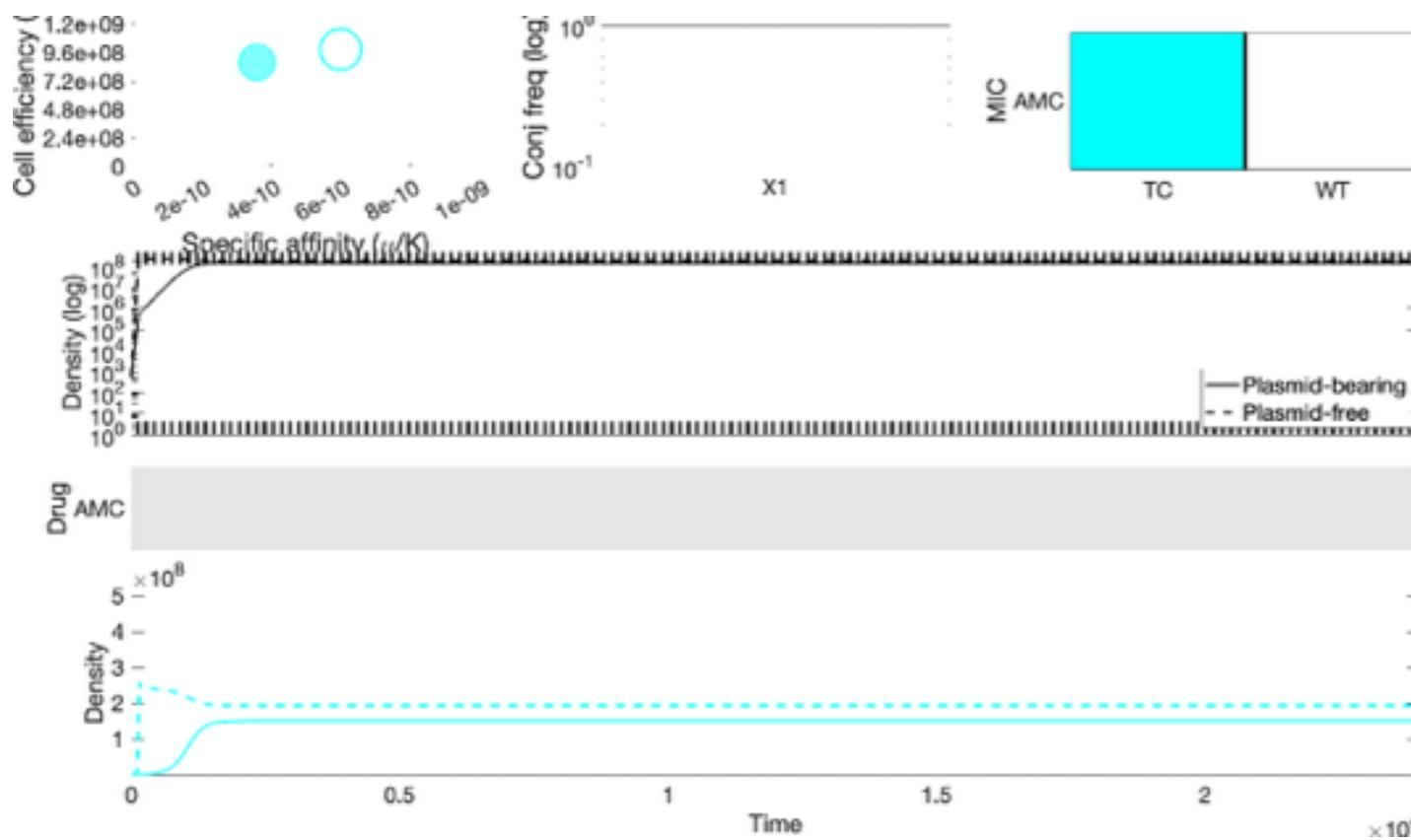
$$\frac{dA}{dt} = -\alpha A(t) \cdot \sum_{j=1}^N (B_p^j(t) + B_0^j(t)).$$

$$\frac{dB_0^i}{dt} = (G(R; \psi_0^i) - \kappa_0 A) \cdot B_0^i(t) + \sigma G(R; \psi_p^i) \cdot B_p^i(t) - \gamma^i B_0^i(t) \sum_{j=1}^N B_p^j(t)$$

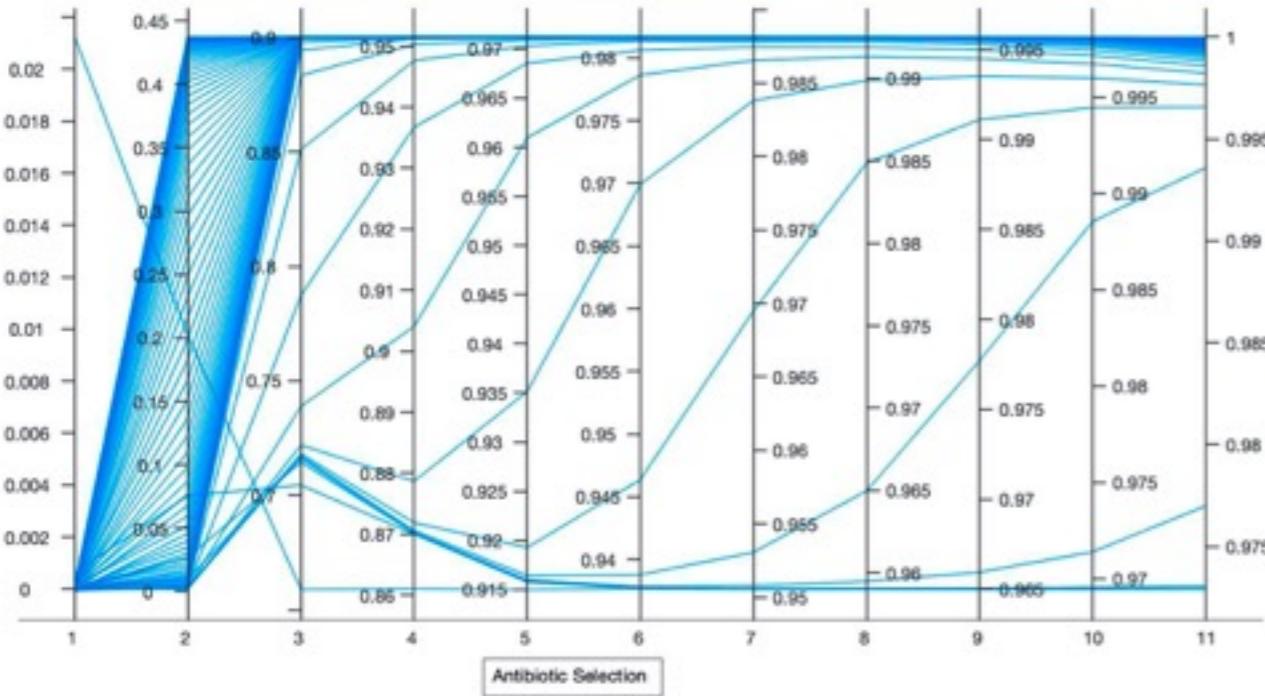
$$\frac{dB_p^i}{dt} = (G(R; \psi_p^i) - \kappa_p A - \sigma) \cdot B_p^i(t) + \gamma^i B_0^i(t) \sum_{j=1}^N B_p^j(t)$$



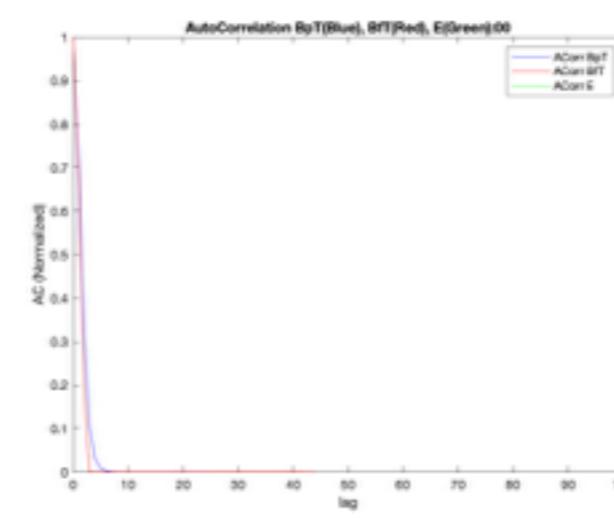
Ciclo de Vida en Plásmidos: Ambientes Selección CTEs



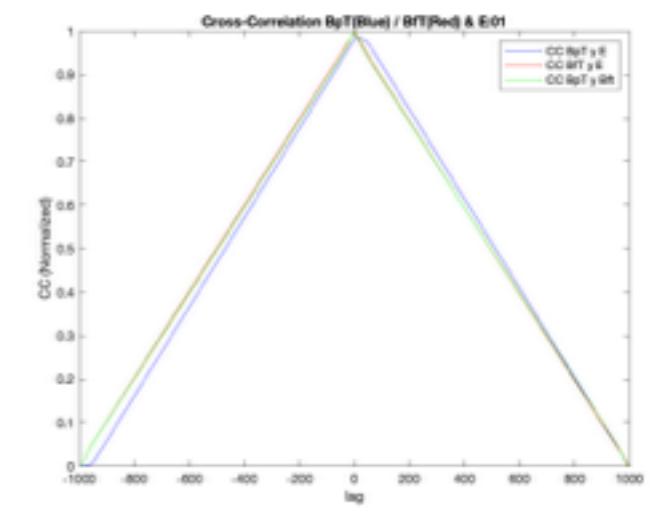
Plasmid Fraction



AutoCorrelación

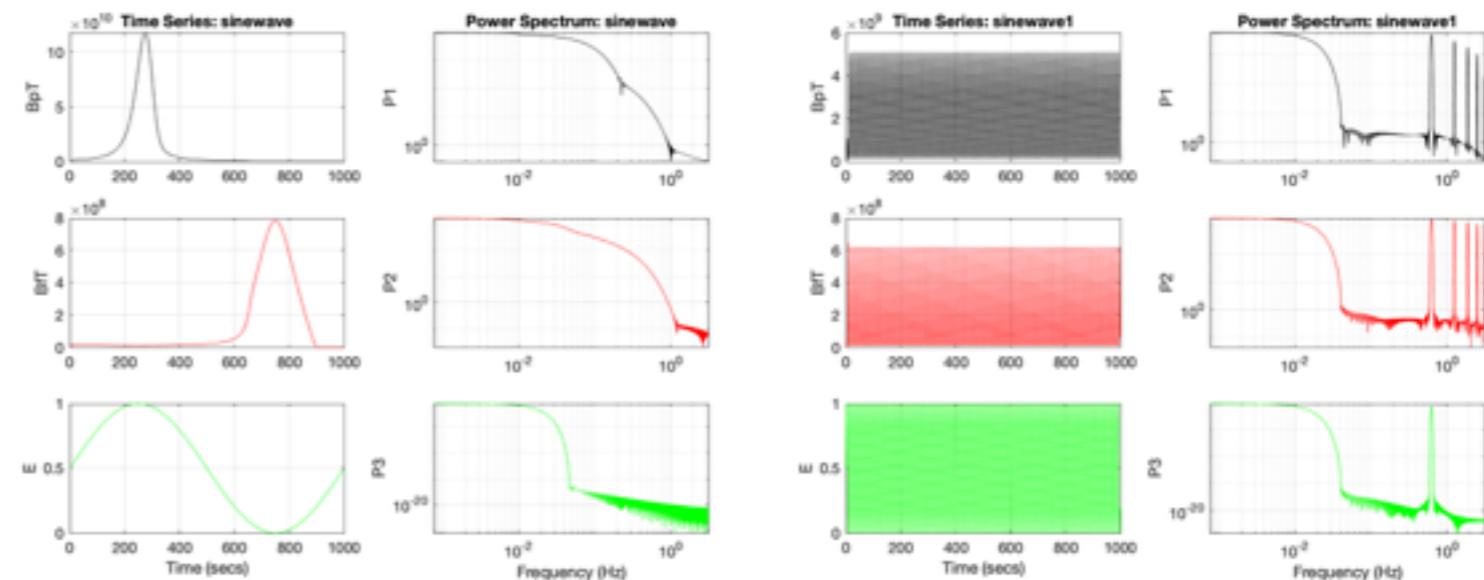
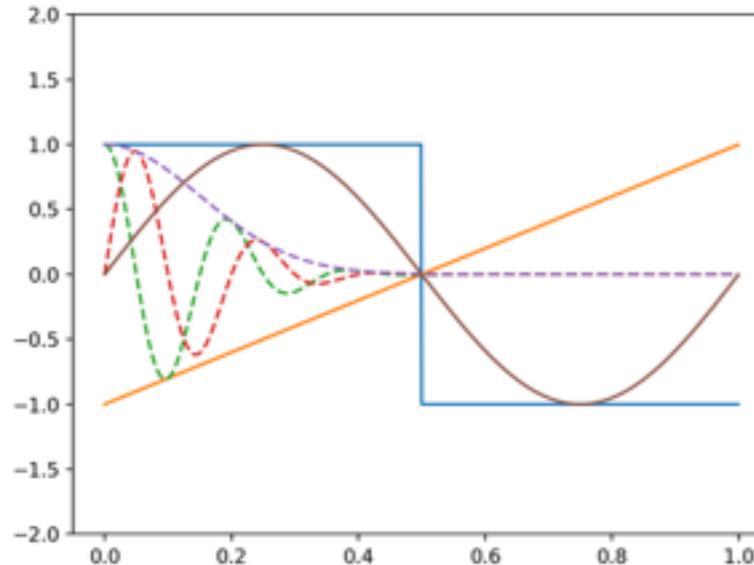


Correlación Cruzada

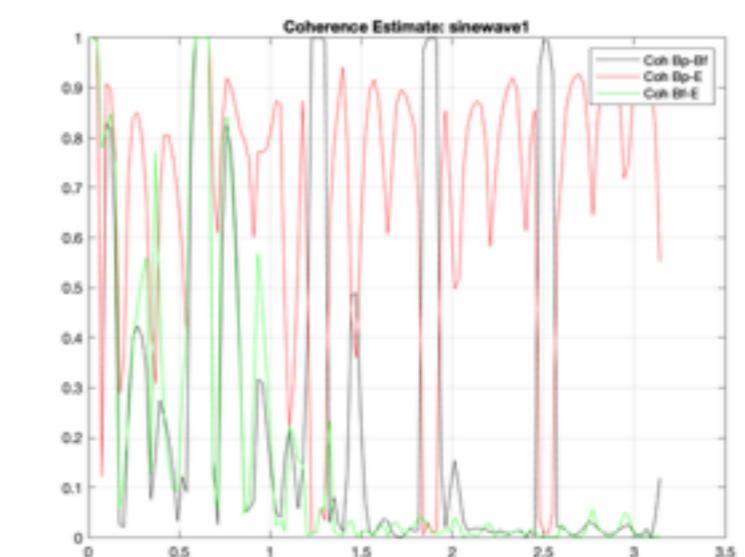
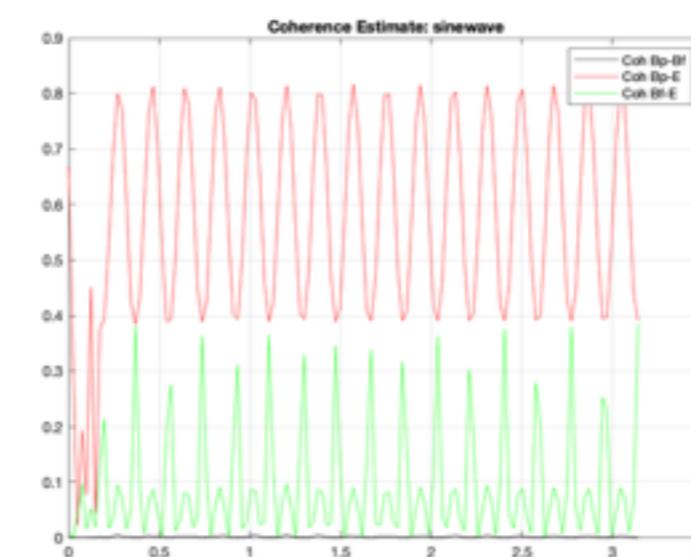
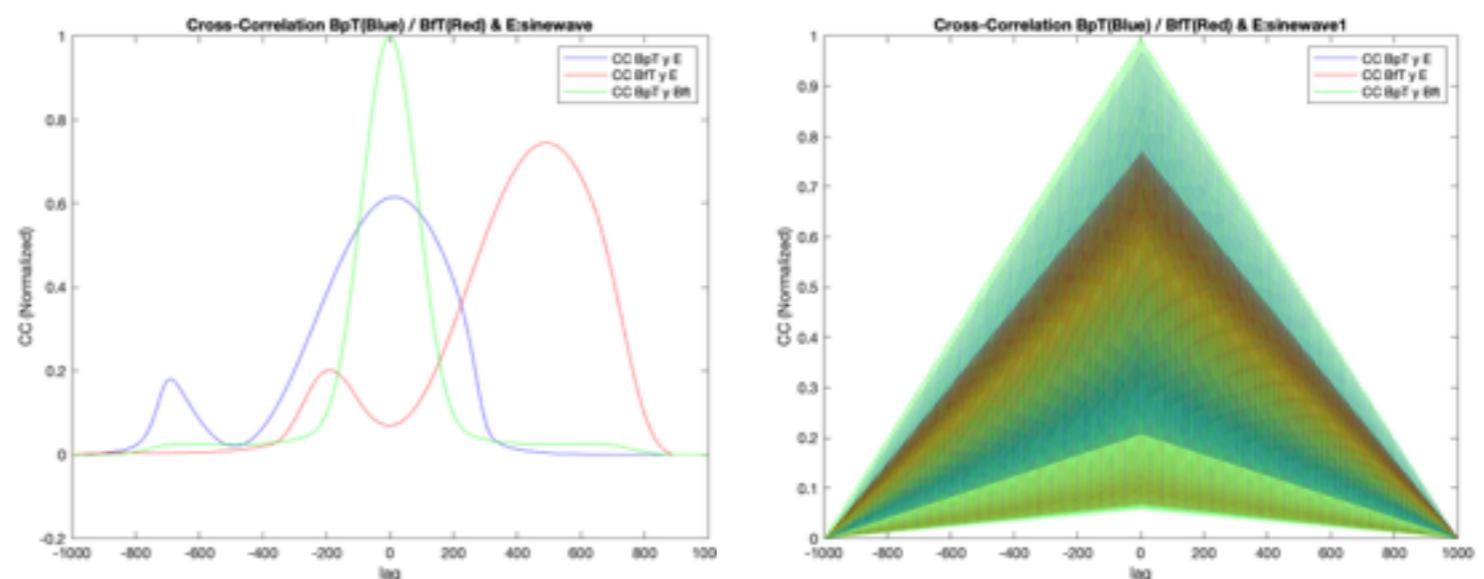
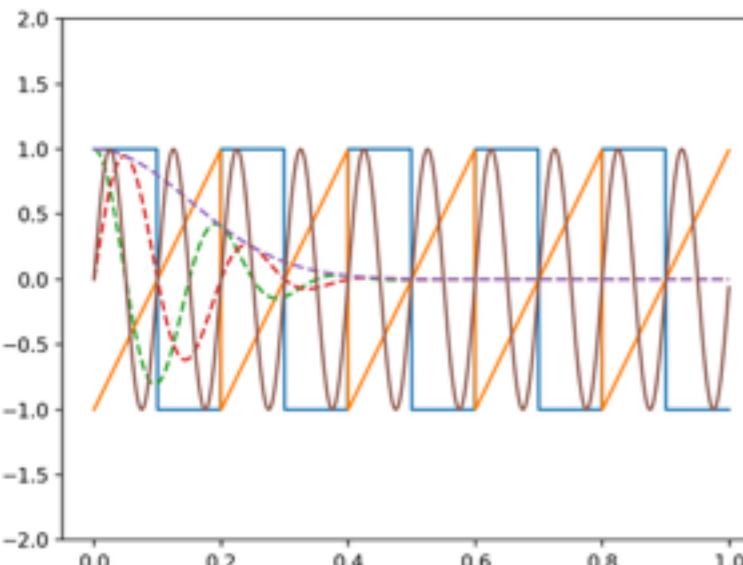


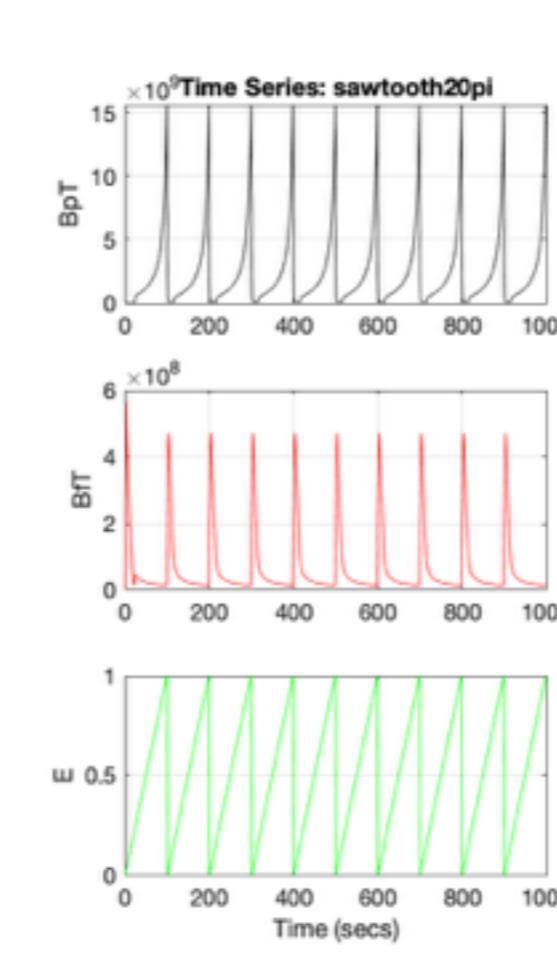
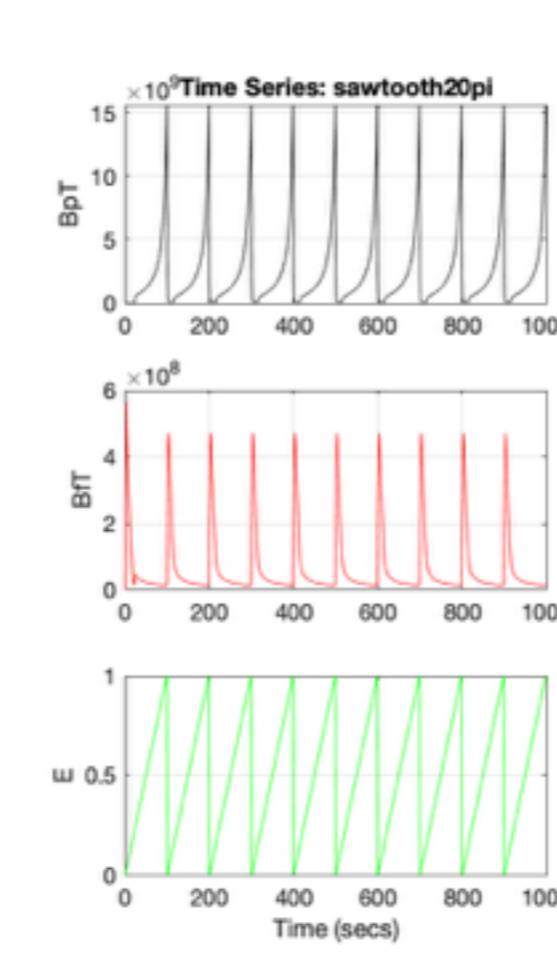
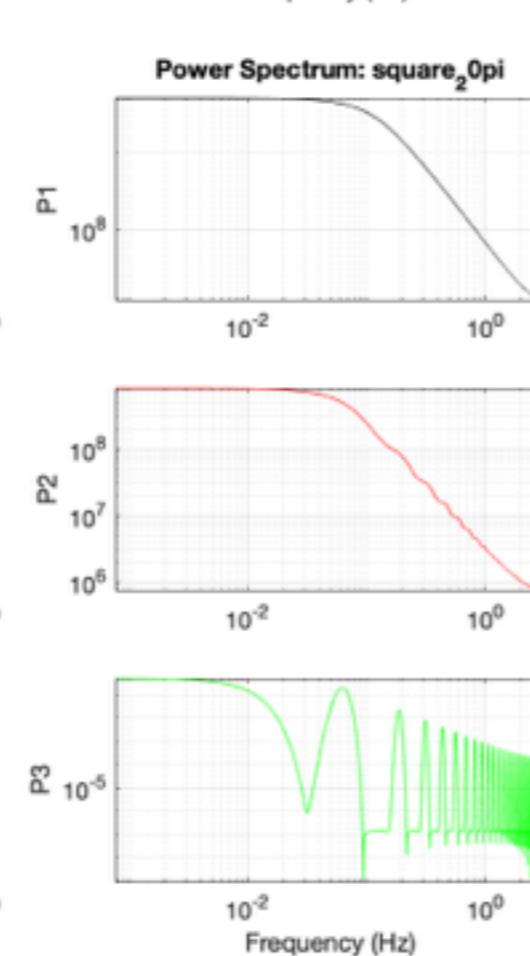
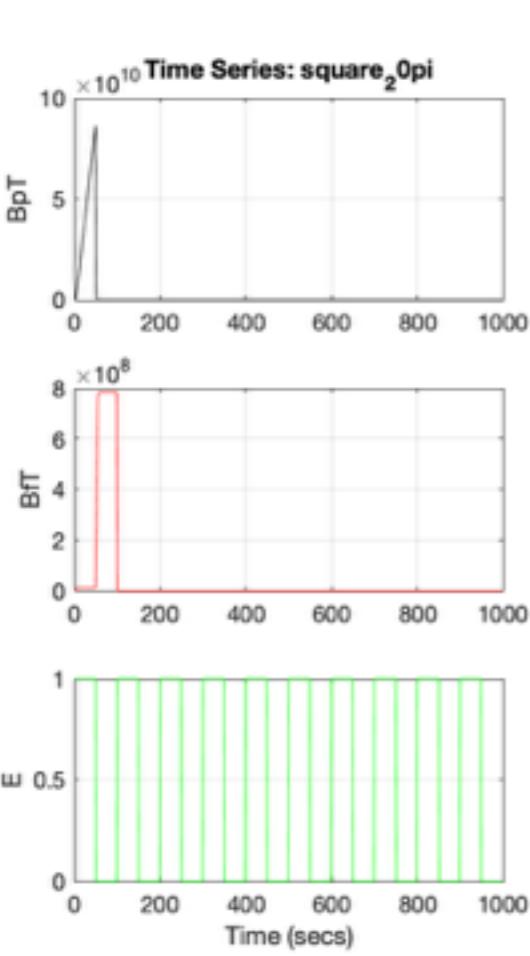
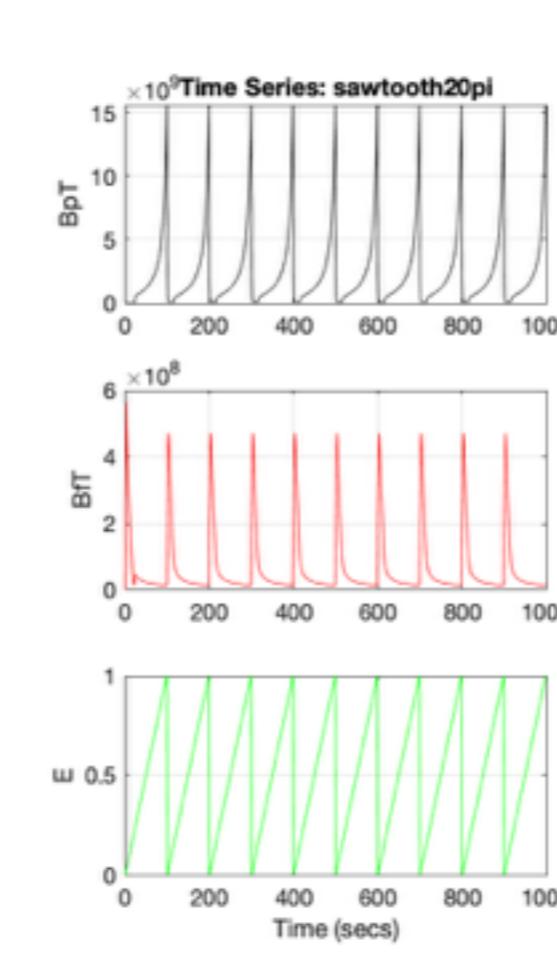
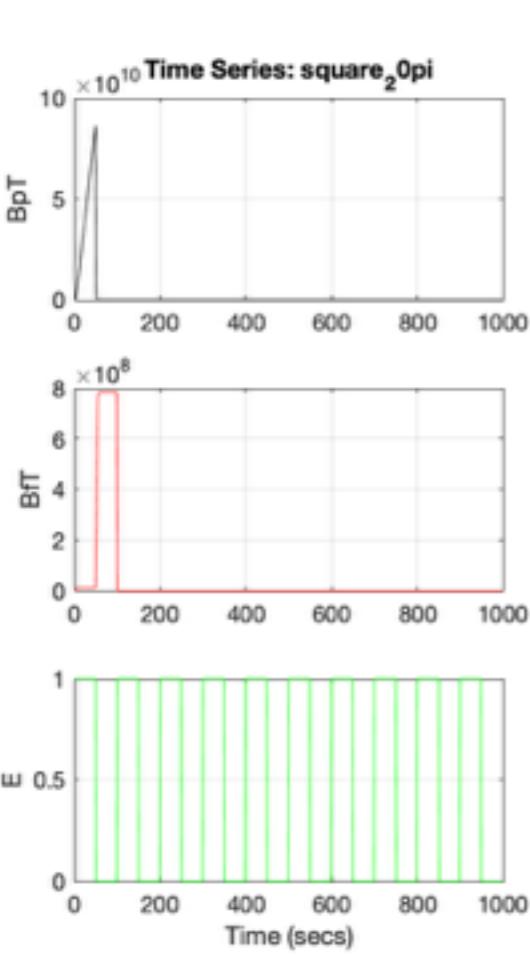
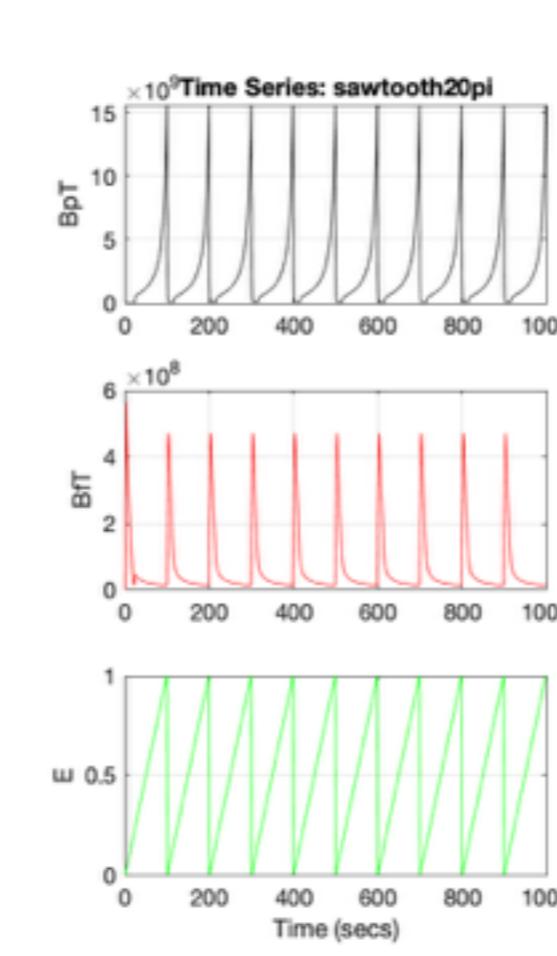
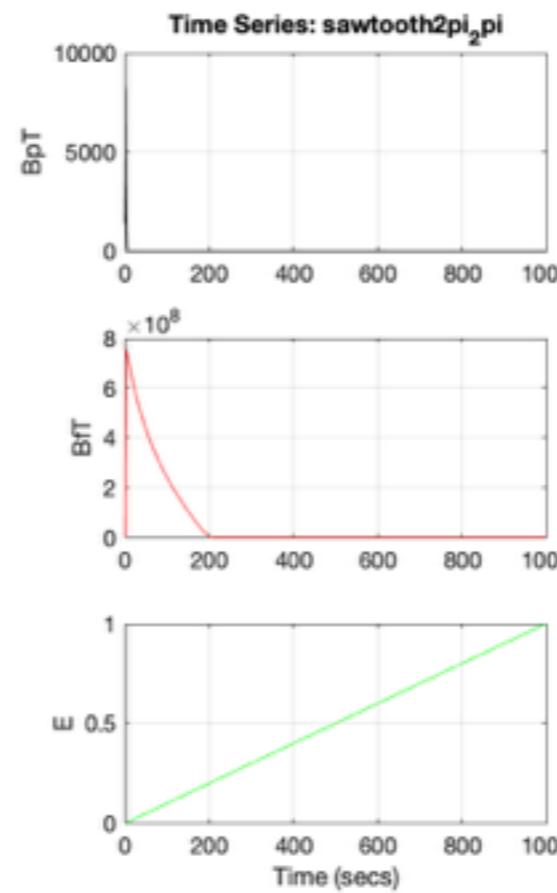
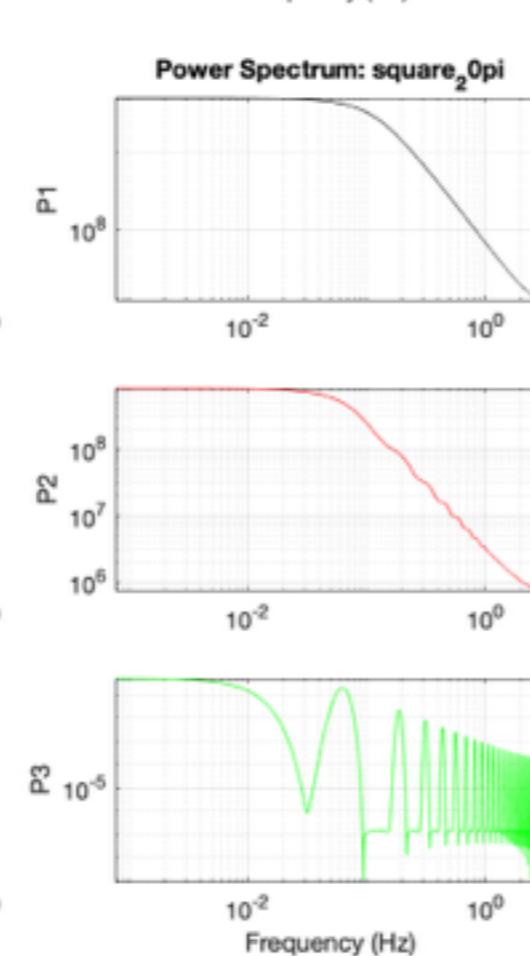
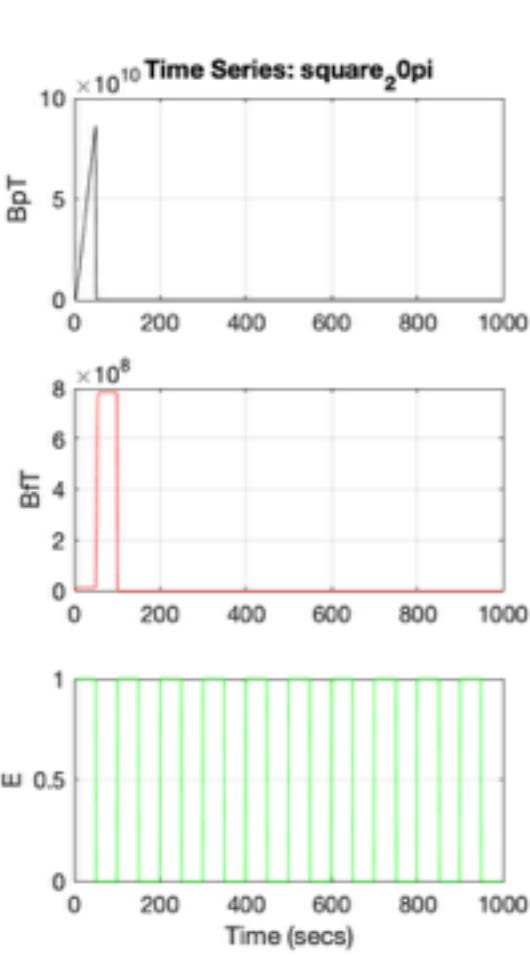
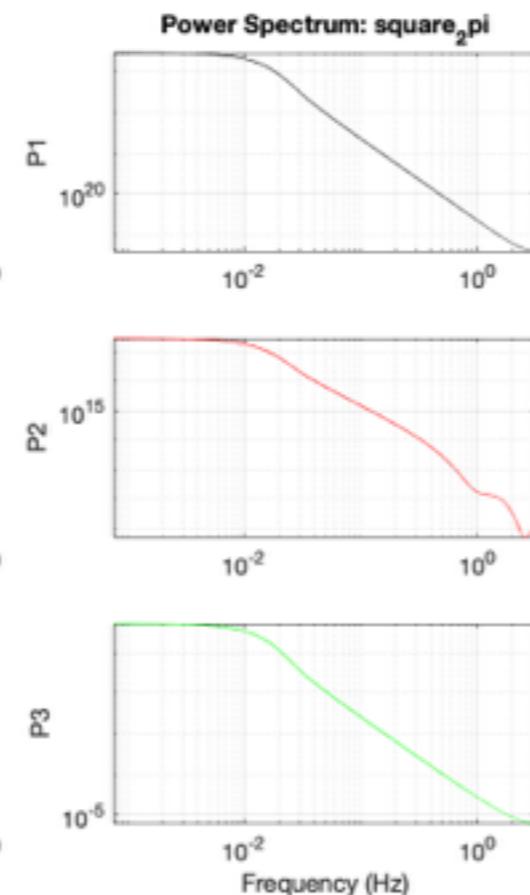
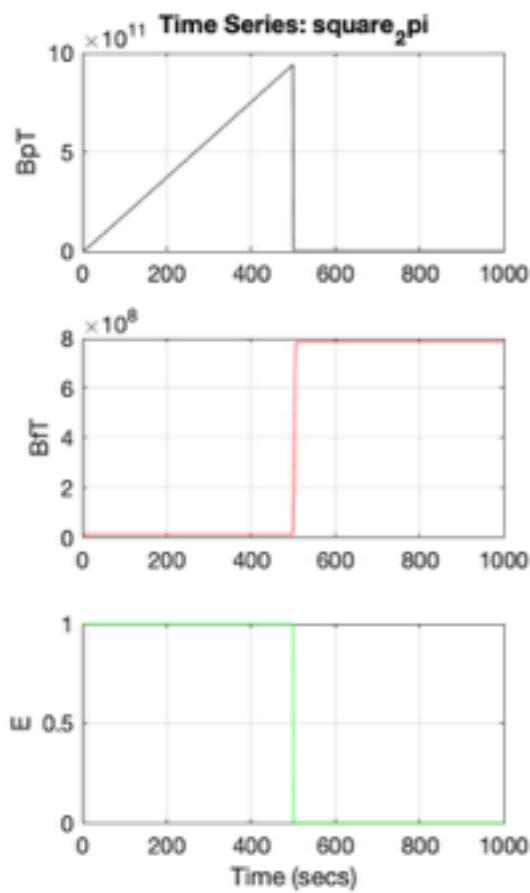
Ciclo de Vida en Plásmidos: Ambientes Selección Periódicos

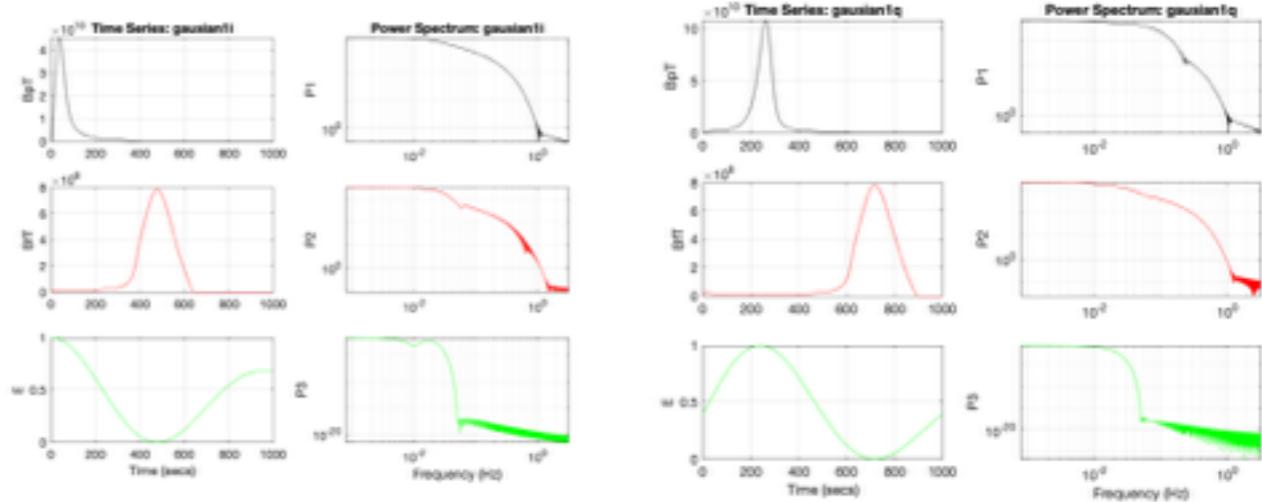
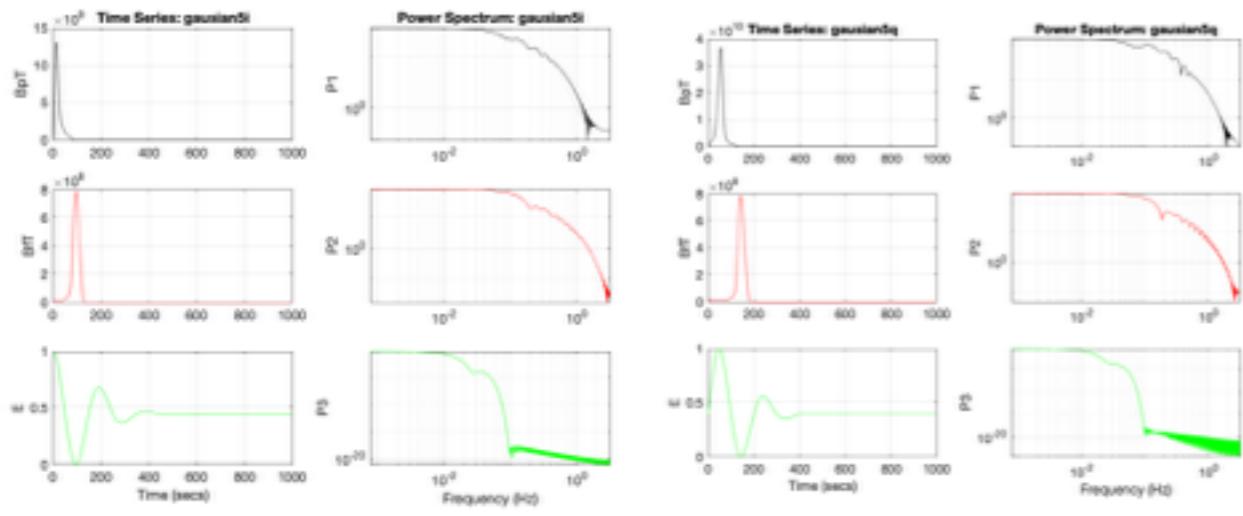
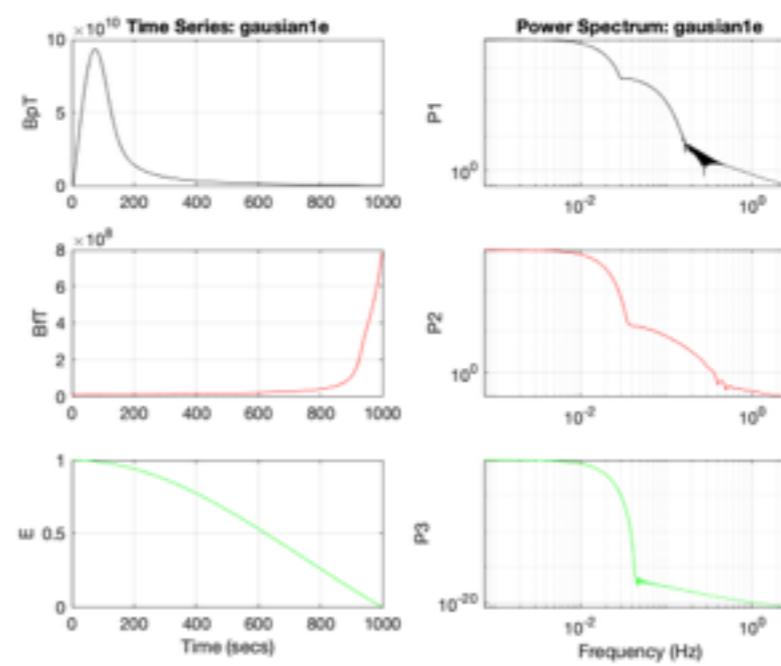
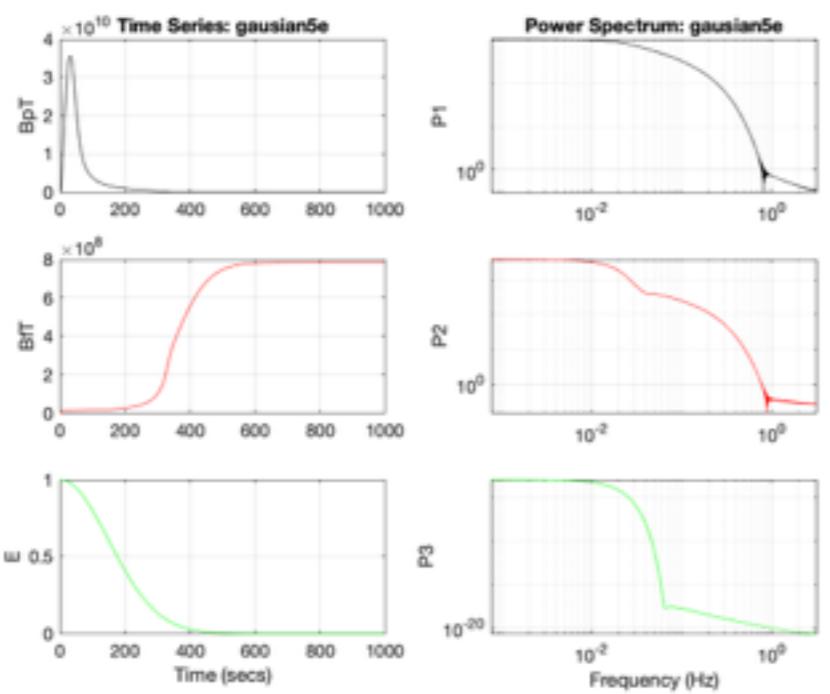
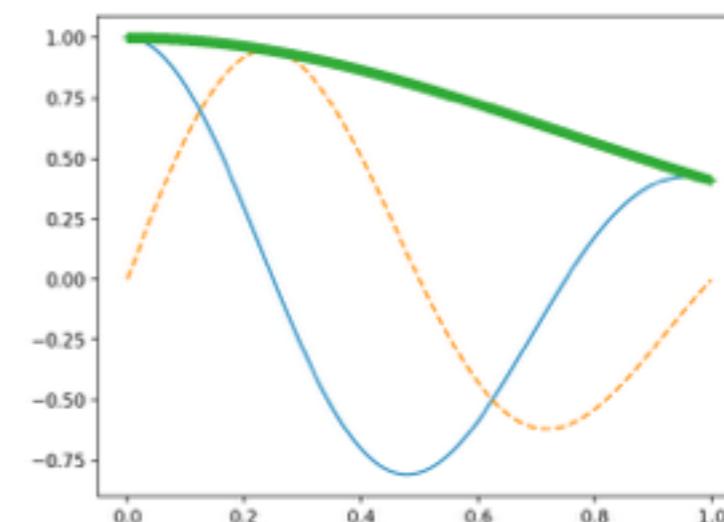
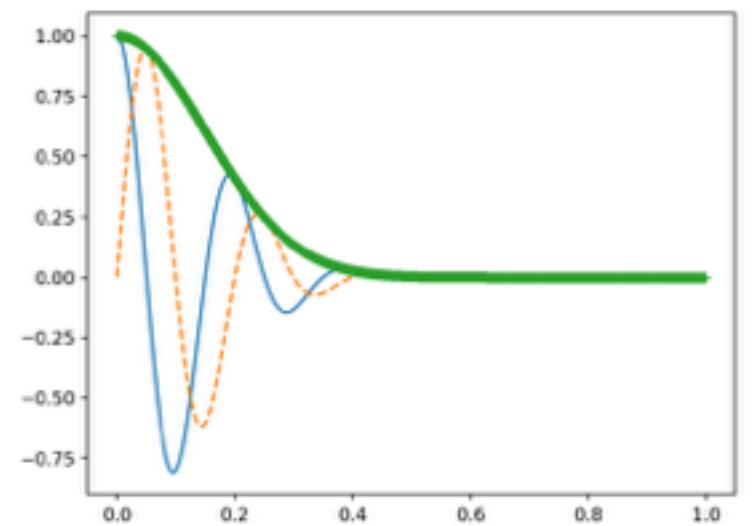
Periódicos ($2^*\pi$)



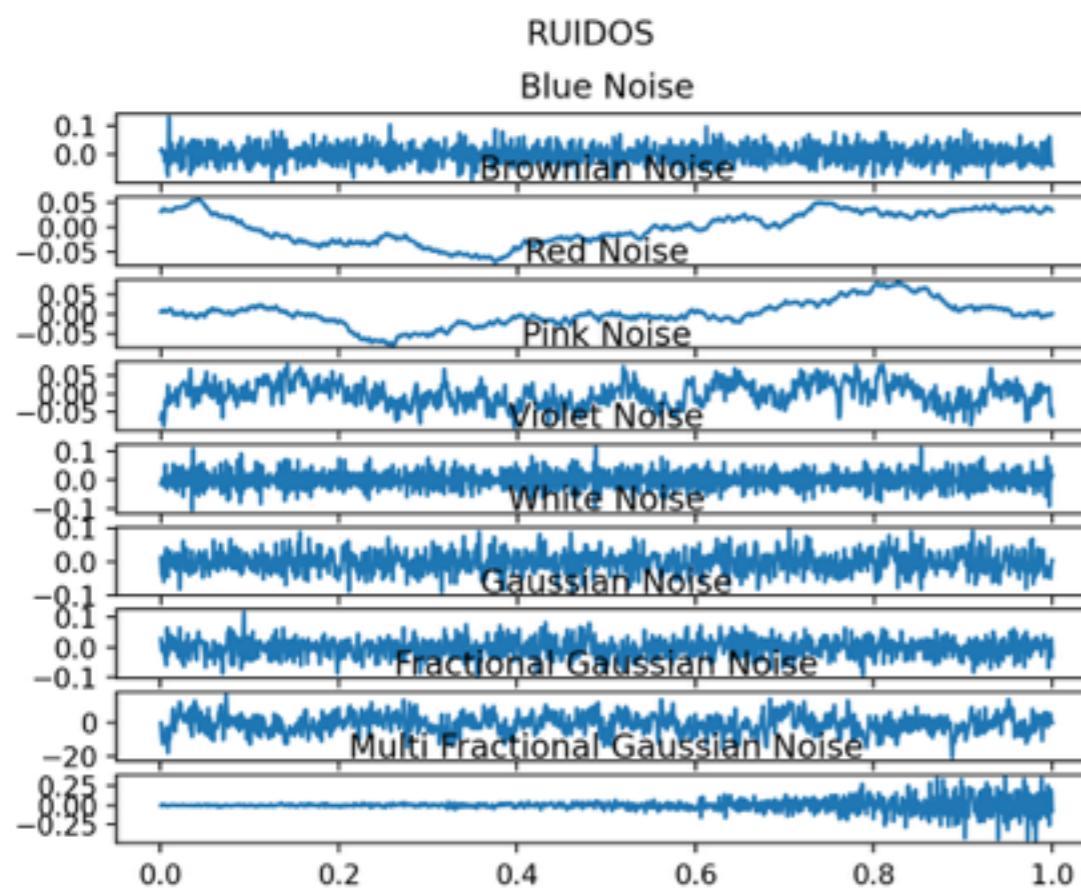
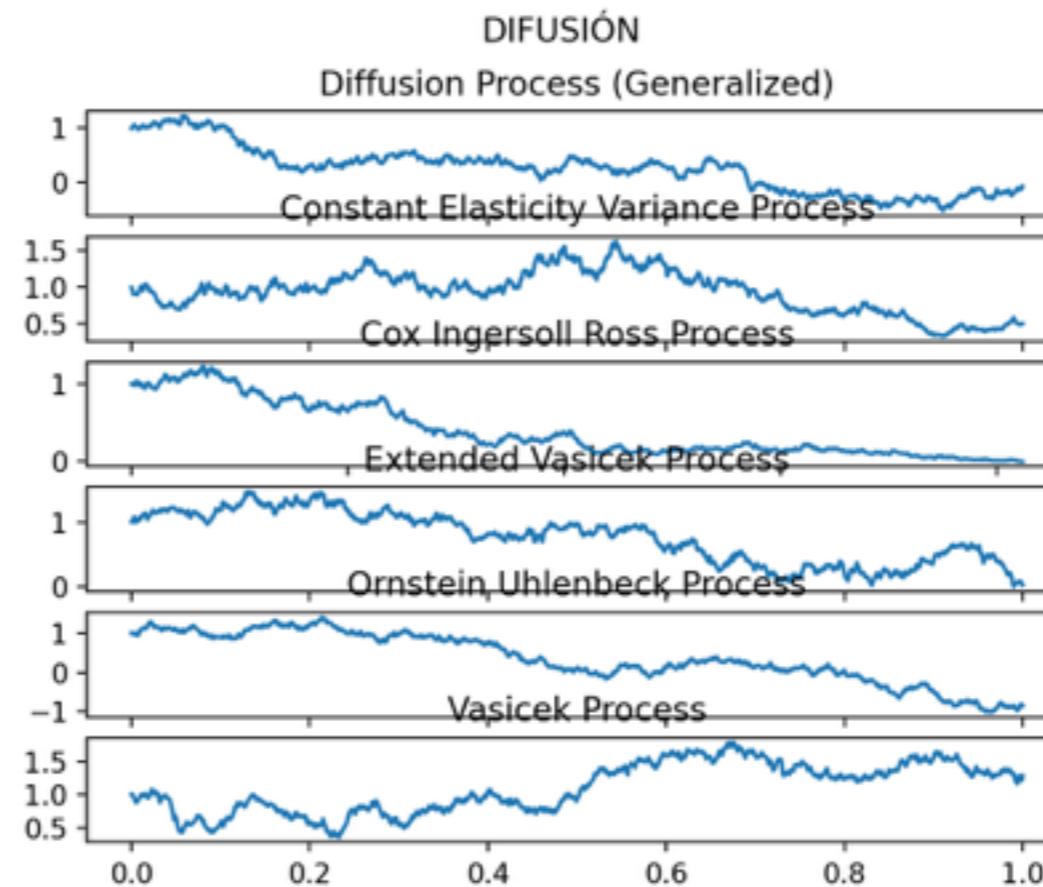
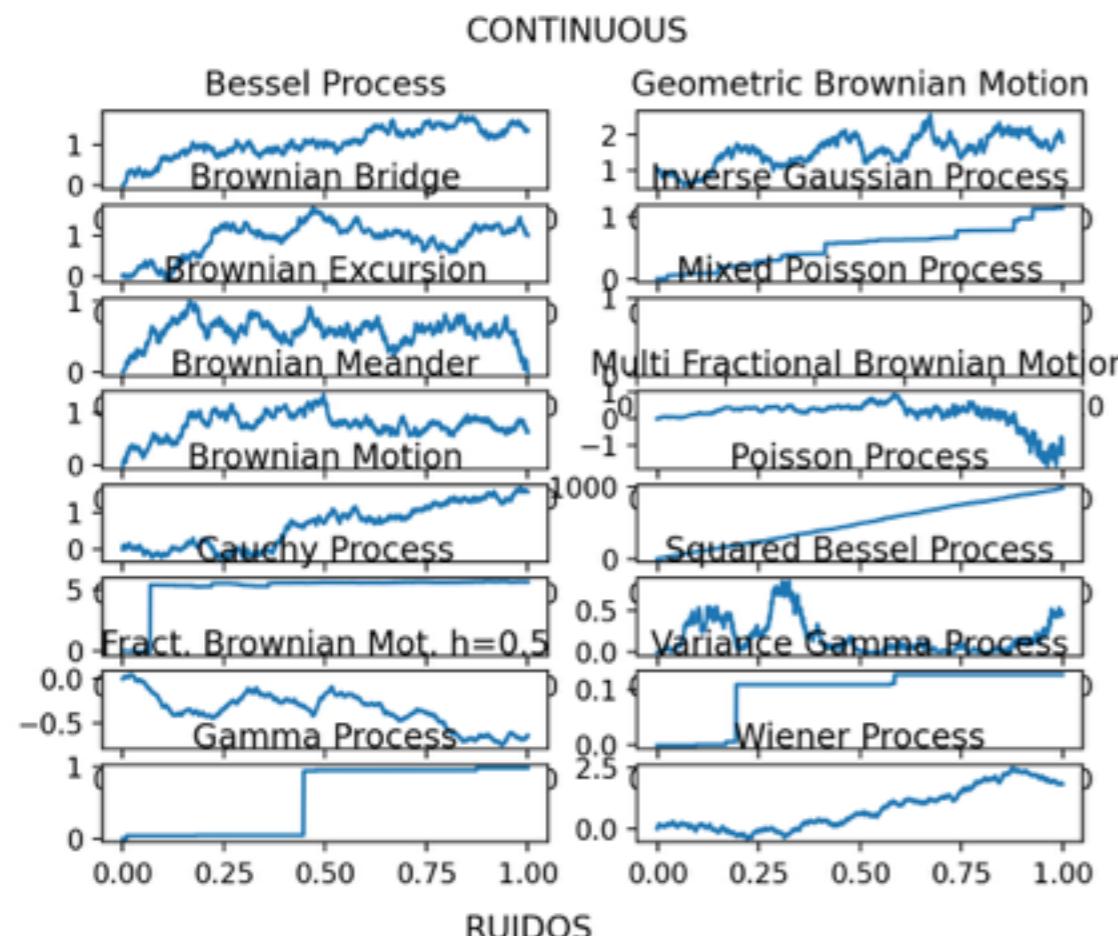
Periódicos ($20^*\pi$)



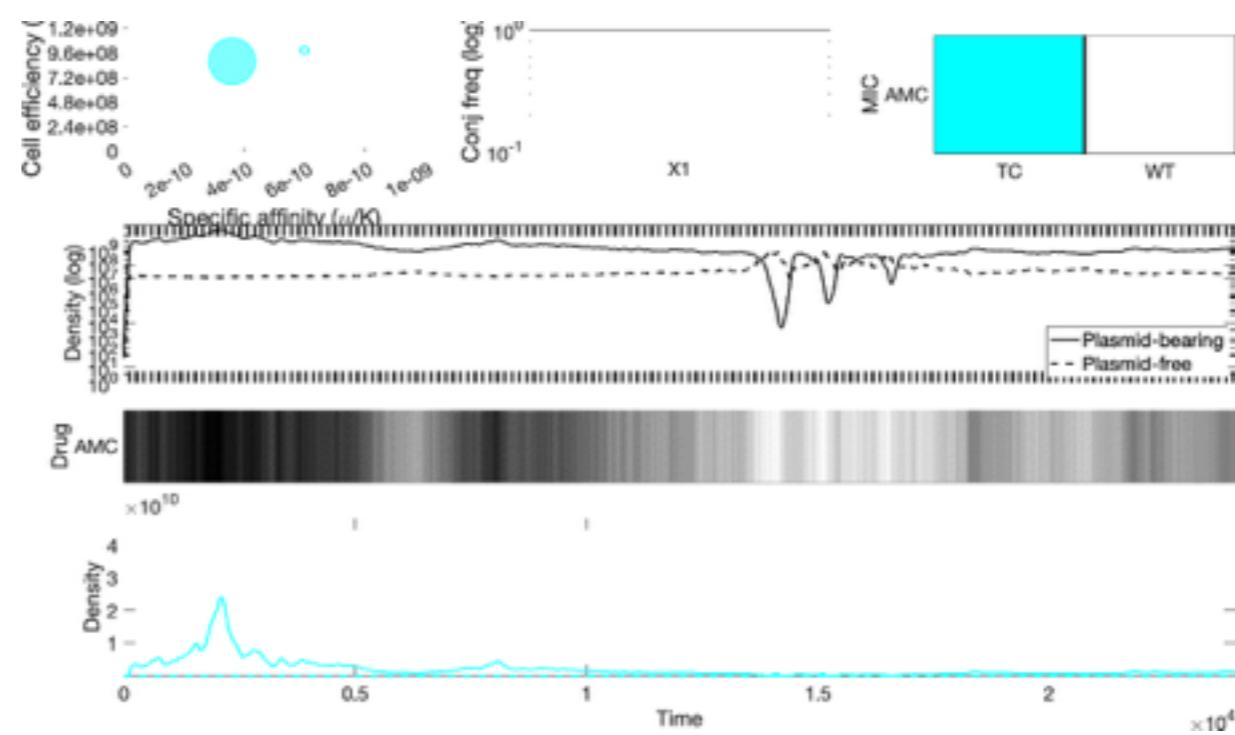




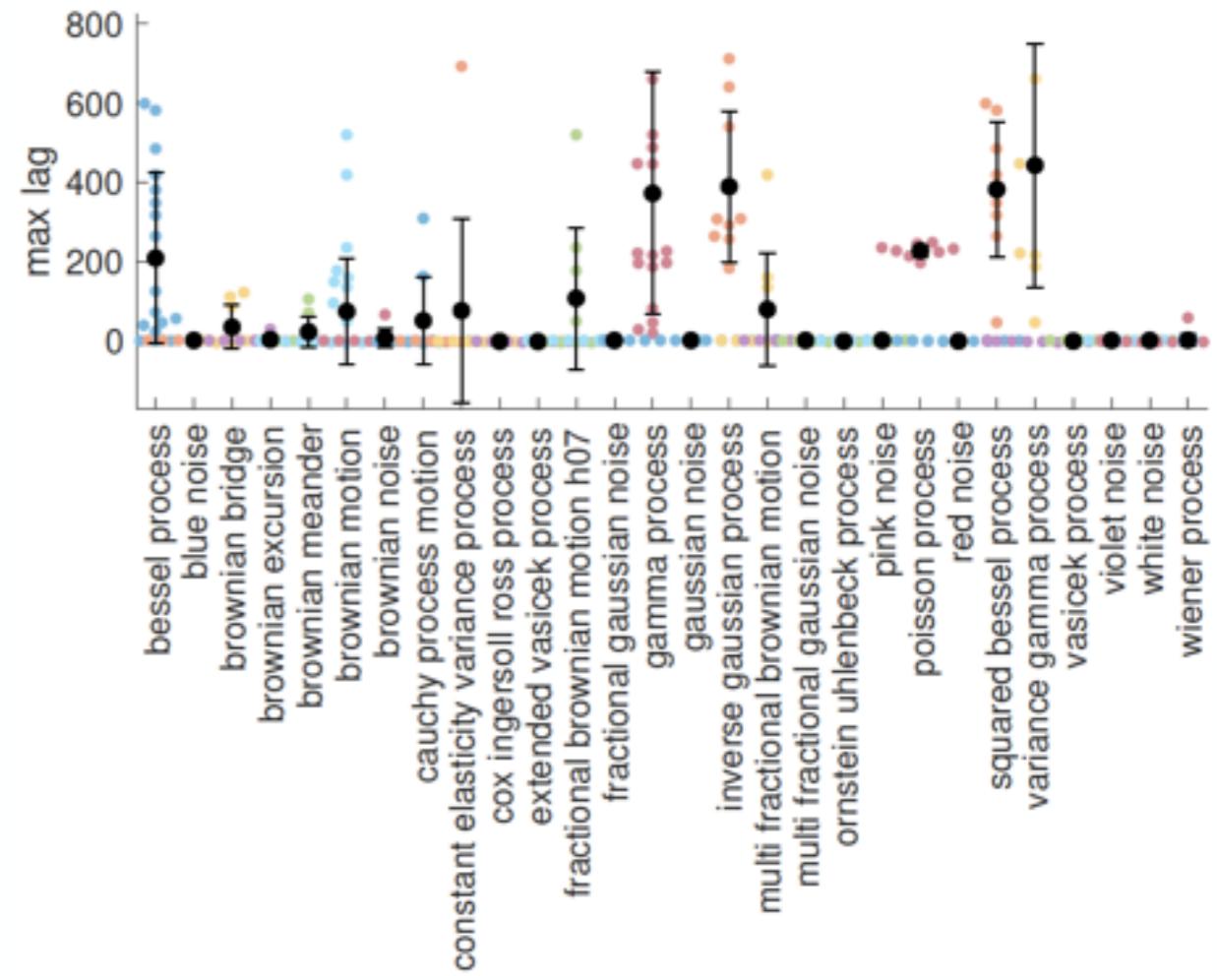
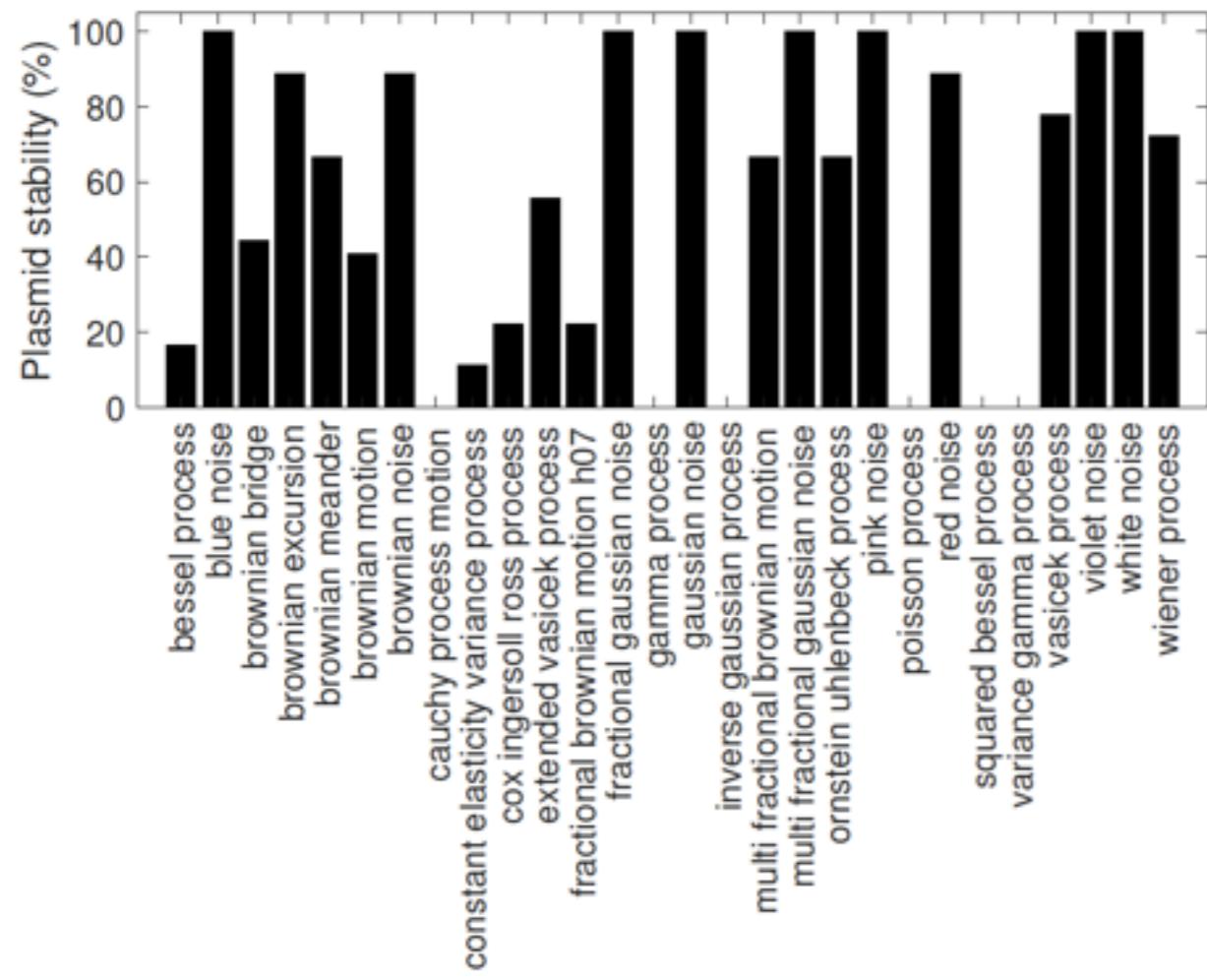
Ciclo de Vida en Plásmidos: Ambientes Selección Estocásticos



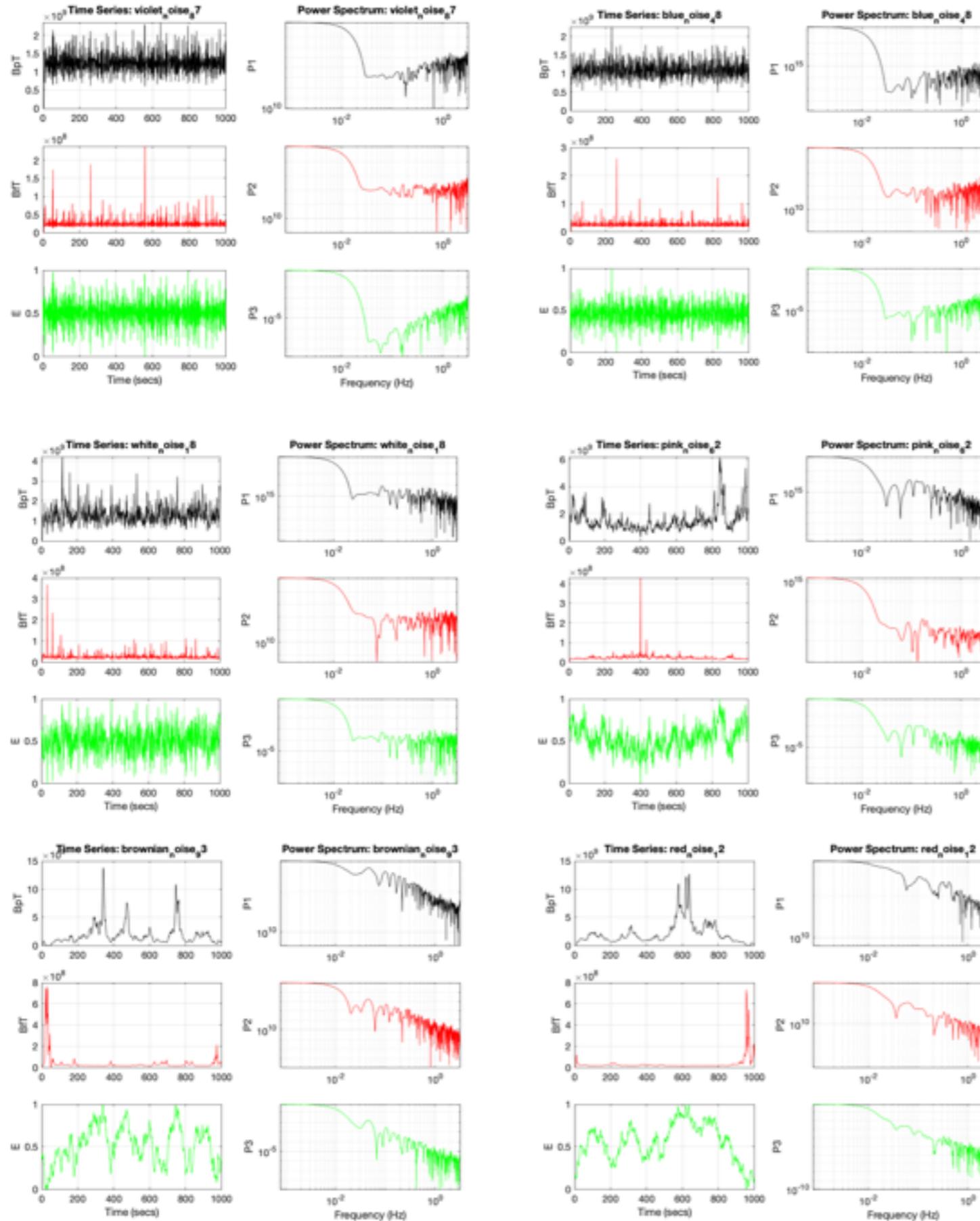
Ex. Proceso Ornstein-Uhlenbeck: $\dot{x}(t) = -\frac{k}{\gamma}(x(t) - x_0) + \sigma\xi(t)$



Ciclo de Vida en Plásmidos: Ambientes Selección Estocásticos



Ciclo de Vida en Plásmidos: Ambientes de Ruido (fGn)



$$C(k) = \frac{(k+1)^{2H} - 2k^{2H} + (k-1)^{2H}}{2}$$

$$\rightarrow C(k) \simeq \frac{H(2H-1)}{k^{2-2H}}$$

Hurst exponente, $H \in (0, 1)$

Wiener-Kinchin th: $S(f) = \int_{-\infty}^{\infty} C(k) e^{-2\pi i f \tau} dk$

$$\rightarrow S(f) \sim \frac{1}{f^{2H-1}} \equiv \frac{1}{f^\beta},$$

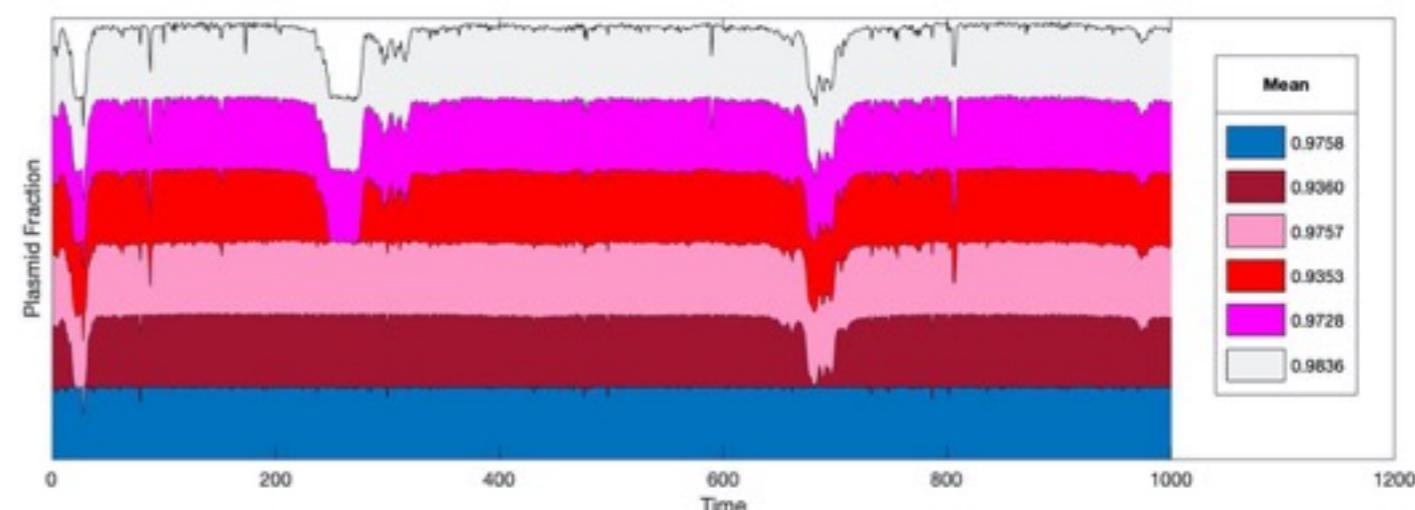
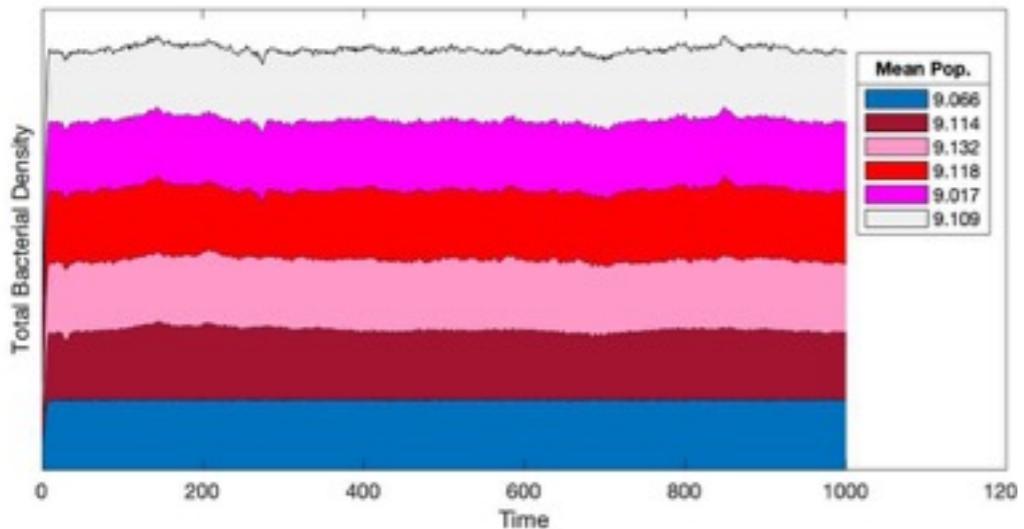
$\beta = 2H - 1$ con $\beta \in (-1, 1)$

$\beta \rightarrow 1 \implies$ LRD (Persistance)

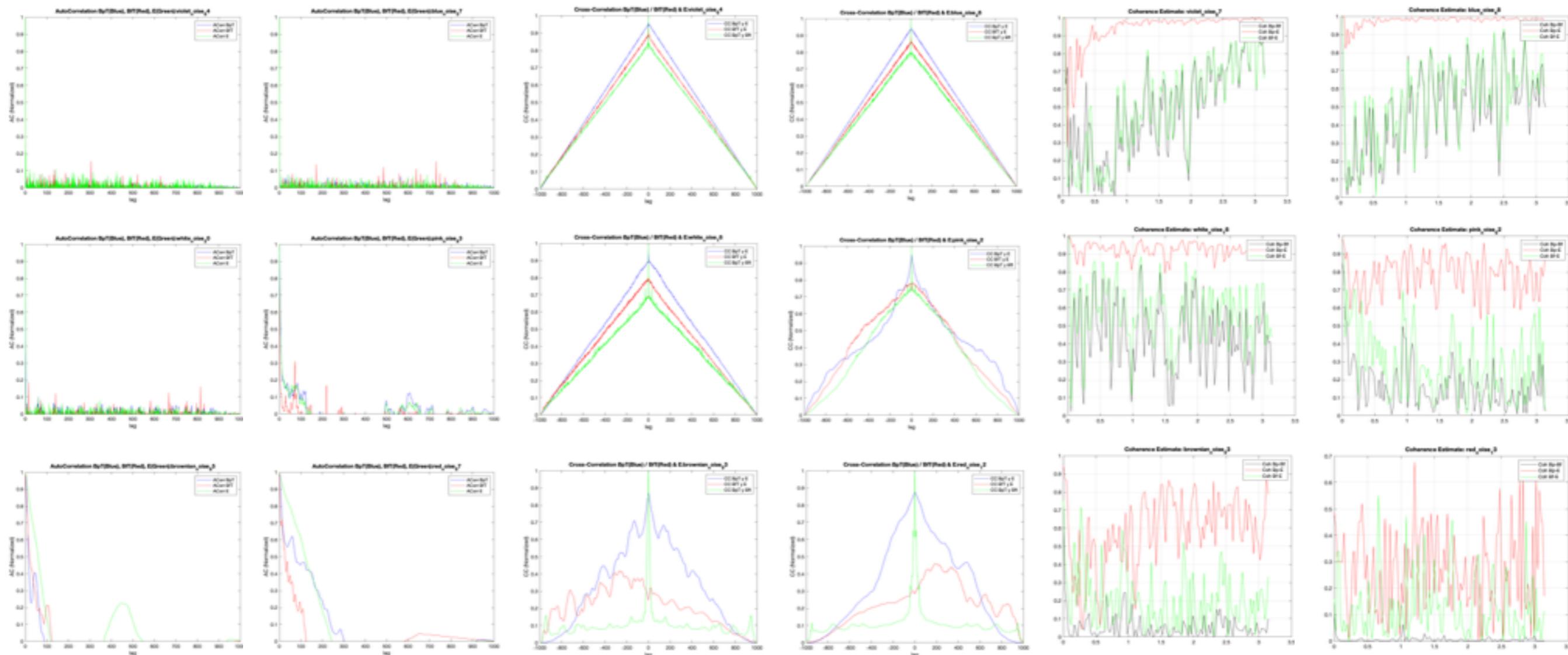
$\beta \rightarrow 0 \implies$ Ausencia de LRD

$\beta \rightarrow -1 \implies$ Anti-Persistencia (Fluct.)

Dinámica Poblacional Estable vs Eventos de Segregación



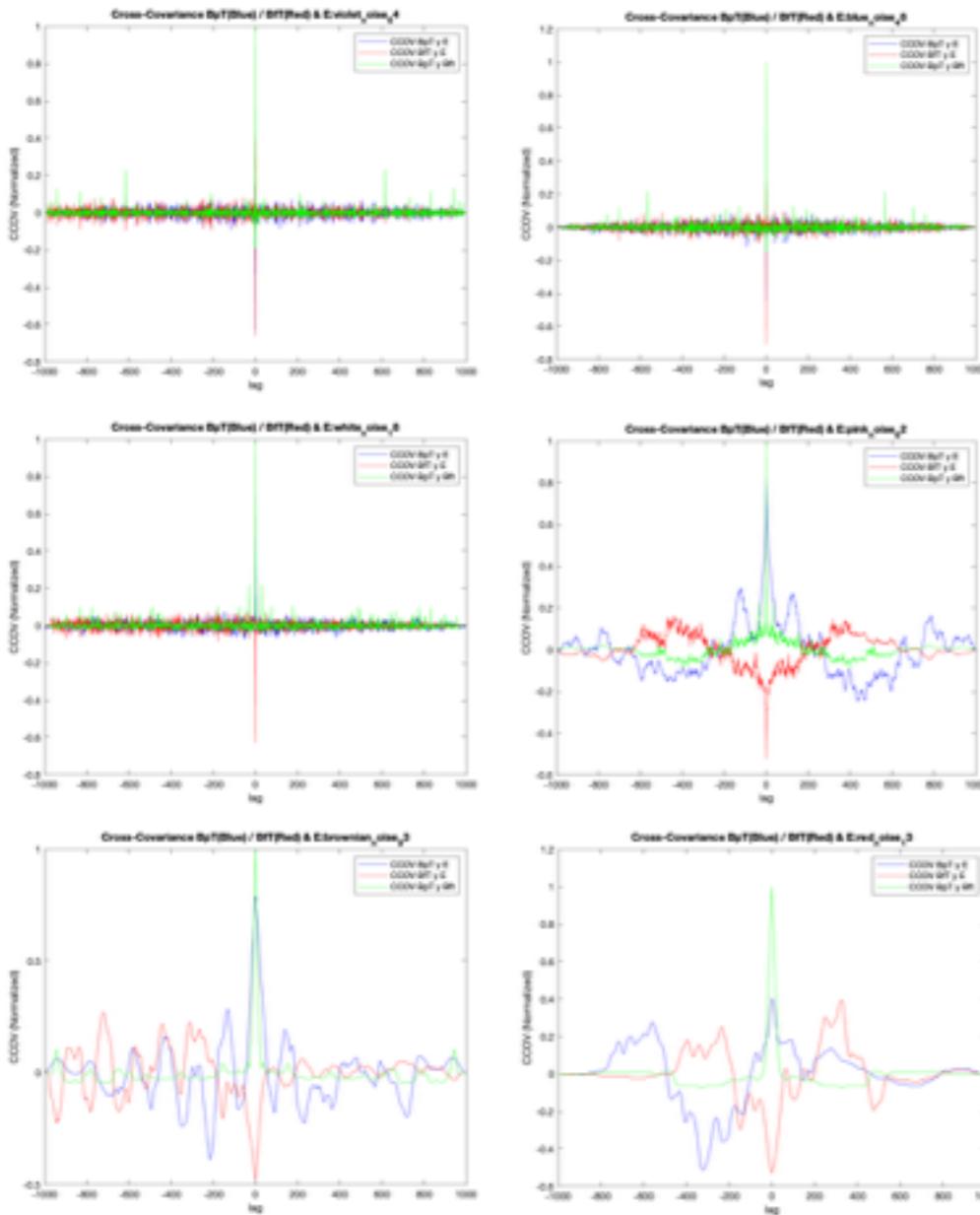
AutoCorrelación



Correlación Cruzada

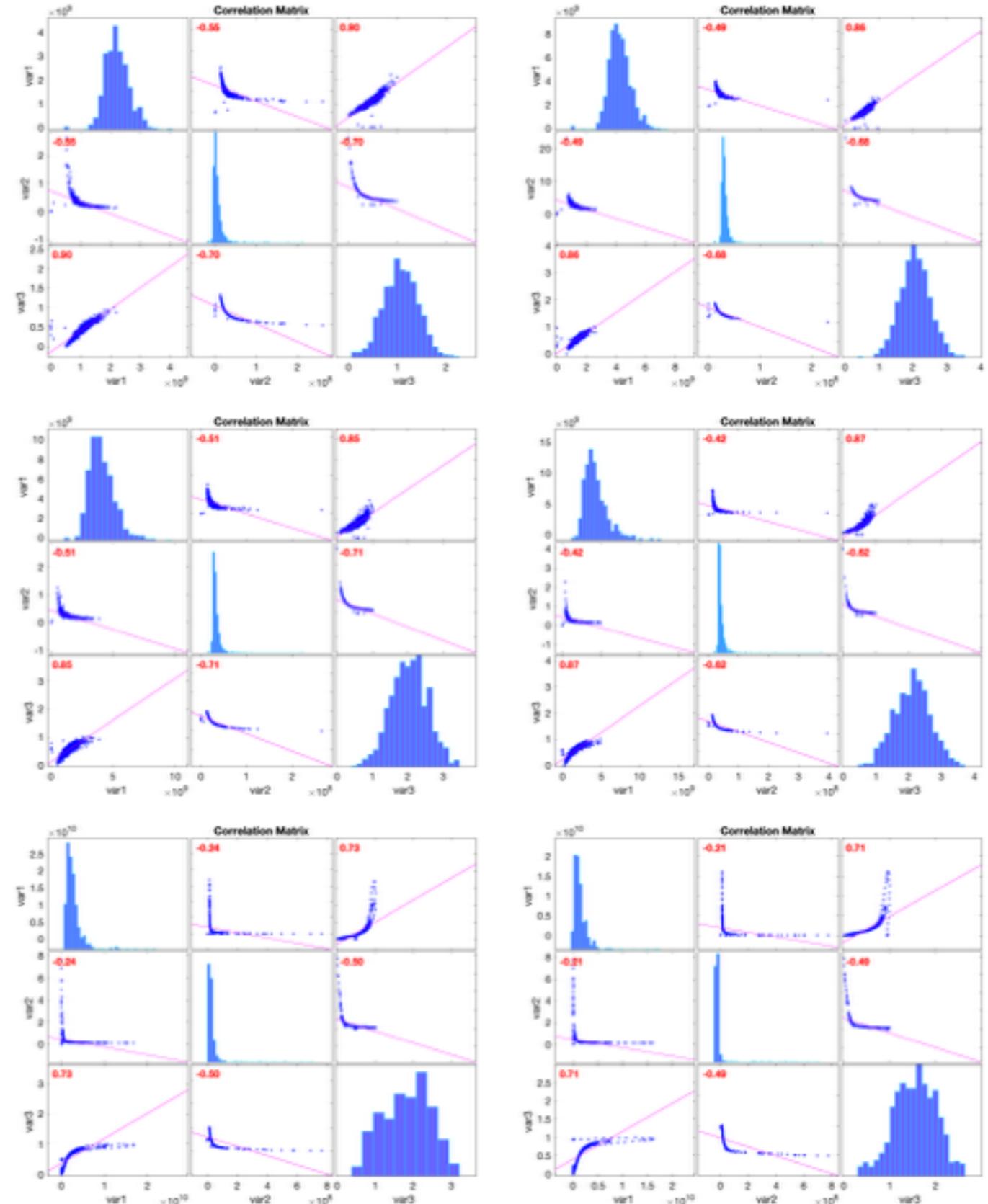
Coherencia Espectral Cruzada

Covariancia Cruzada

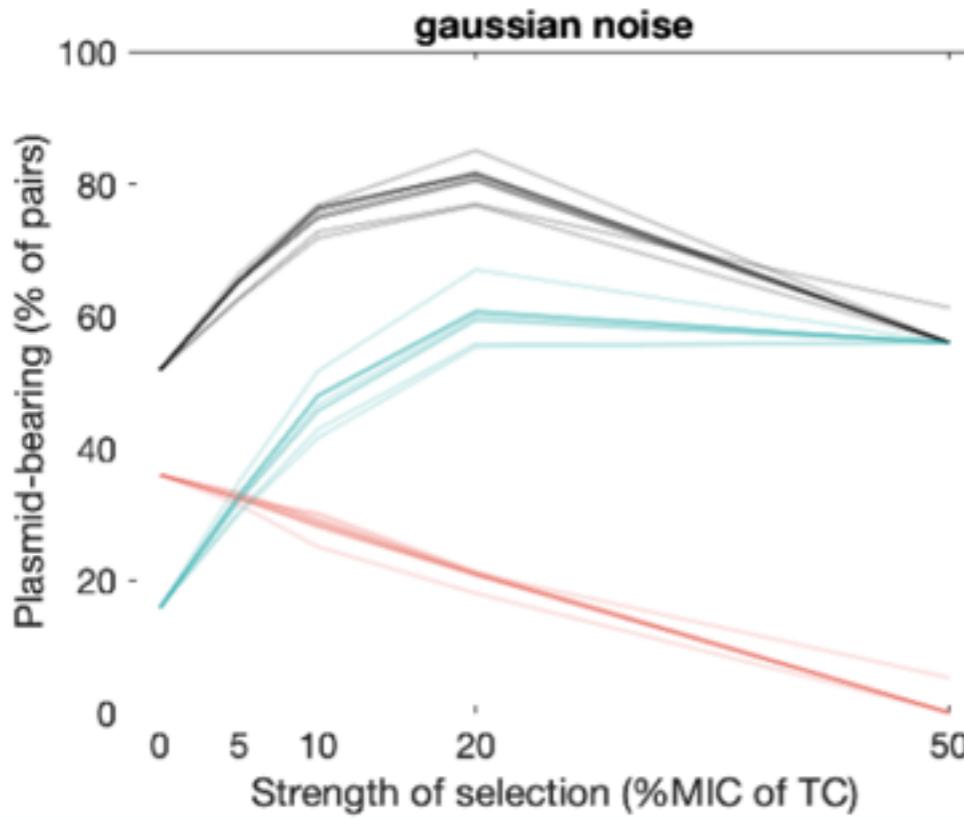
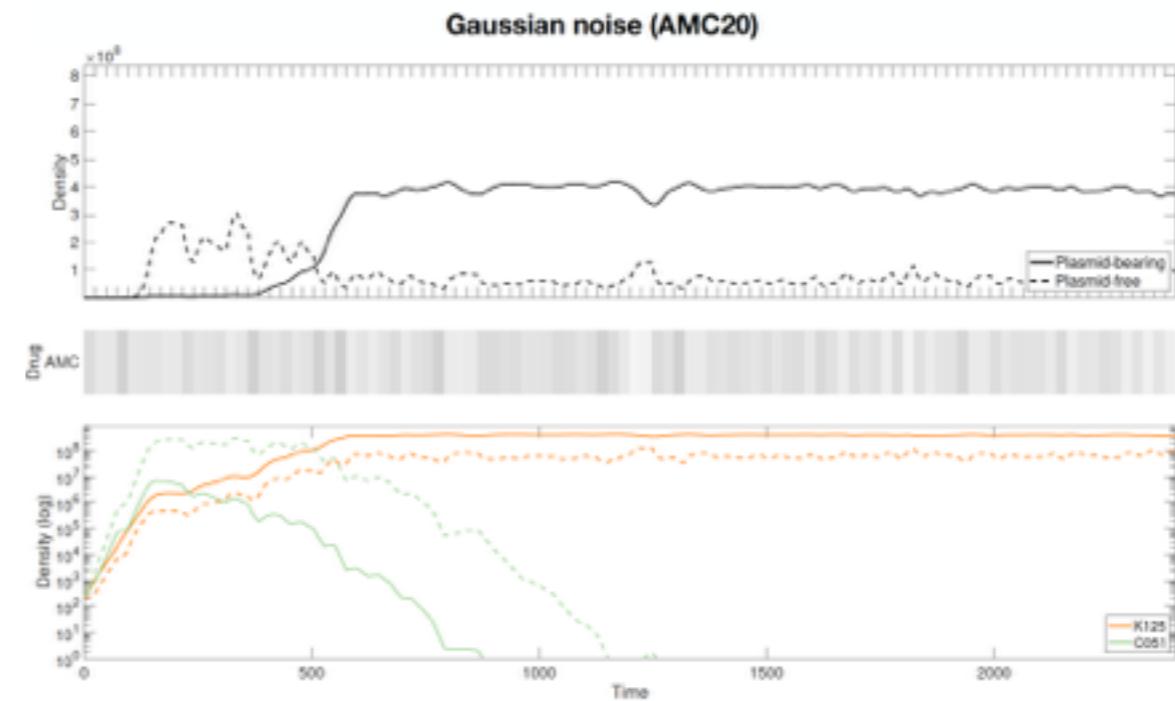
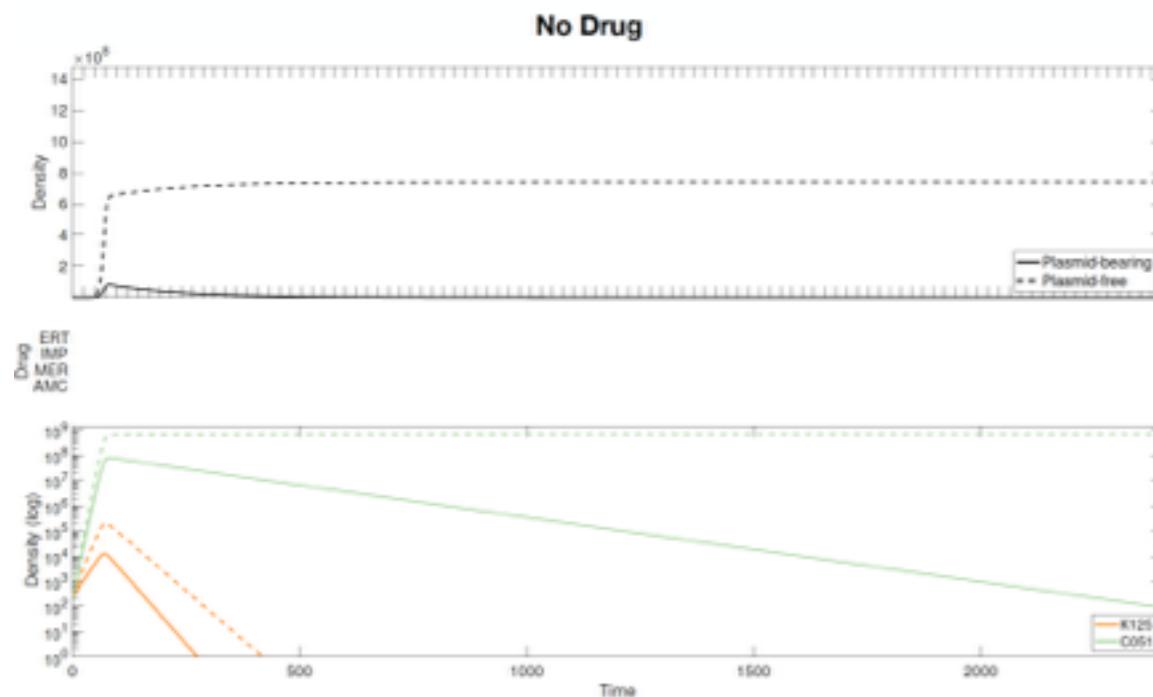


Hurst Exponent	BfT	BpT	Environment
Violet	-0.0600757138880163	-0.0513753350919102	-0.0631055163532985
Blue	-0.0369885601334580	-0.0097127150355180	-0.0503869724652171
White	-0.004757096993490	0.104292448719559	0.0214105829245383
Pink	0.136975291348946	0.364288122900233	0.178299855984500
Red	0.621258690099793	0.802832146440975	0.571907367367835
Brownian	0.557166606087888	0.737673752330808	0.588951004974829

Matriz de Correlación Pearson-
 $[var1, var2, var3] = [daily_BpT, daily_BfT, E]$

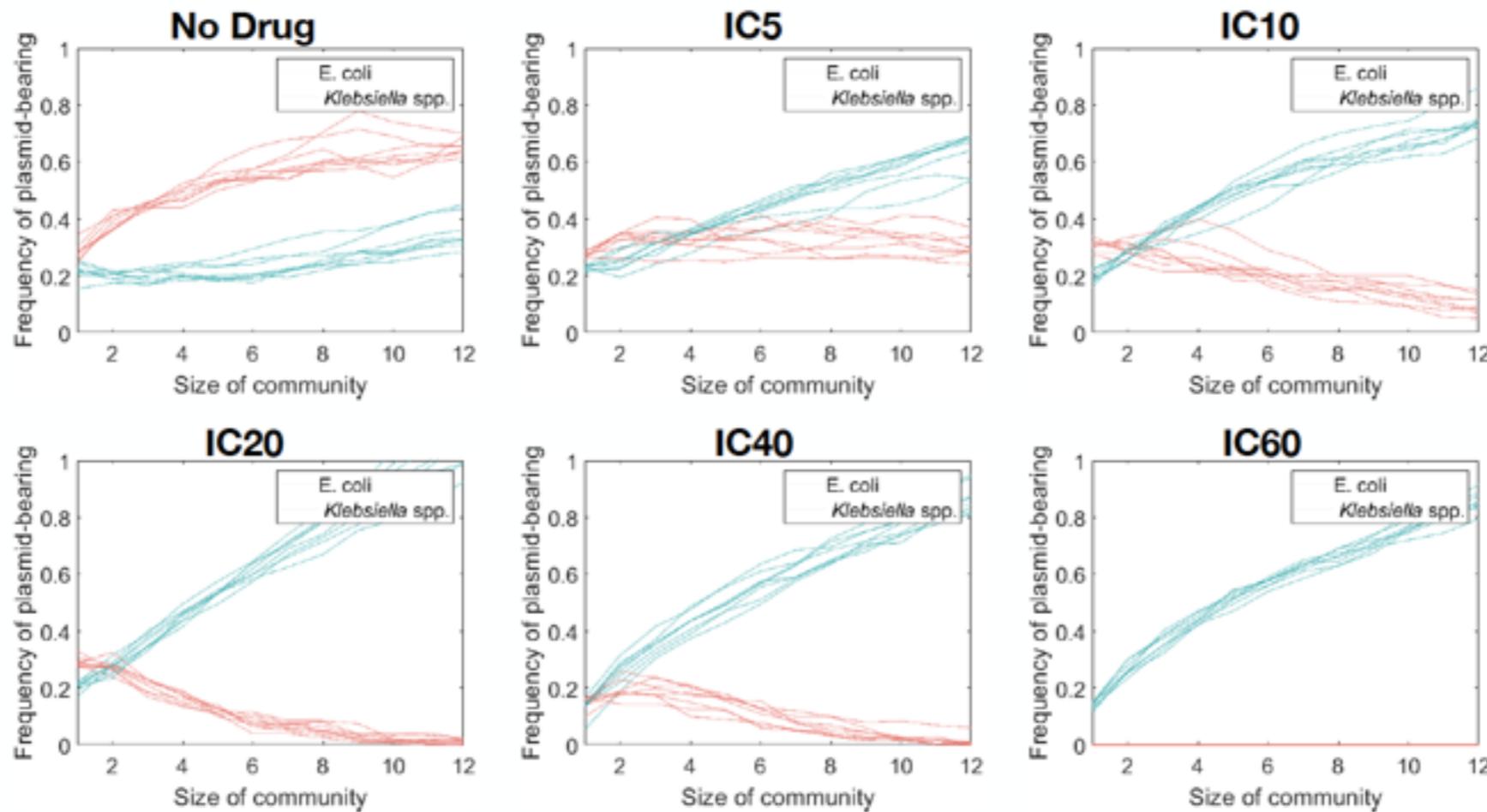


Ciclo de Vida en Plásmidos: Comunidades Sintéticas (Pares)



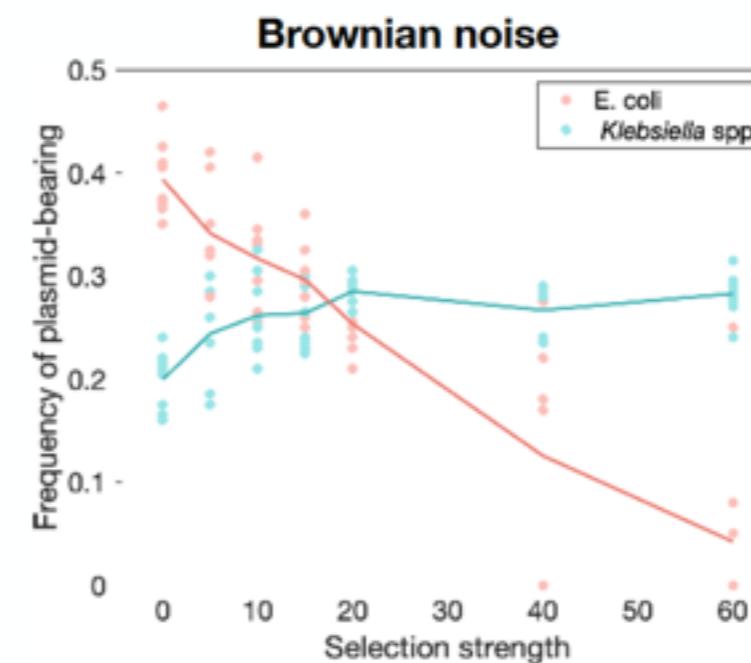
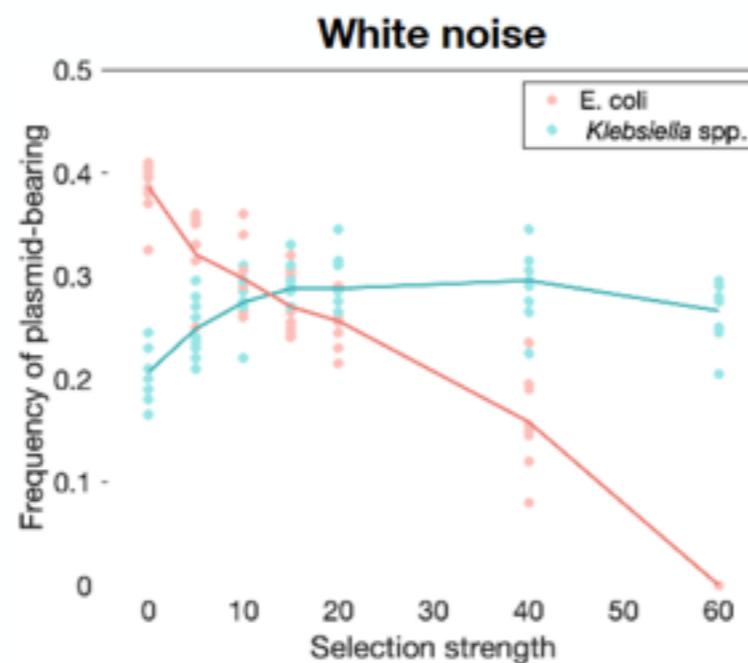
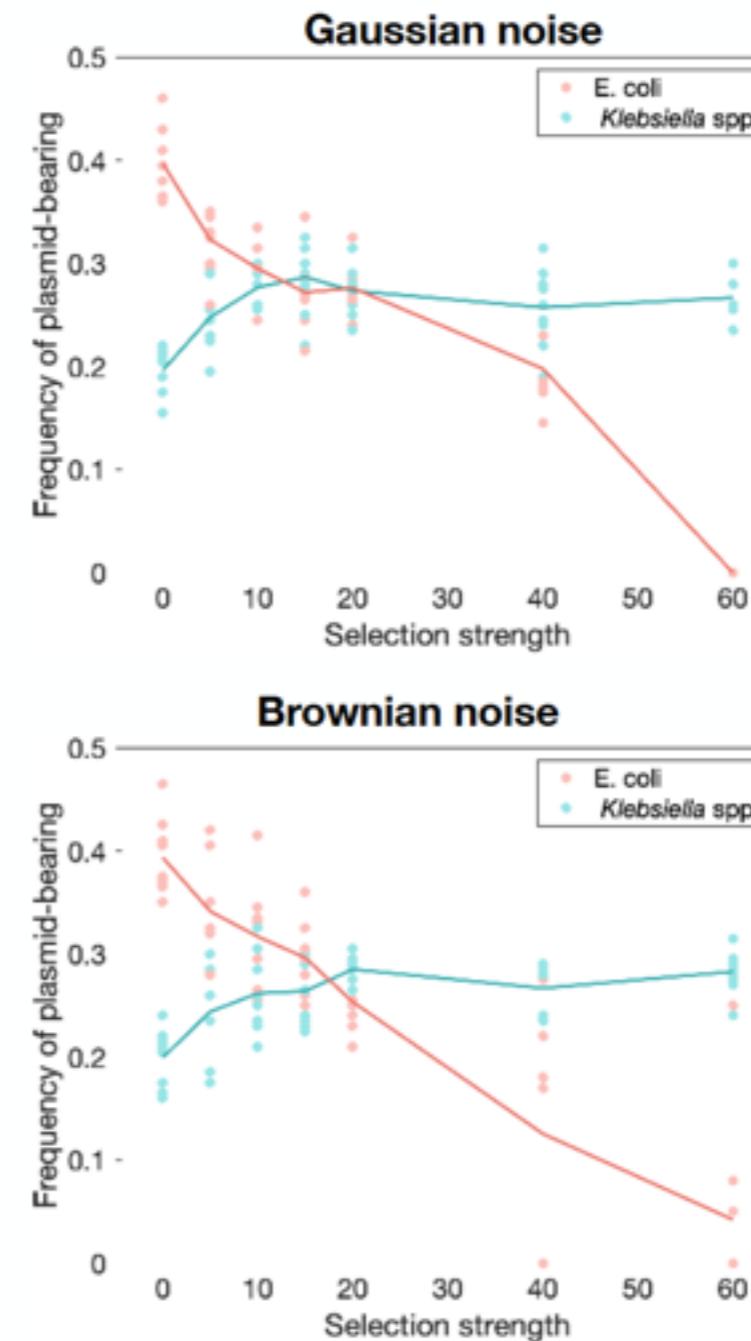
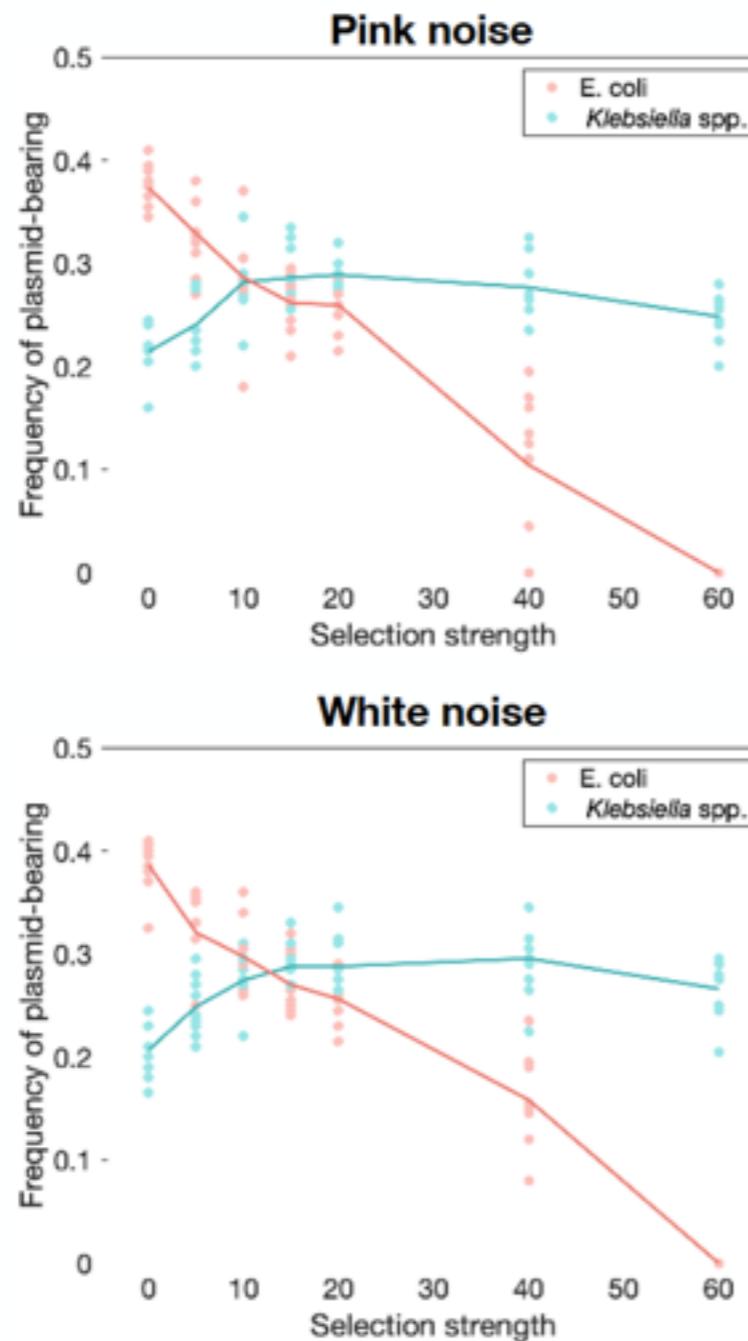
Ciclo de Vida en Plásmidos: Comunidades Sintéticas (Size)

Gaussian noise



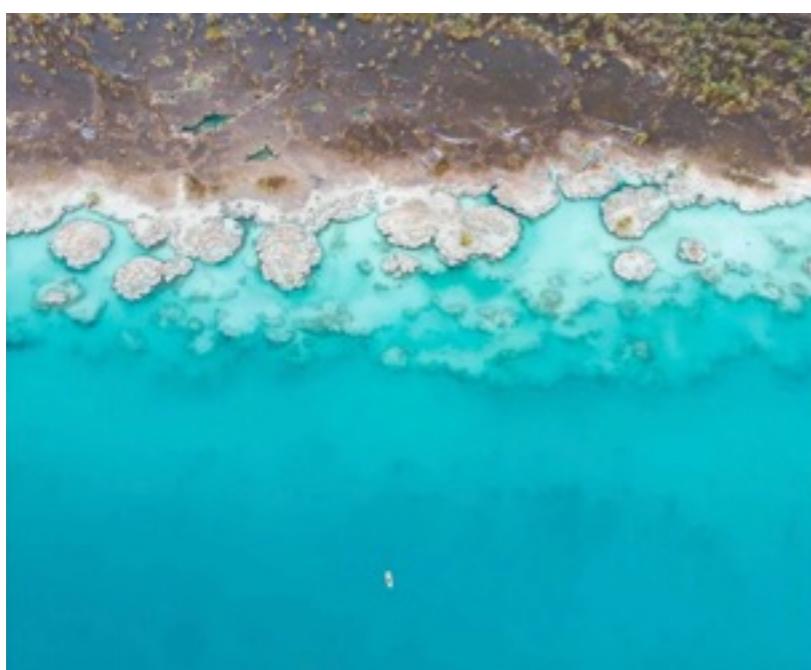
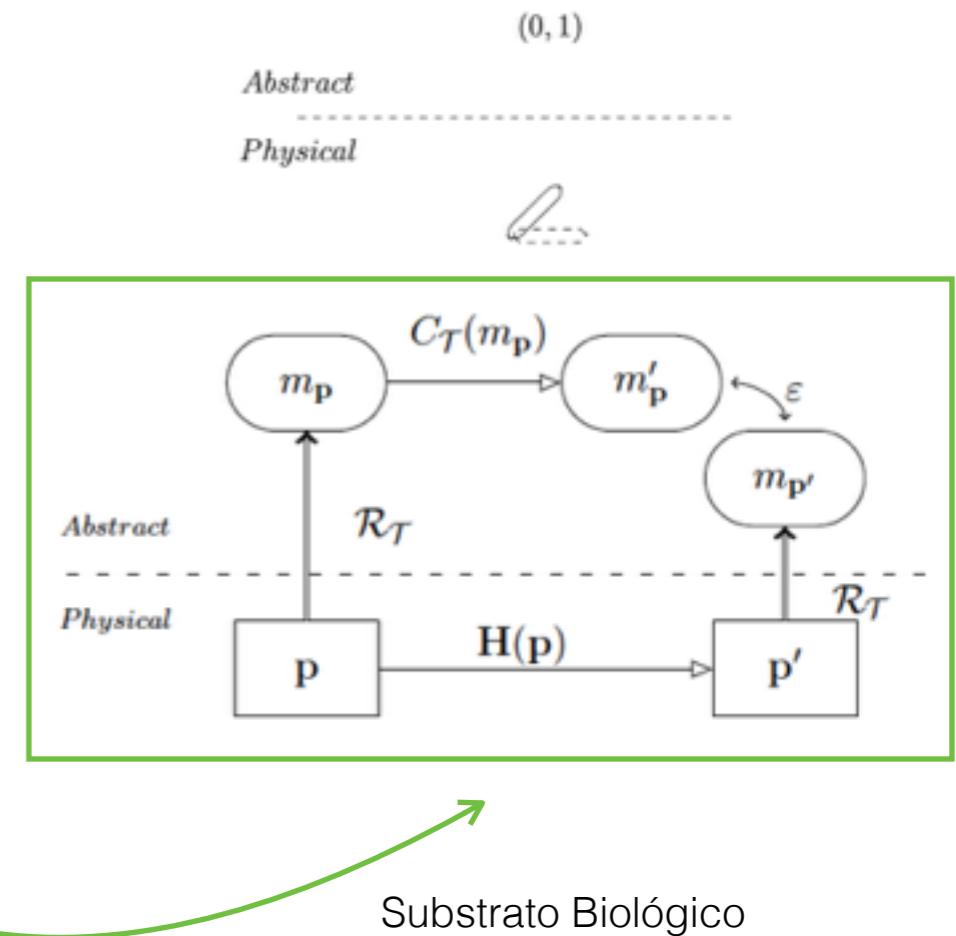
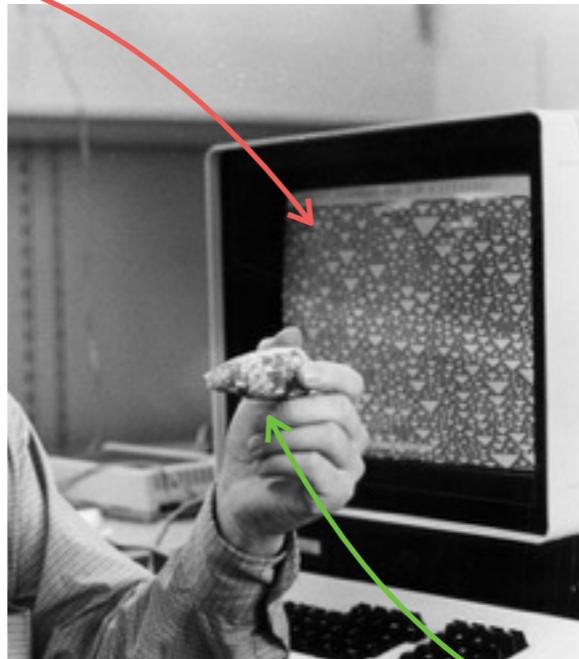
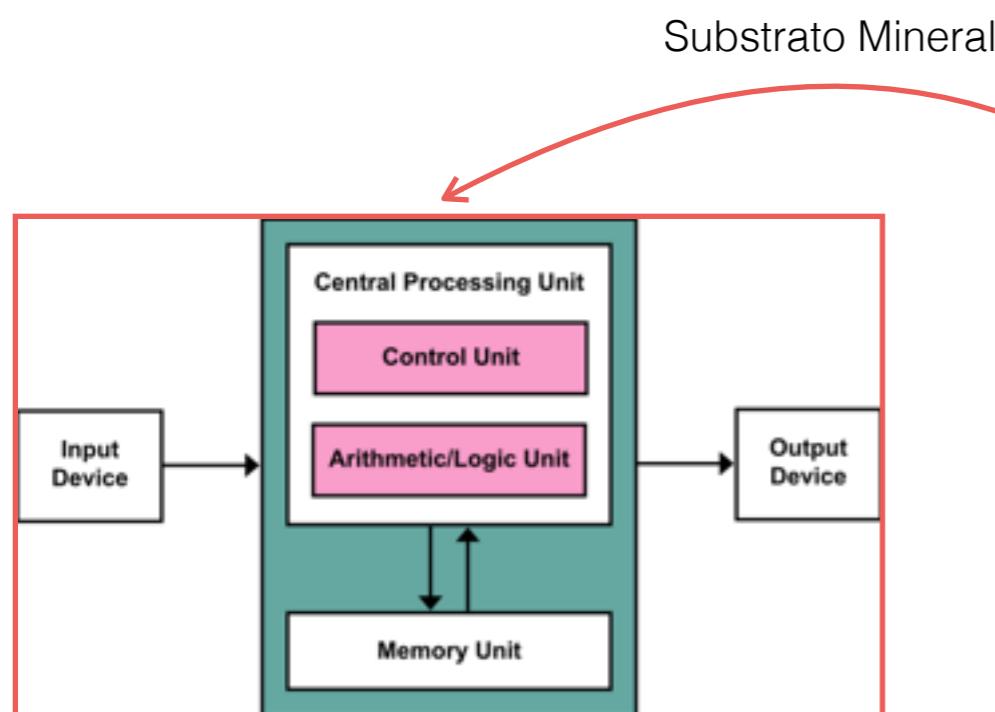
Random communities (variable N)
10 stochastic environments
100 replicate simulations per environment

Ciclo de Vida en Plásmidos: Comunidades Sintéticas (IC)

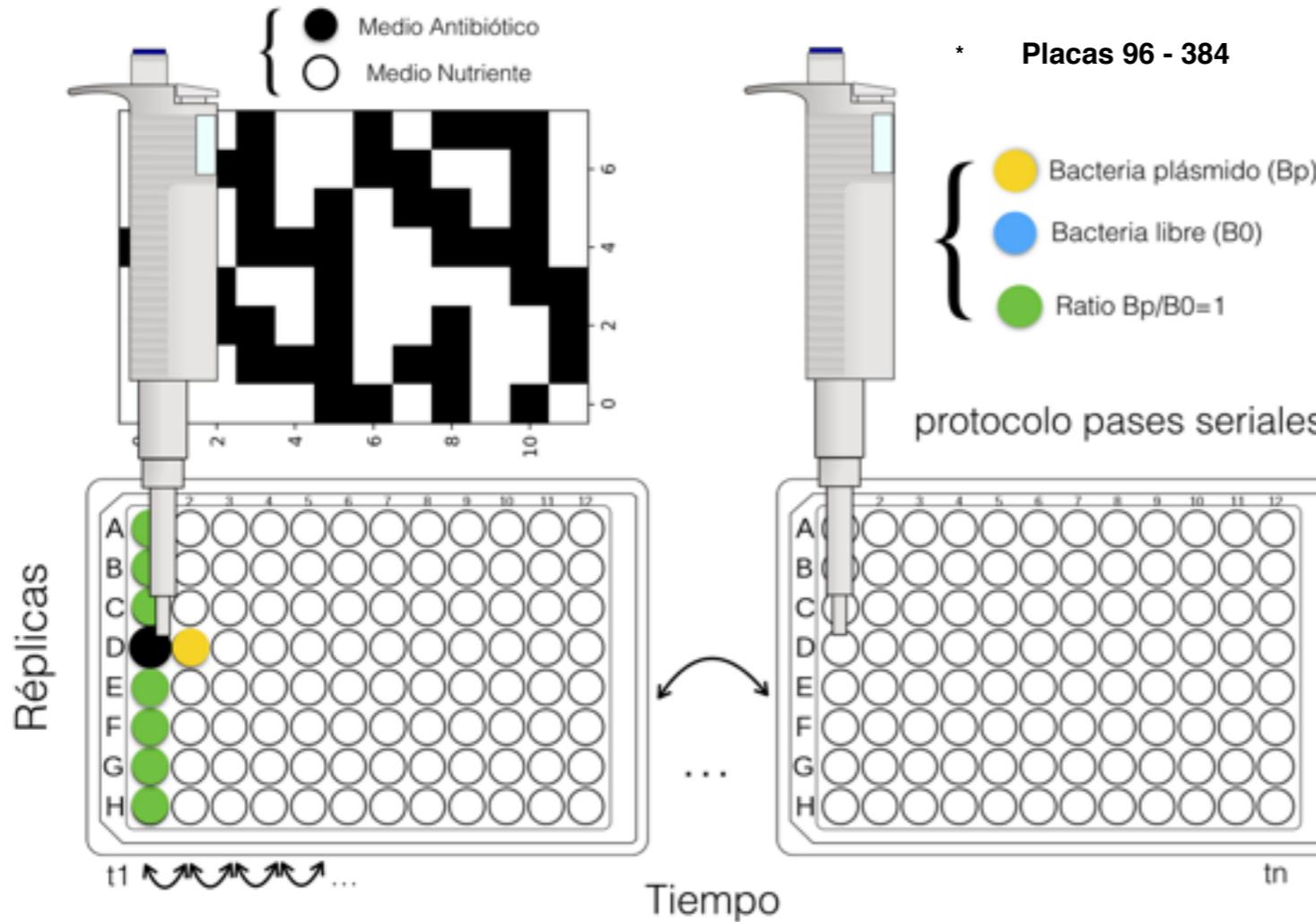


Random communities (N=2)
10 stochastic environments
100 replicate simulations per environment

Series Temporales: Autómatas Celulares

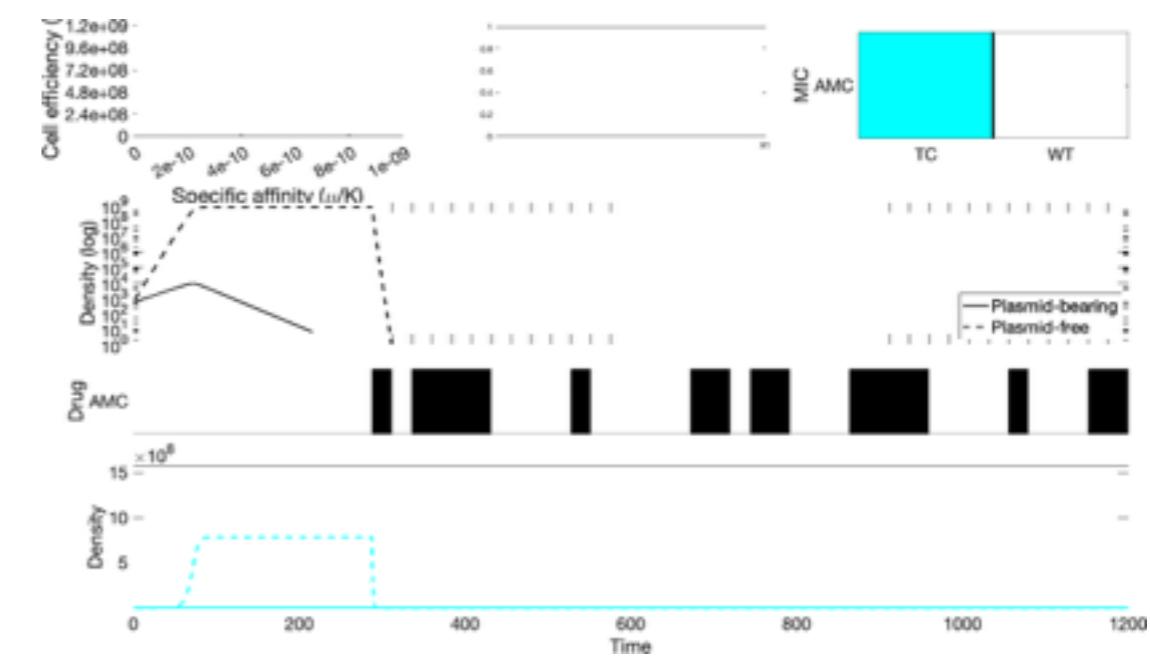
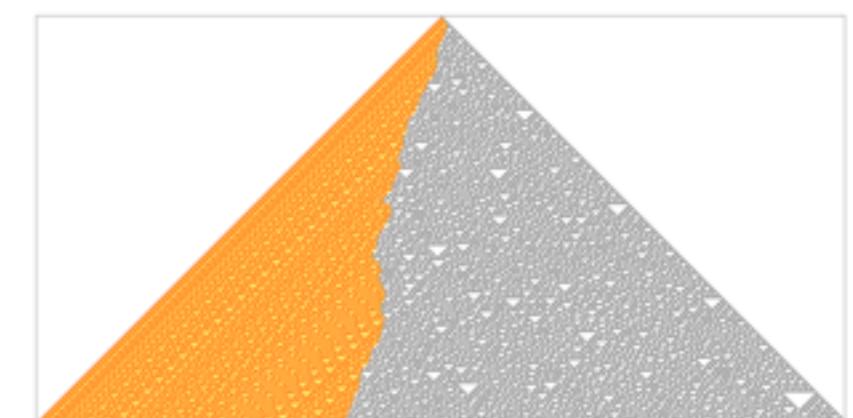


Series Temporales: Autómatas Celulares

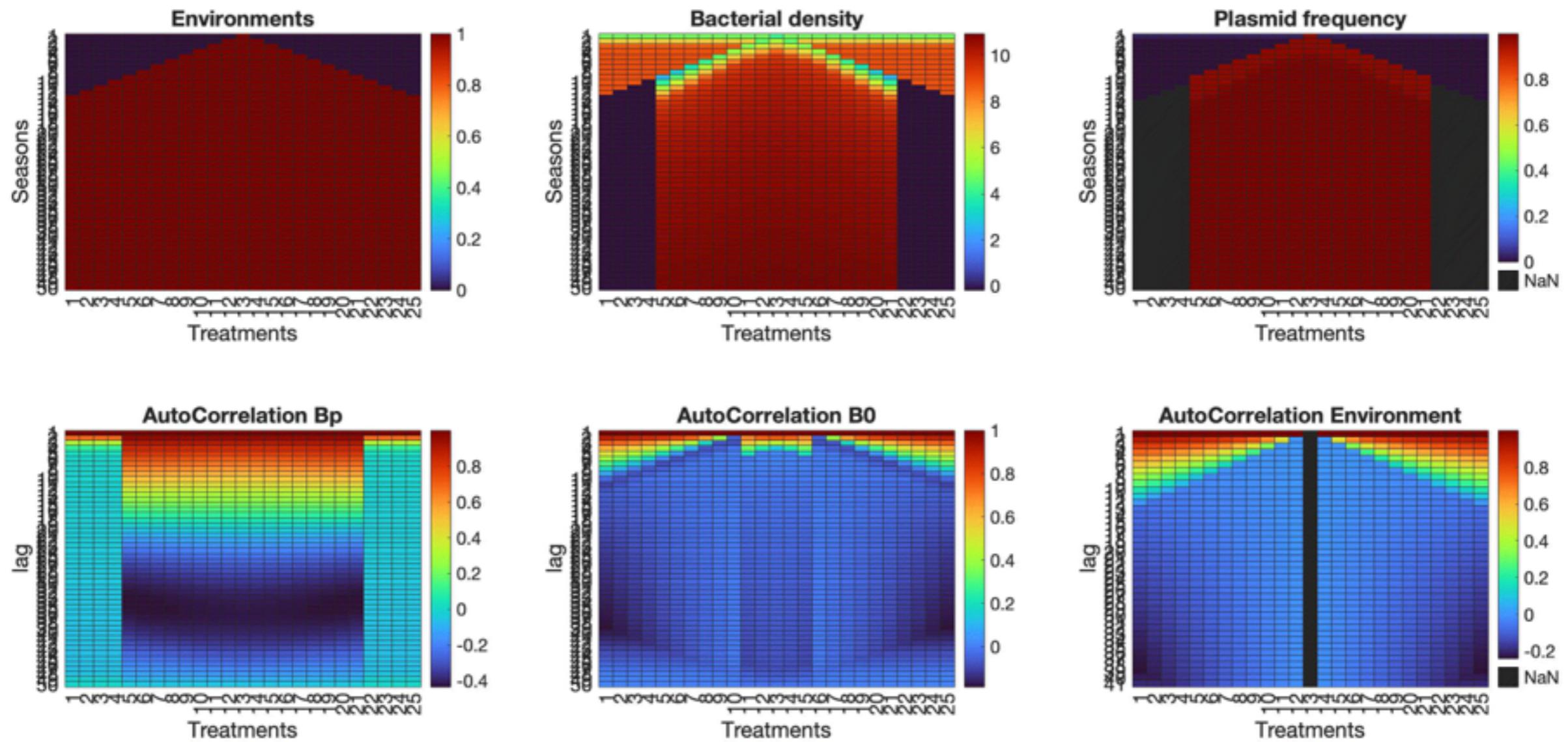


Comportamiento Aperiódico-Caótico:

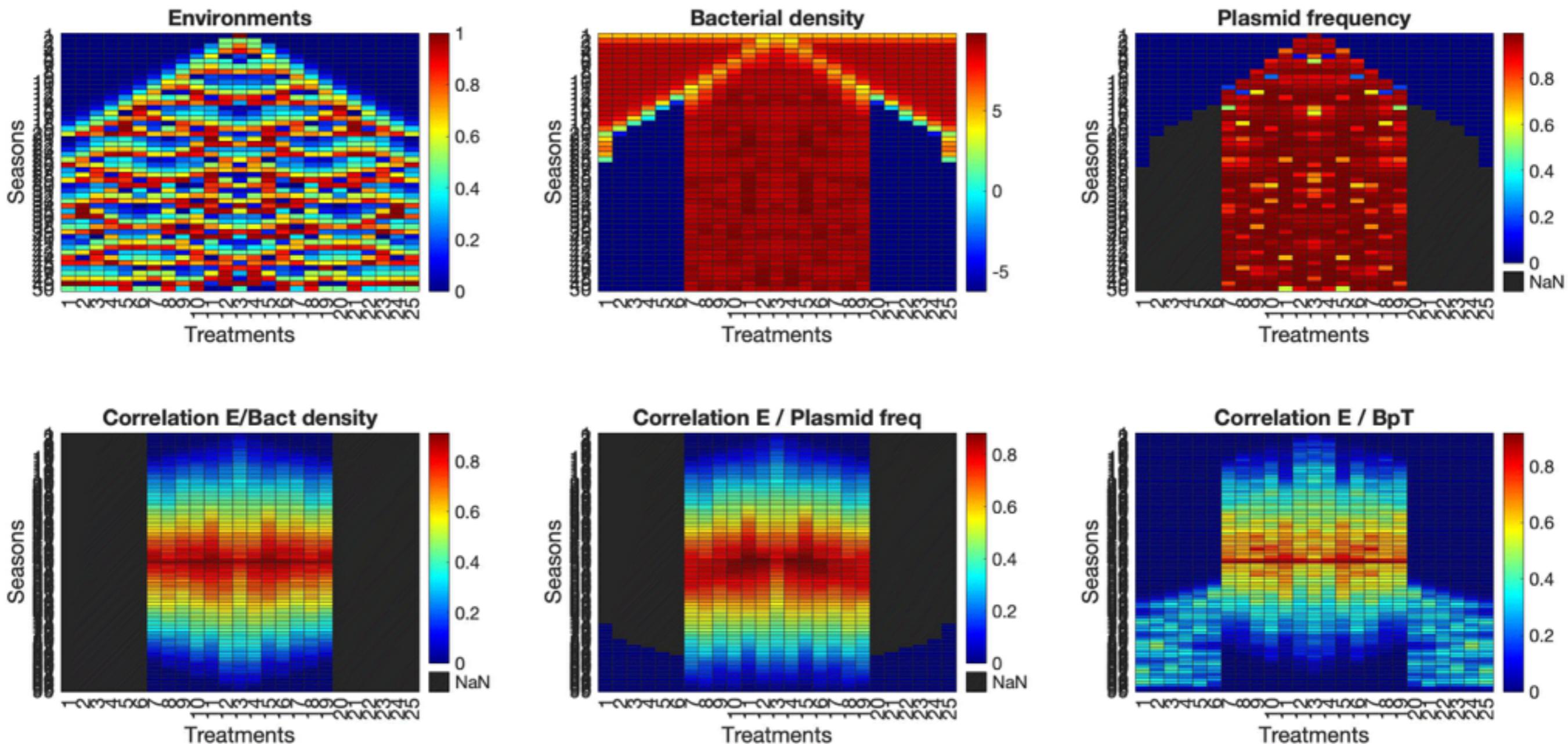
- ¿La columna central siempre permanece no periódica?
- ¿Cada color de celda aparece en promedio con la misma frecuencia en la columna central?
- ¿El cálculo de la n-ésima celda de la columna central requiere al menos $O(n)$ esfuerzo computacional?



Rule 222 / Rule 30 /Rule 94 / Rule 62 / CA Continuo

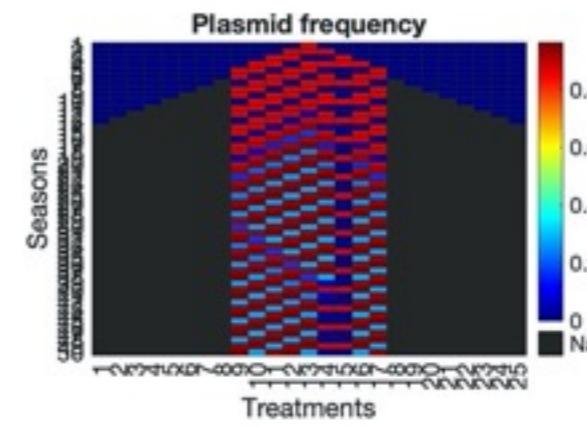
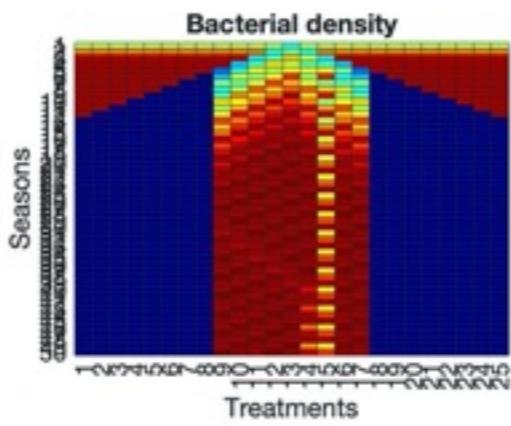
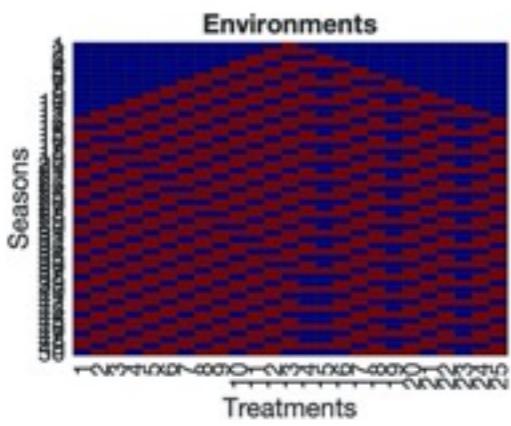
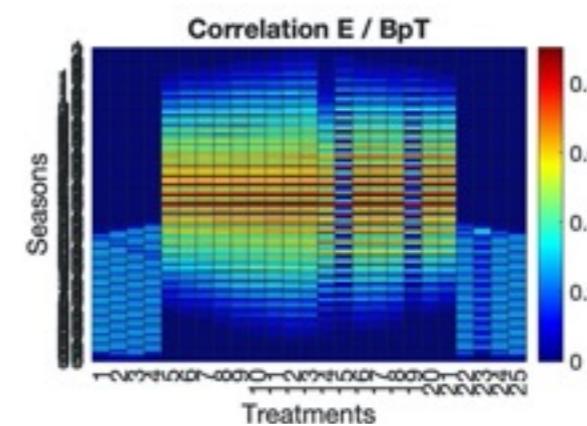
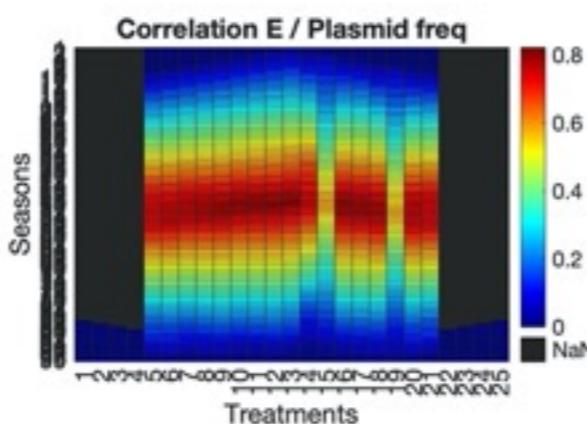
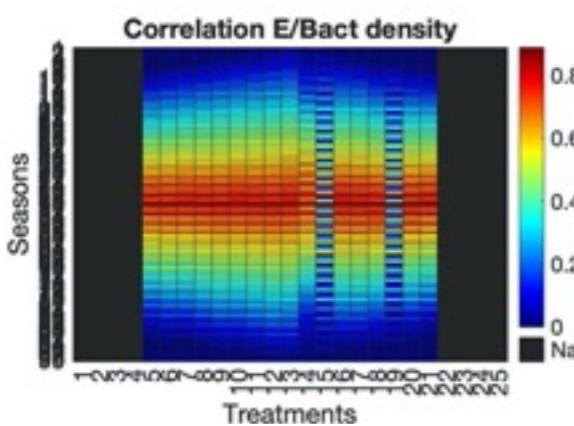
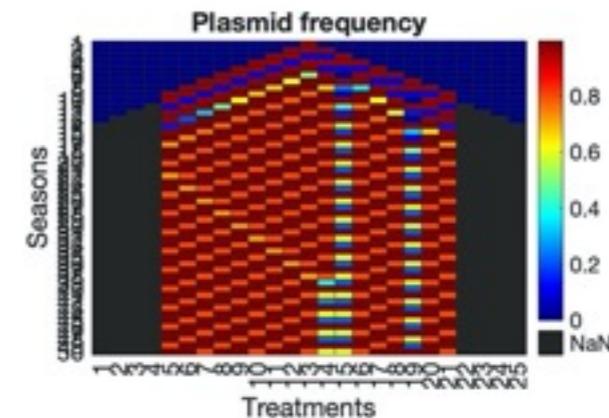
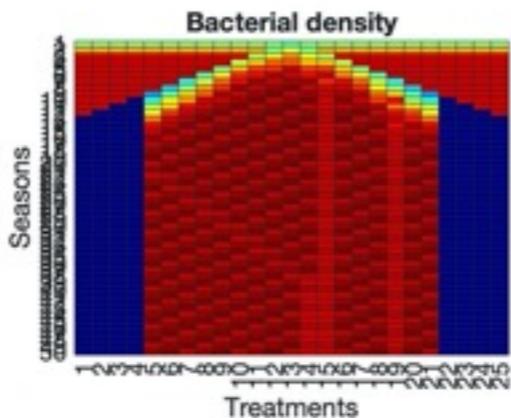
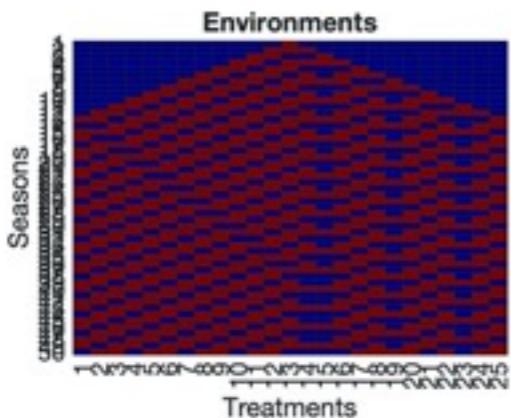


Rule 222 / Rule 30 /Rule 94 / Rule 62 / CA Continuo

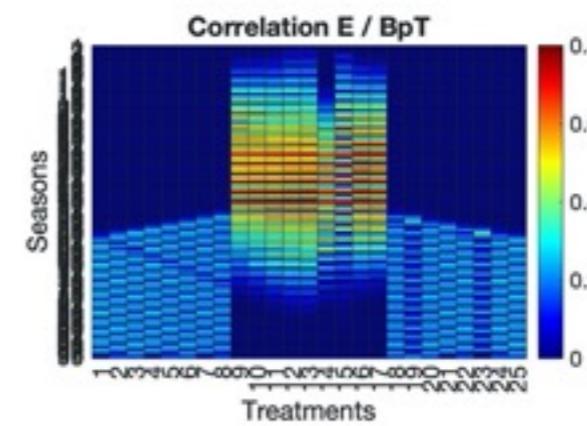
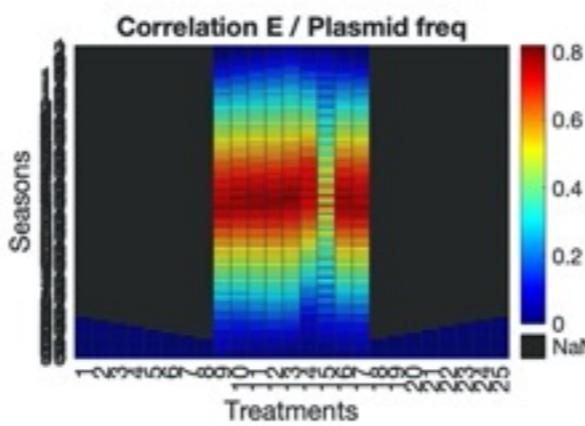
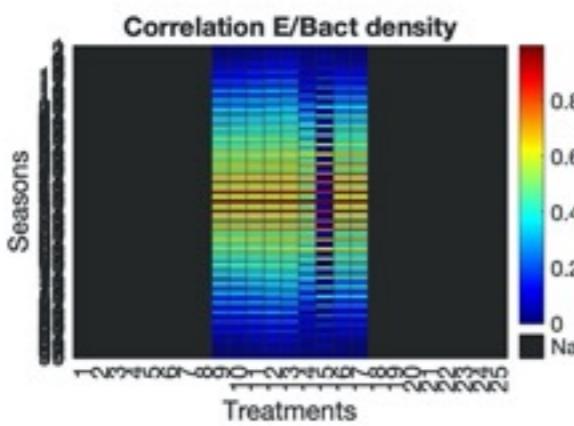


Rule 94

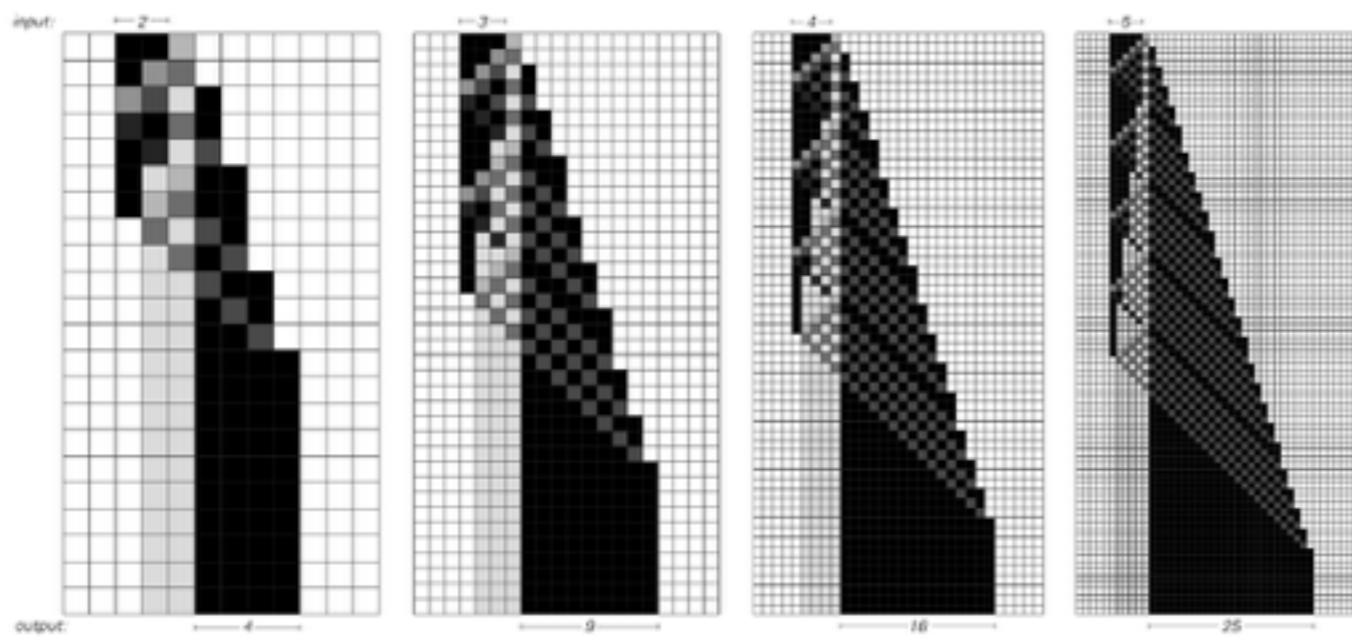
seg_rate=.1



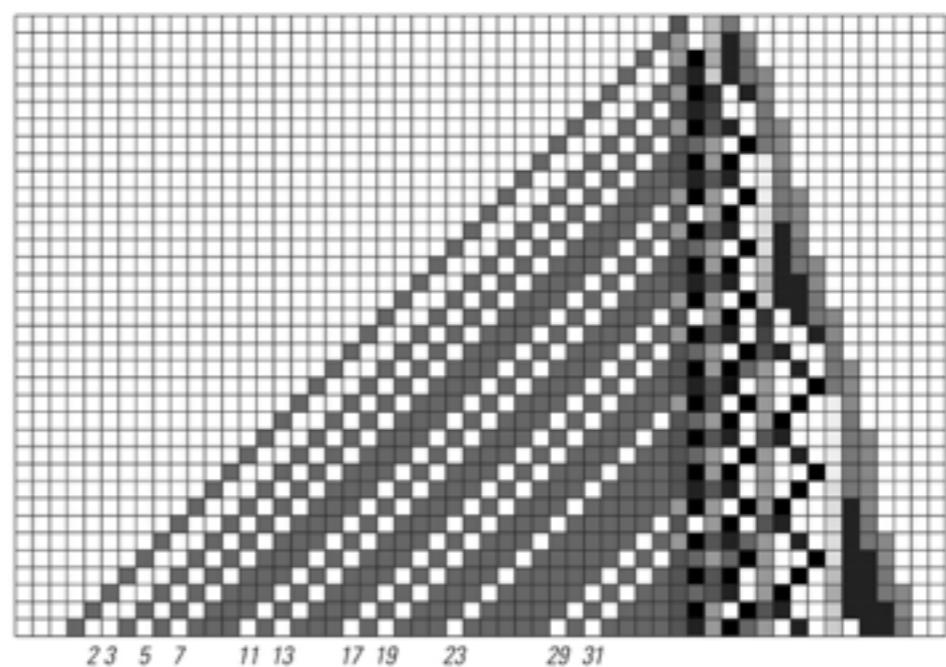
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Cálculo de Cuadrados



Cálculo de Primos



Cellular Automata Approaches to Biological Modeling

G. B. ERMENTROUT AND L. EDELSTEIN-KESHET

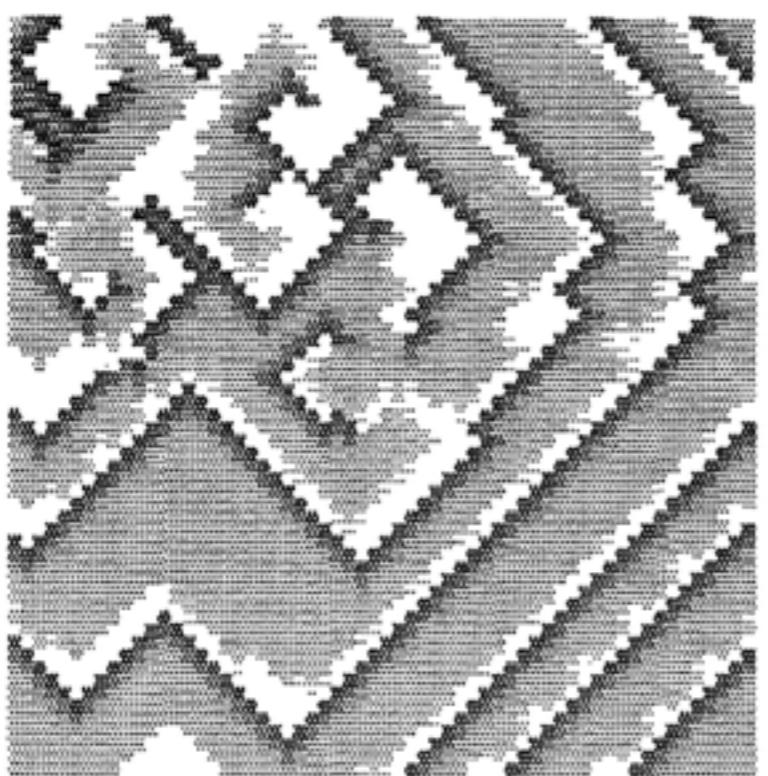
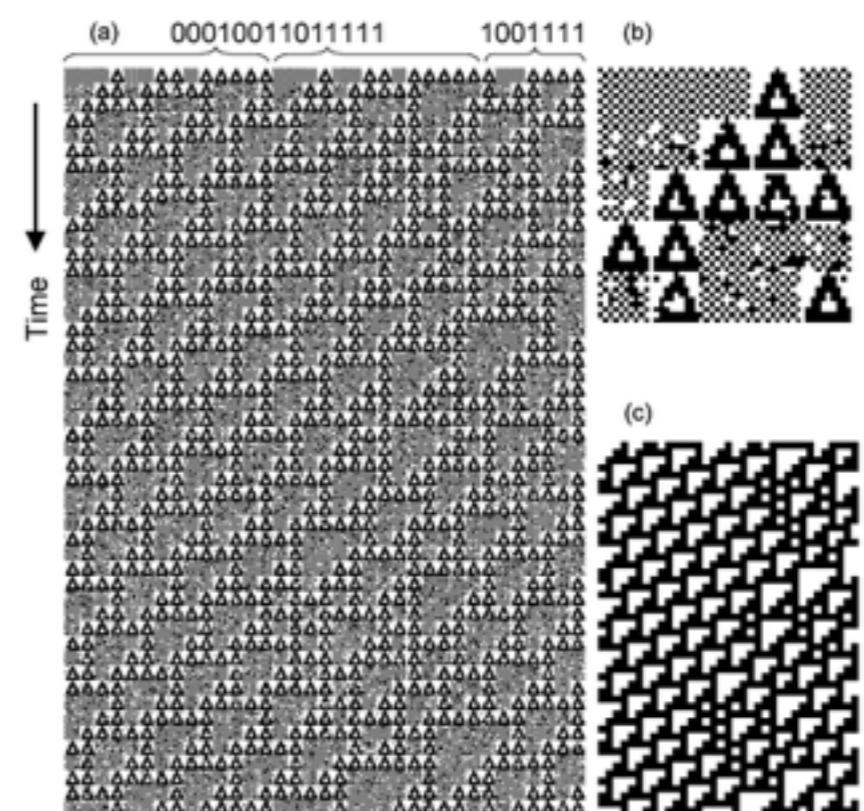


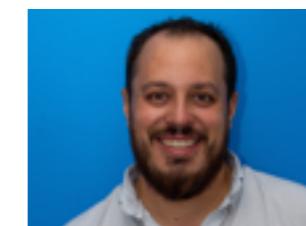
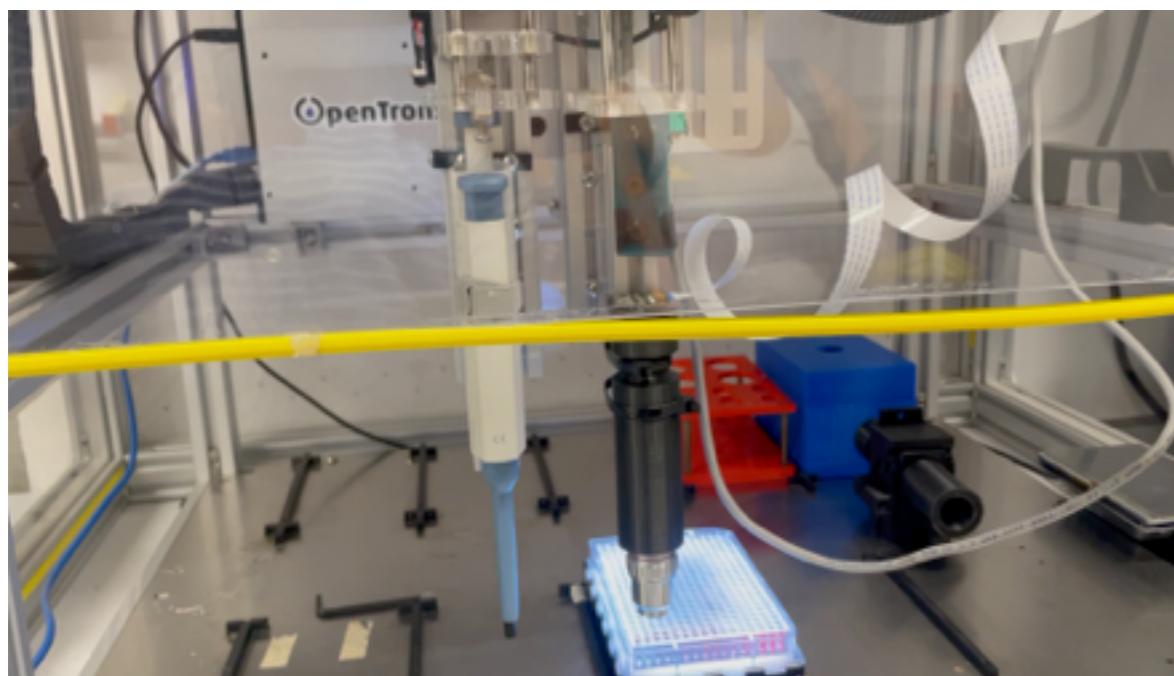
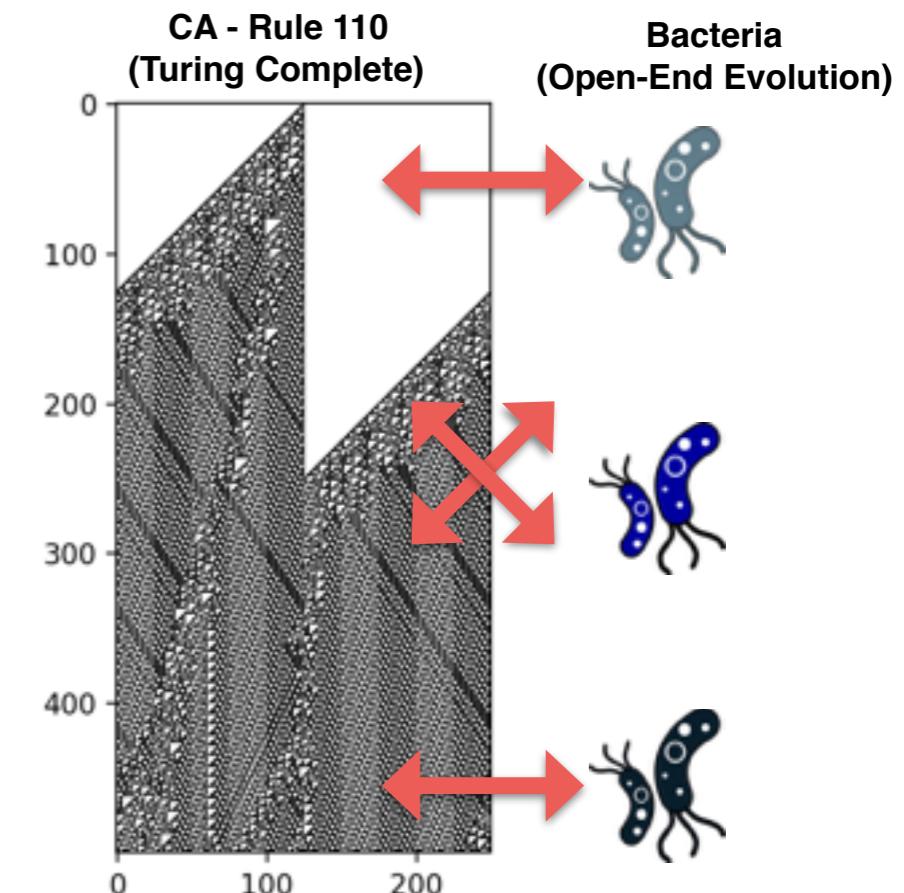
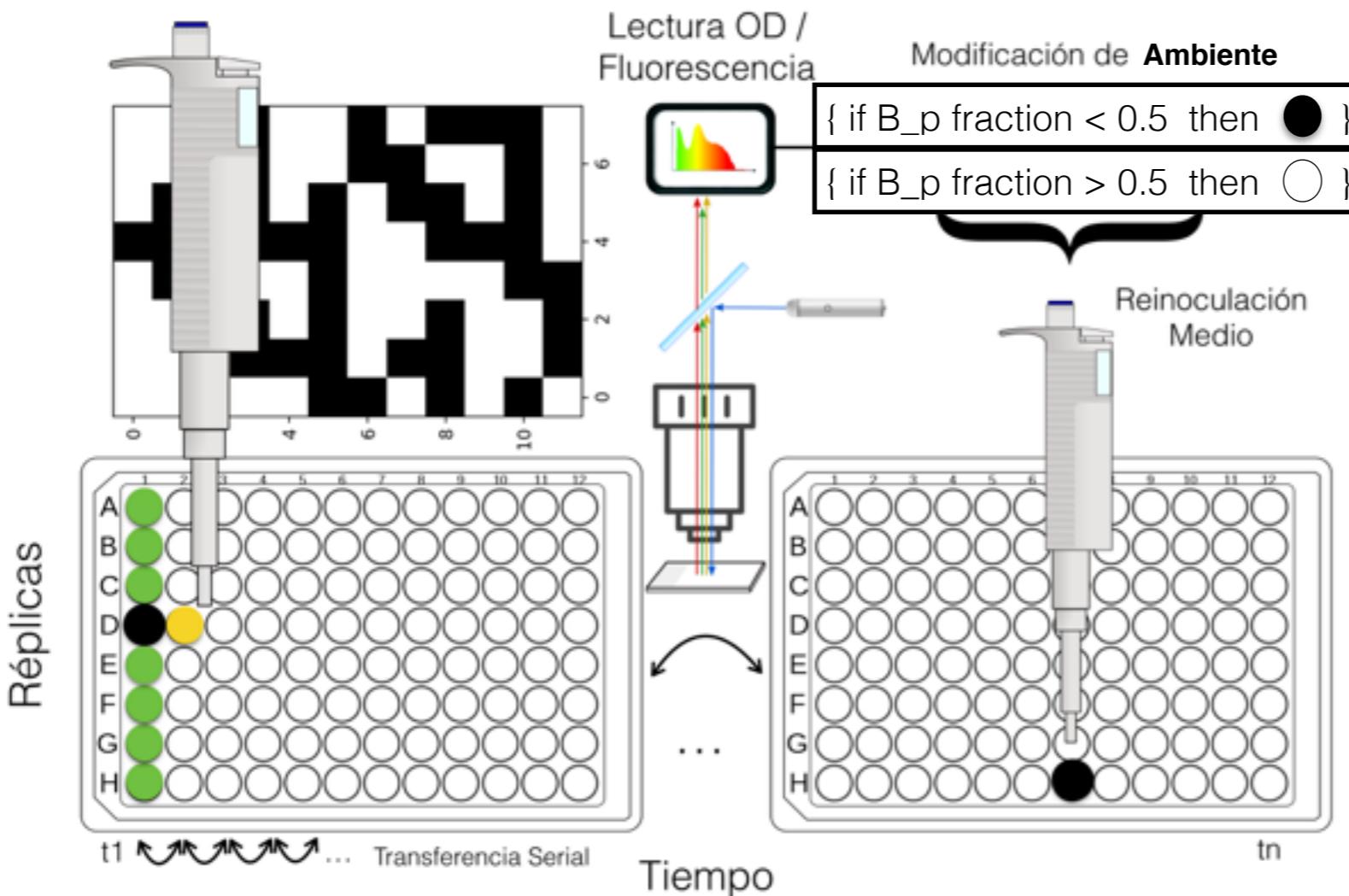
FIG. 3. Host-parasitoid automata. White is state 0 and dark grey is state 8.

Noise-robust realization of Turing-complete cellular automata by using neural networks with pattern representation

M. Oku, K. Aihara / Physics Letters A 374 (2010) 4859–4863



BACTOMATA (*Heterotic hybrid computing device*): dispositivo que involucra la combinación de dos o mas substratos computacionales en un sólo sistema de computación cuyo poder computacional es mayor al de su suma de sus componentes individuales (Stepney, 2015)



Rafael Peña-Miller



Centro de Ciencias Genómicas



Financial Support