How might multiscale collectives ‘collect’ across scales?

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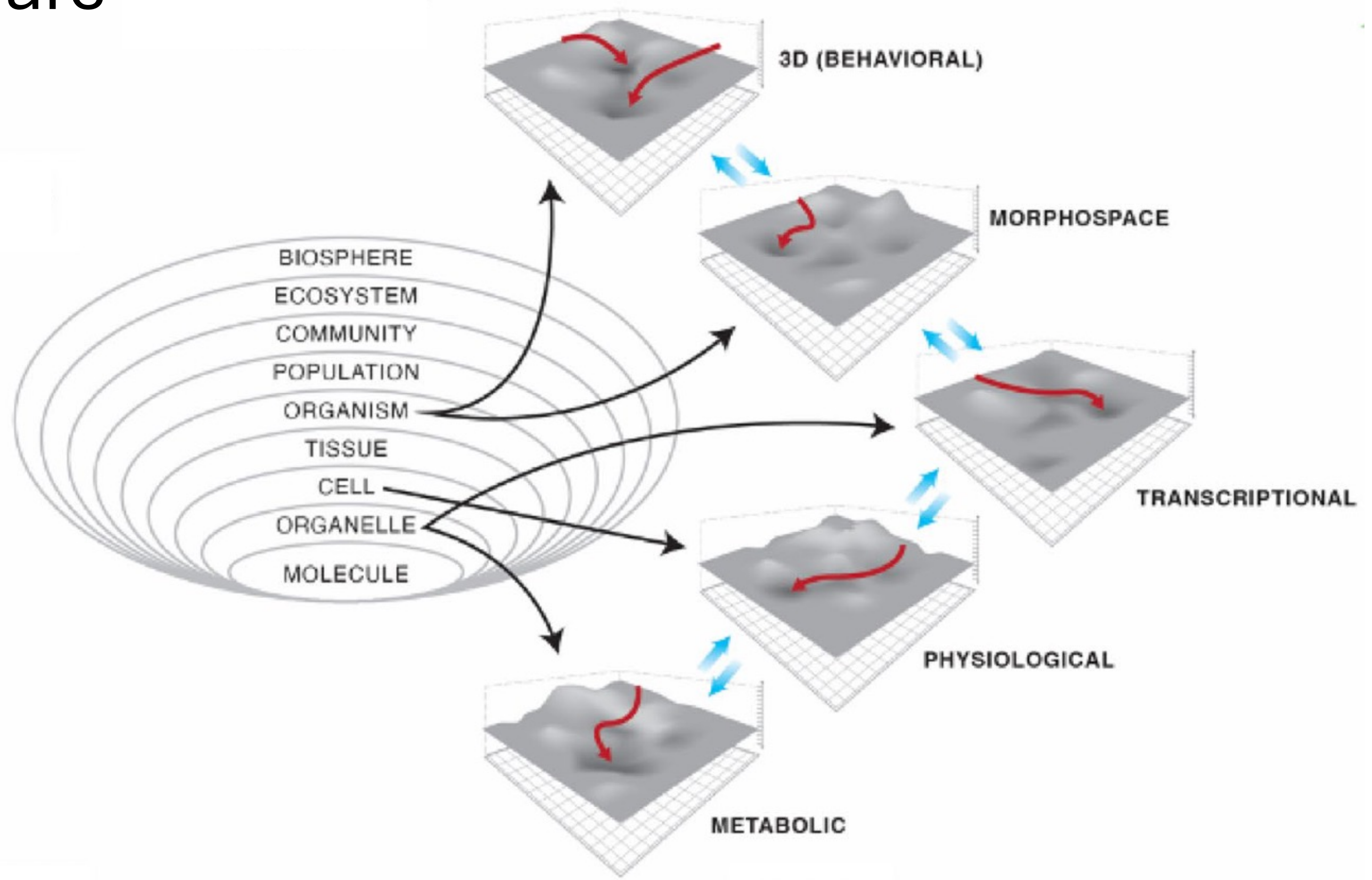
https://www.youtube.com/watch?v=dXpAbezdOho&ab_channel=Jordy

How to characterize the disparate collective phenomena occurring during development using a common language?

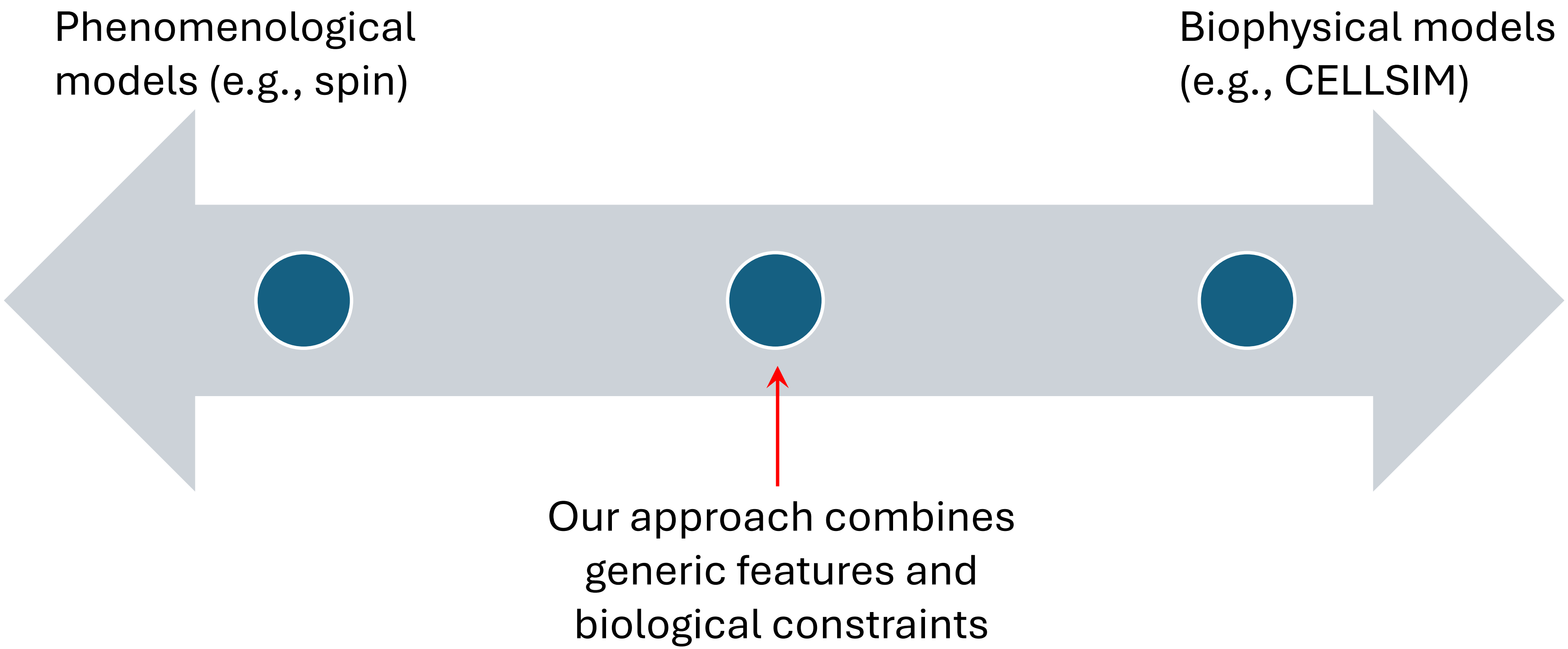
Motivating ideas

Evolution may be searching the lower-dimensional space of high-level strategies rather than the higher-dimensional space of low-level hardware

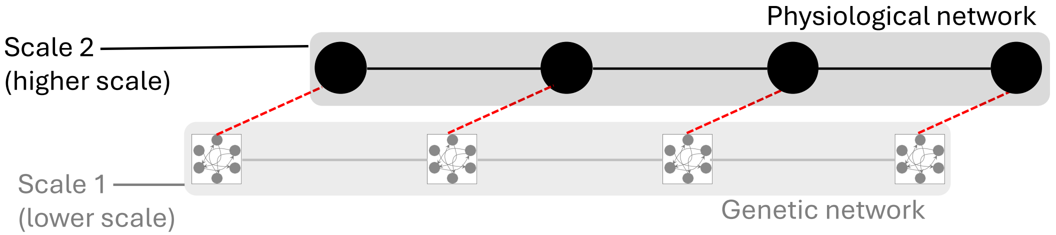


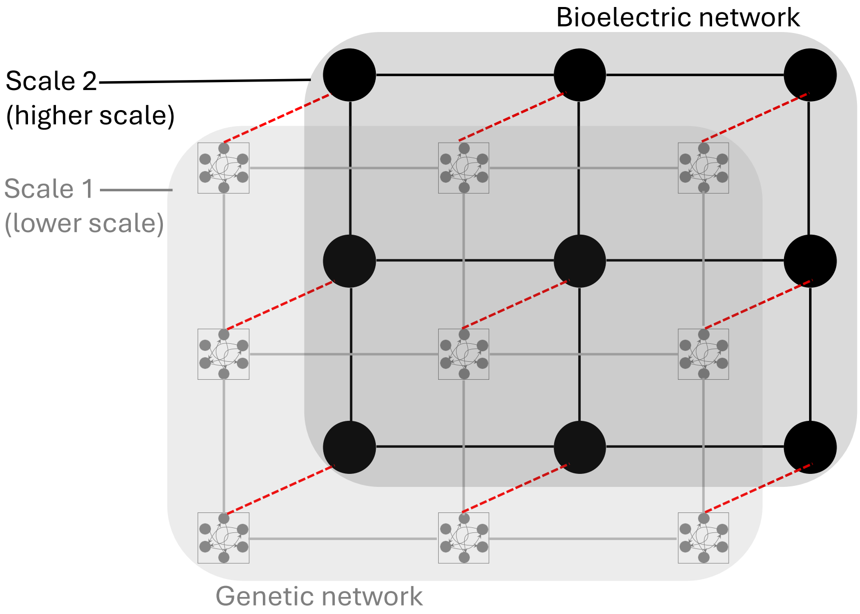
Levin, M. (2023). "Darwin's agential materials: evolutionary implications of multiscale competency in developmental biology." Cell Mol Life Sci **80**(6): 142.

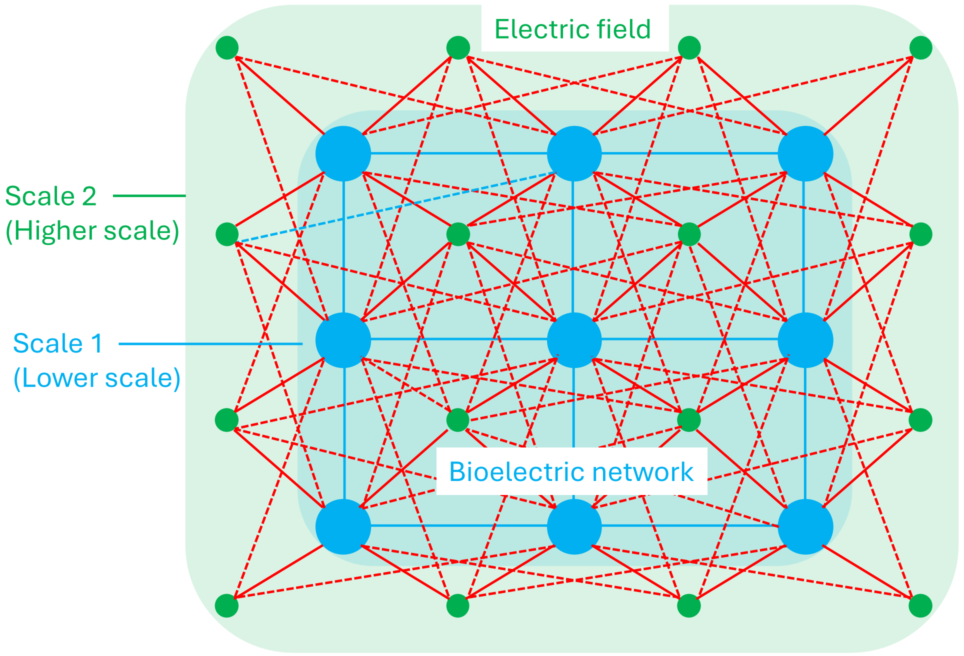
A simple-but-not-simpler modeling approach



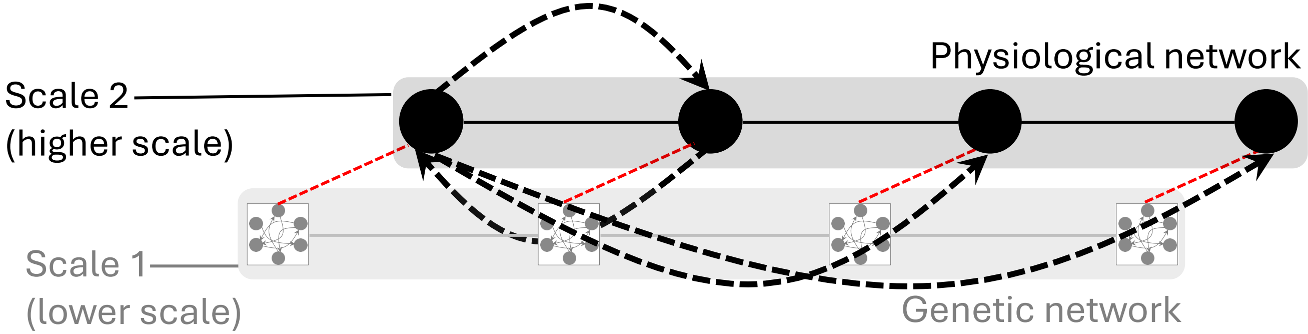
Minimal two-scale models of collective patterning and decision-making



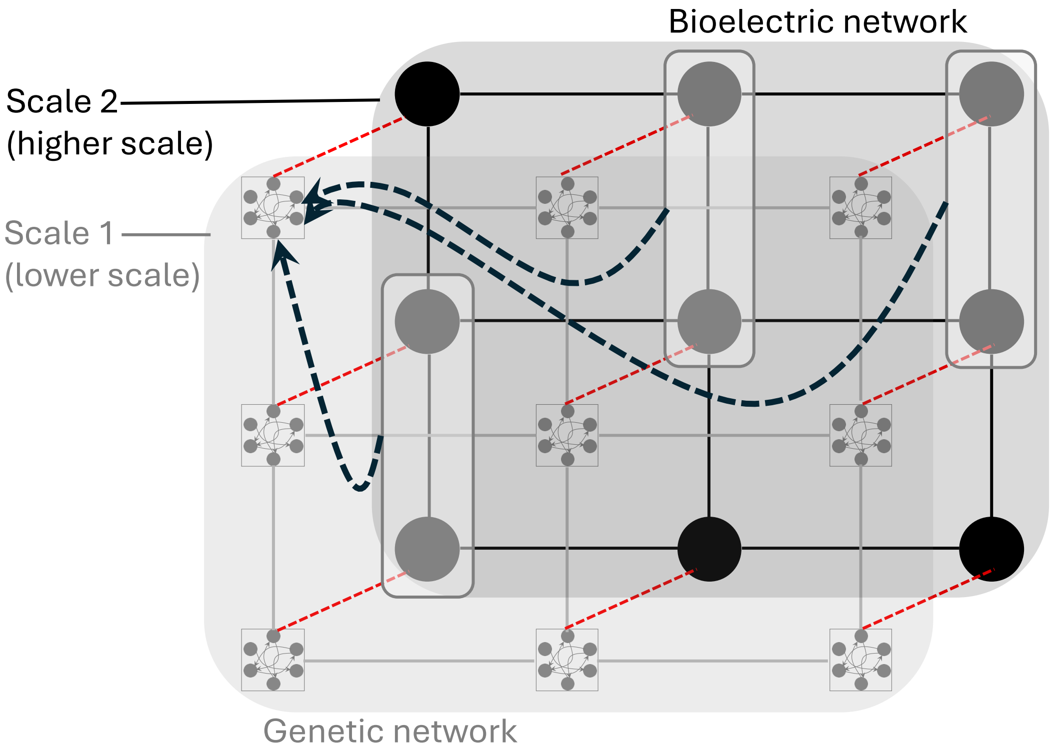


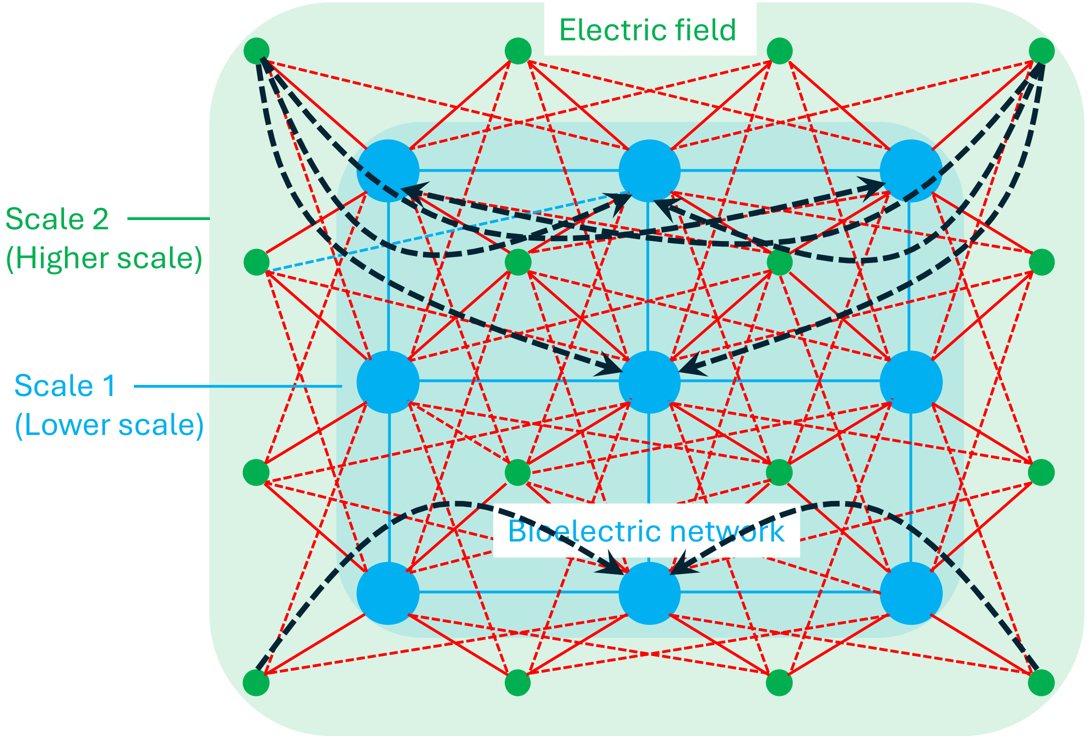


Multiscale collective intelligence = high-level causal influence patterns by which units 'collect' across scales



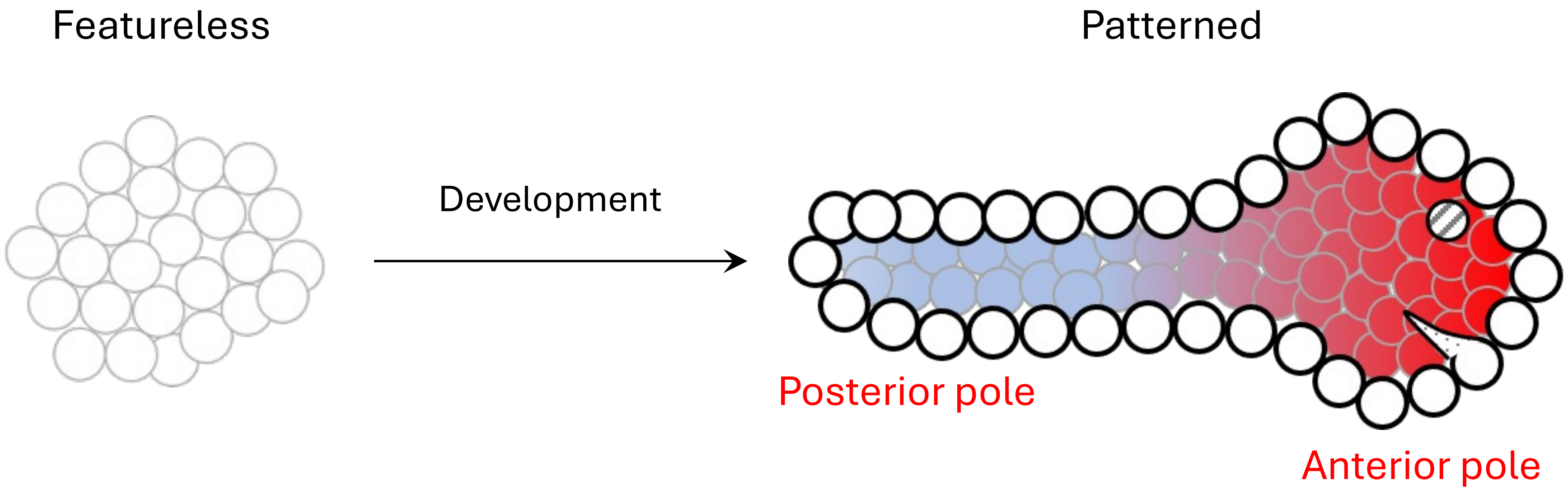
These patterns reflect the collective intelligence strategy that's required to solve a given problem



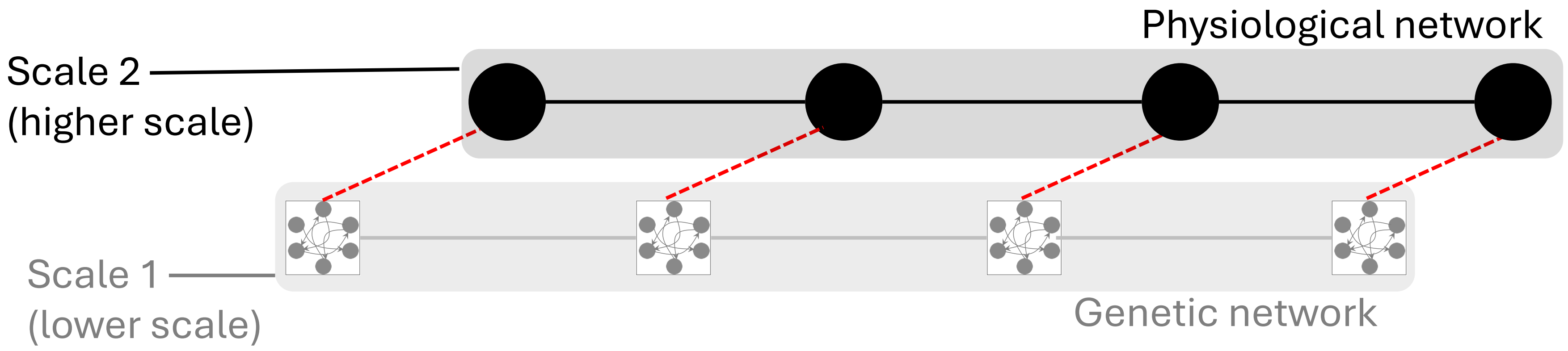


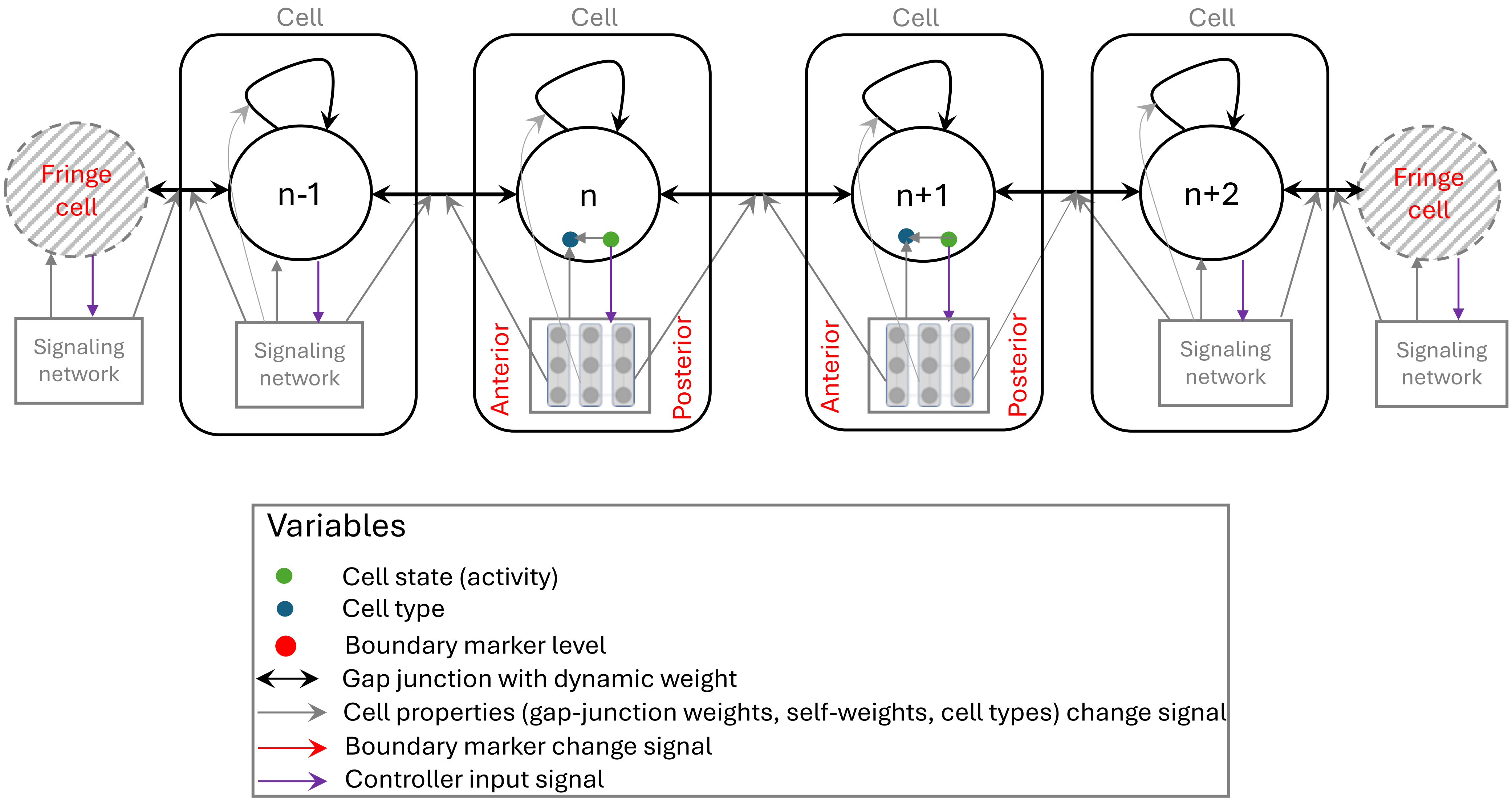
Example 1:
Axial polarity development

How might an embryo develop axial gradients from homogeneous conditions?



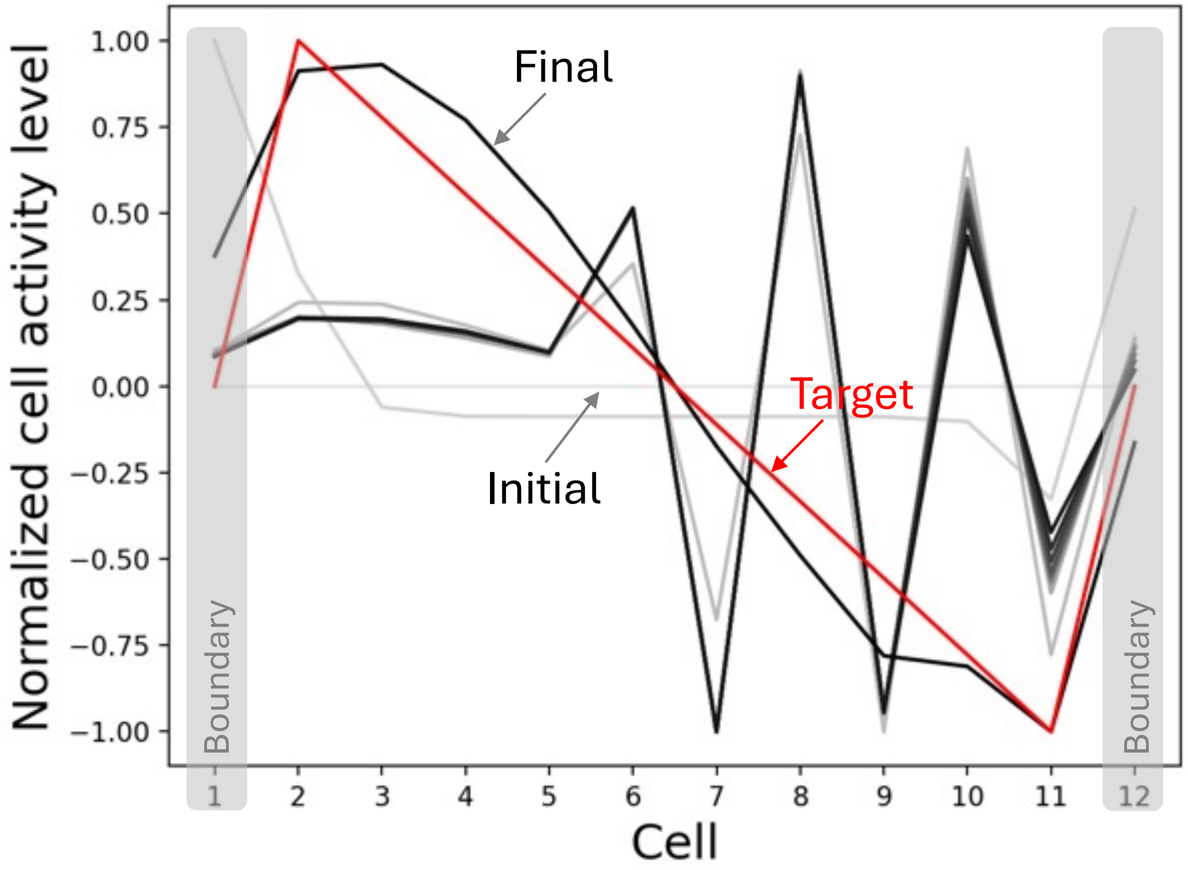
A minimal physiological-genetic network model can demonstrate how simple axial patterns can develop from homogeneous conditions

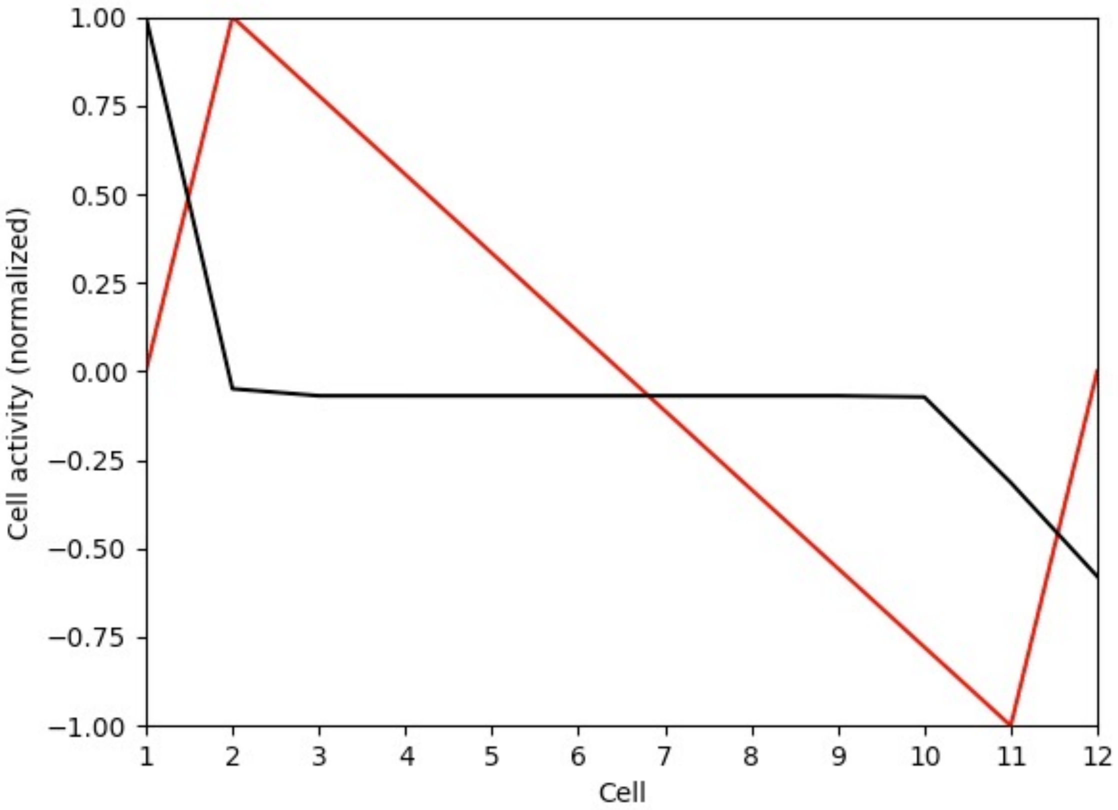




Manicka, S. and M. Levin (2022). "Minimal Developmental Computation: A Causal Network Approach to Understand Morphogenetic Pattern Formation." Entropy **24**(1).

A linear physiological gradient develops from a homogeneous state



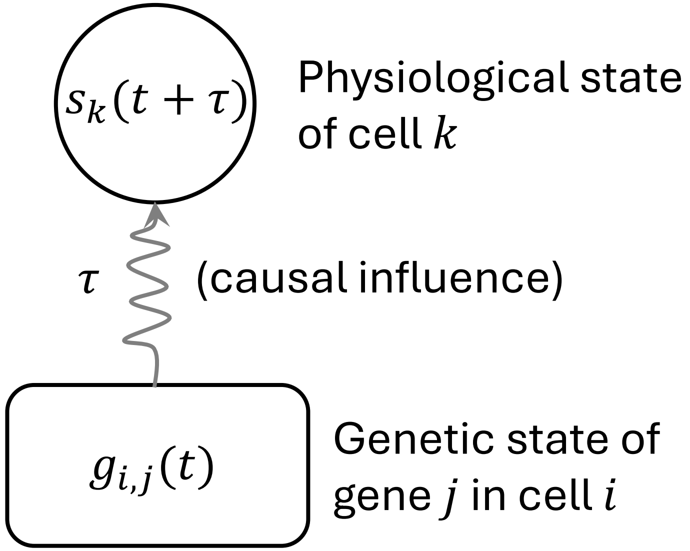


Manicka, S. and M. Levin (2022). "Minimal Developmental Computation: A Causal Network Approach to Understand Morphogenetic Pattern Formation." Entropy **24**(1).

Characterizing collective behavior using spatiotemporal causal influence analysis

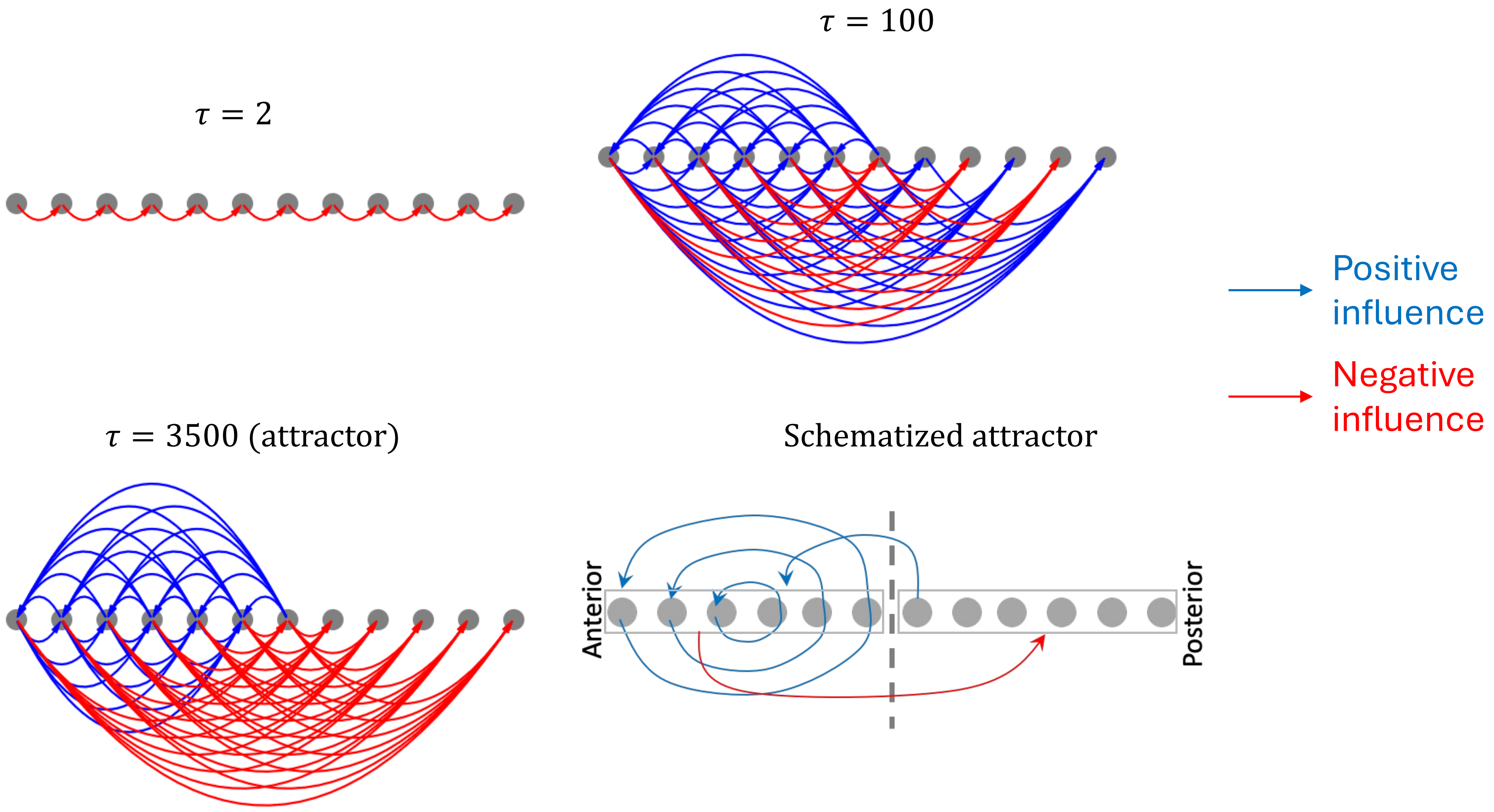
First-order causal influence

$$\left[\frac{\partial s_k(t+\tau)}{\partial g_{i,j}(t)}\right]$$



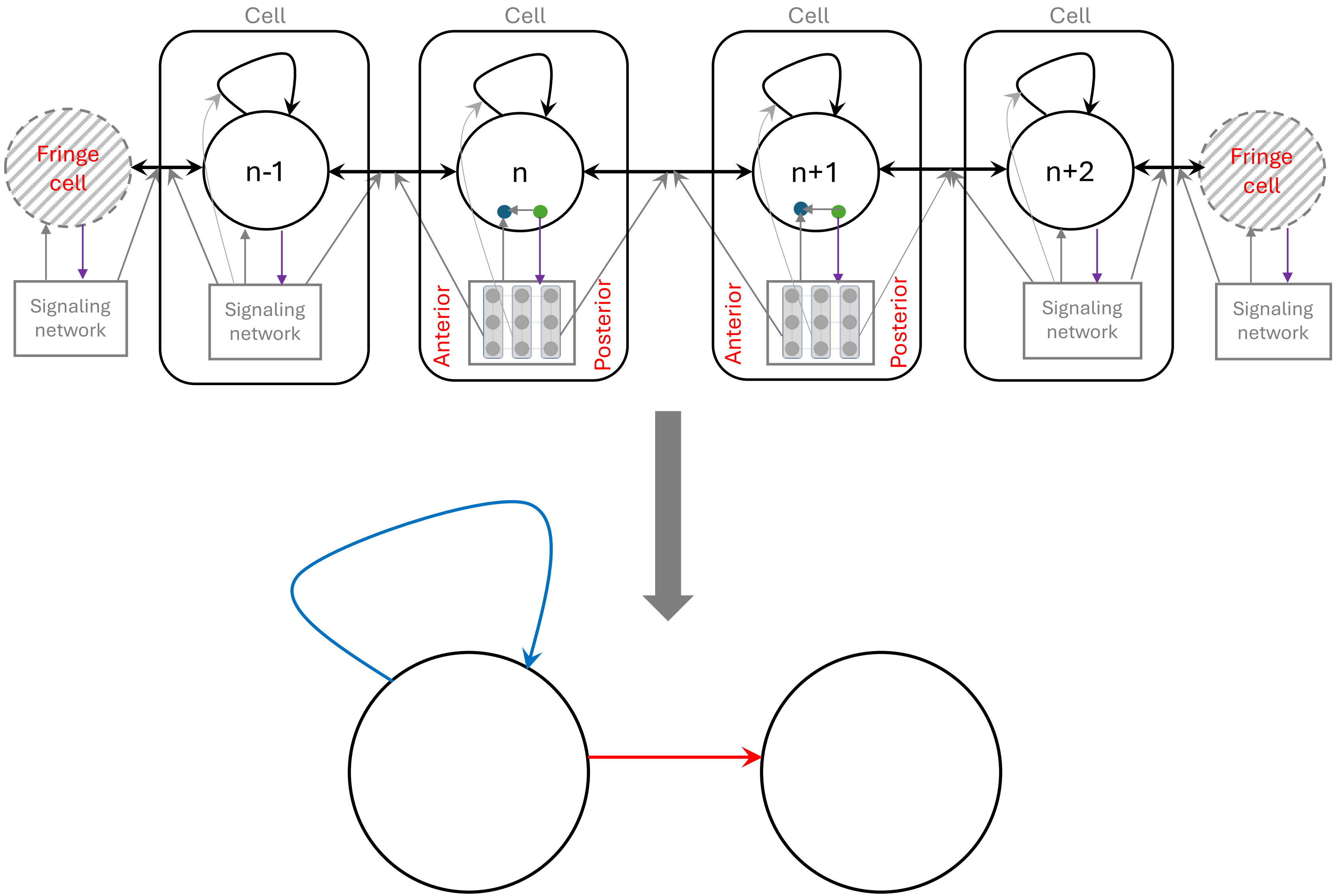
Manicka, S. and M. Levin (2022). "Minimal Developmental Computation: A Causal Network Approach to Understand Morphogenetic Pattern Formation." Entropy **24**(1).

Genetic-physiological causal relations spatially segregate into positive and negative regions over time



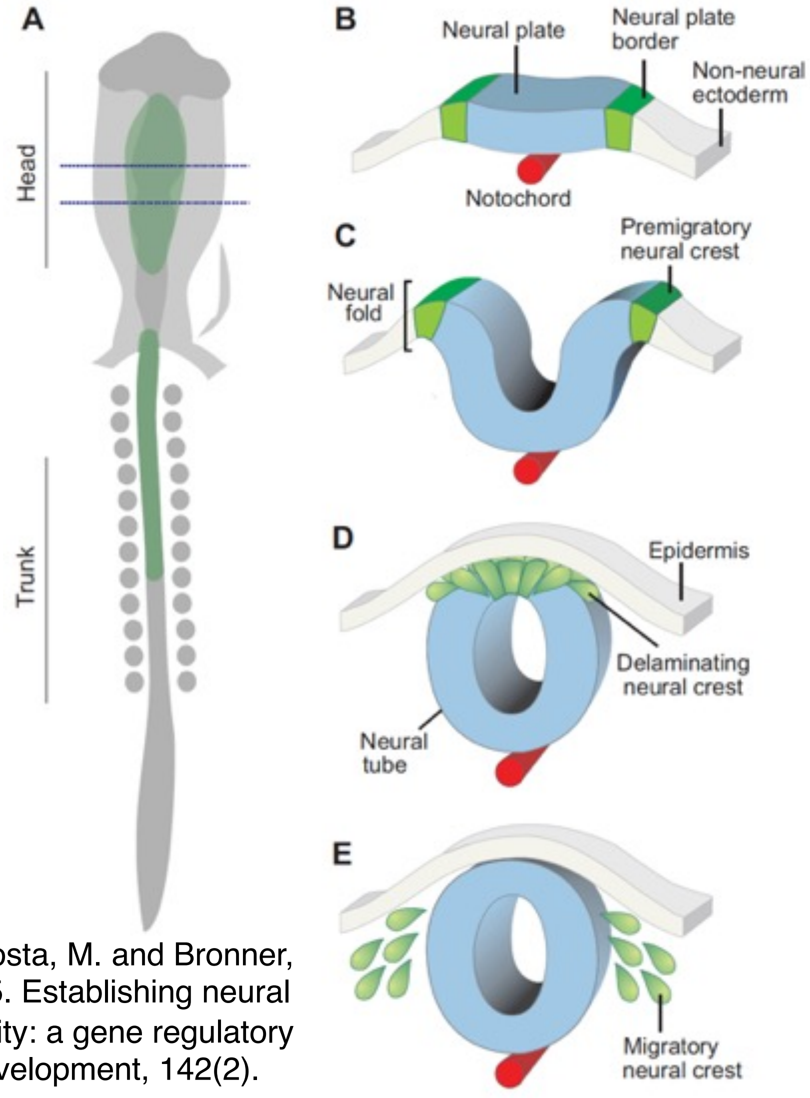
Manicka, S. and M. Levin (2022). "Minimal Developmental Computation: A Causal Network Approach to Understand Morphogenetic Pattern Formation." Entropy **24**(1).

Macroscale pattern of collective behavior

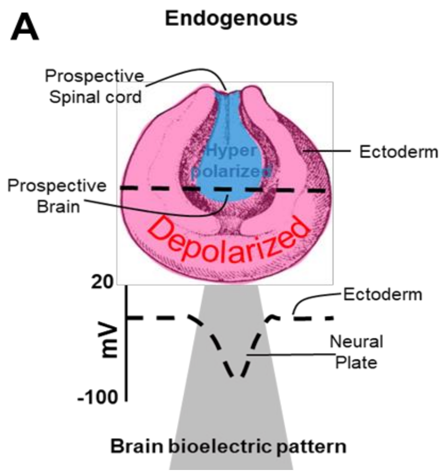


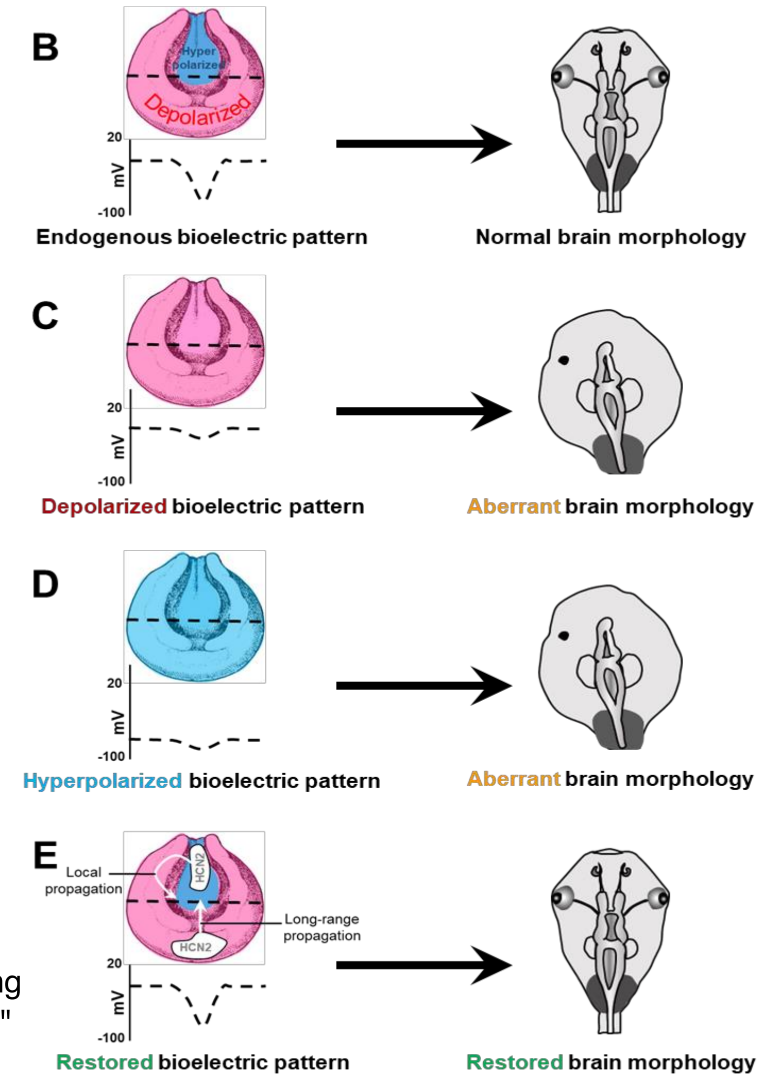
Example 2:
Bioelectric control of morphogenesis

How might bioelectric patterns of the neural plate regulate brain development in frog embryos?



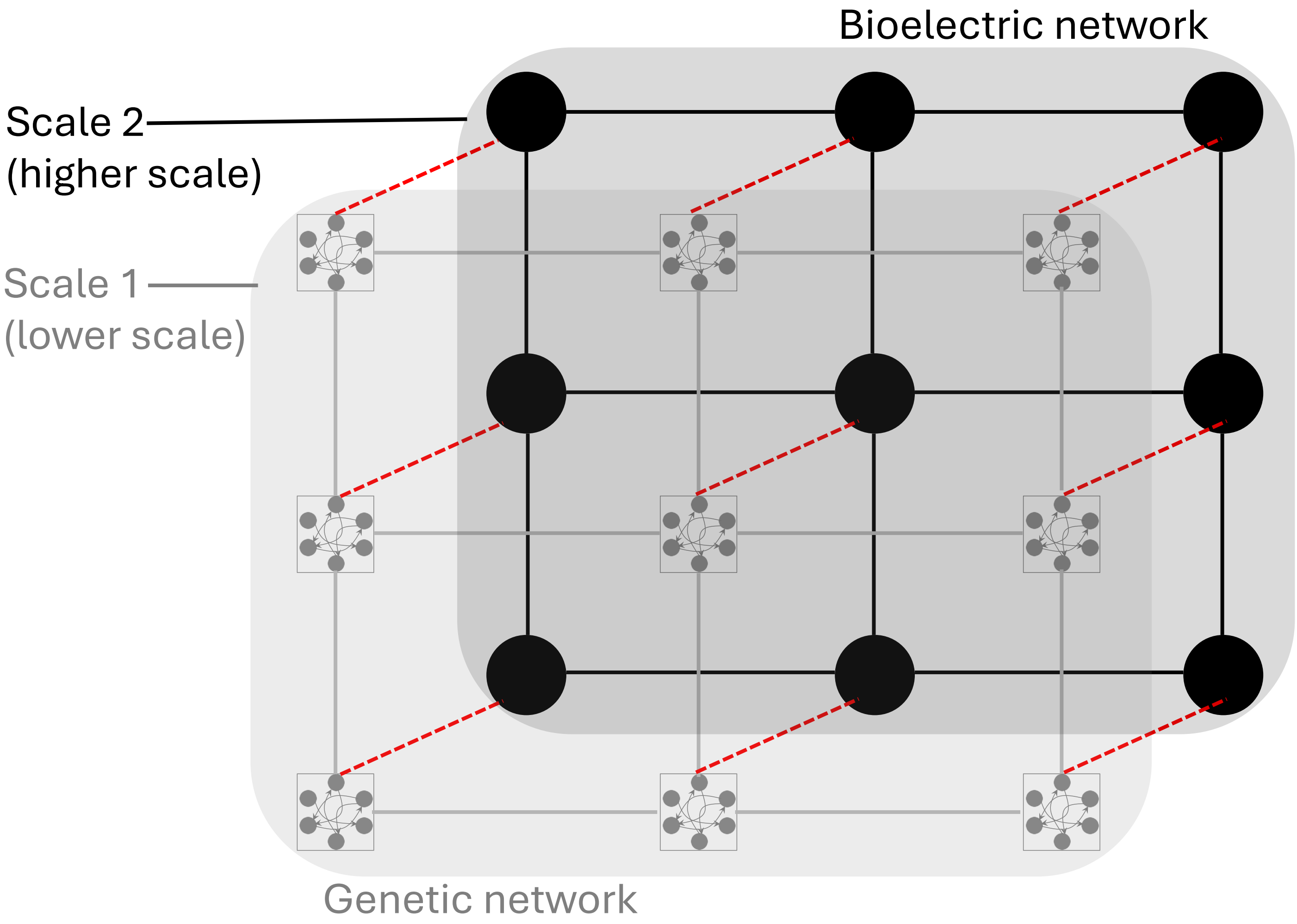
Simões-Costa, M. and Bronner, M.E., 2015. Establishing neural crest identity: a gene regulatory recipe. Development, 142(2).

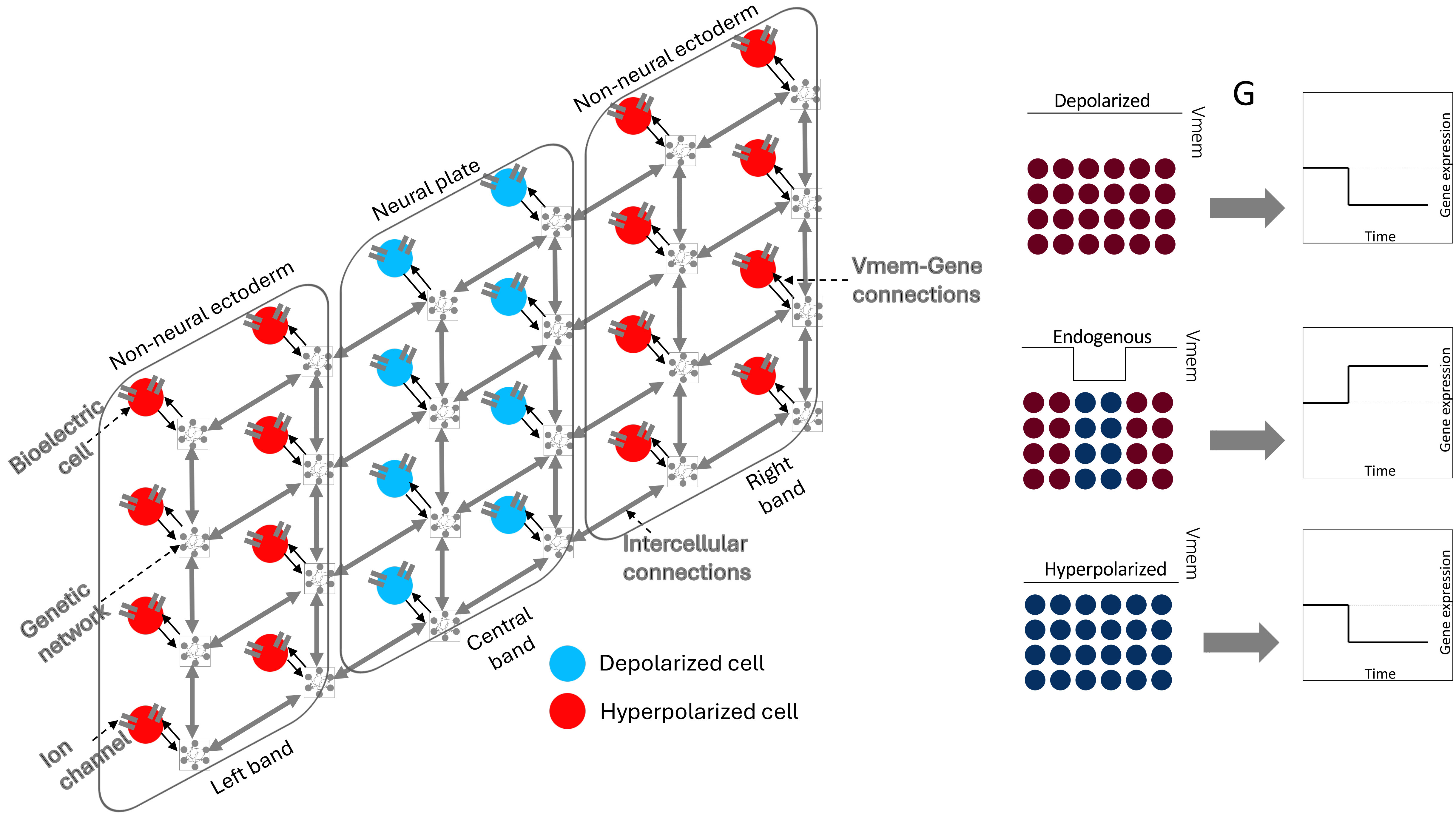




Pai, V. P., et al. (2018). "HCN2 Rescues brain defects by enforcing endogenous voltage pre-patterns." Nat Commun **9**(1): 998.

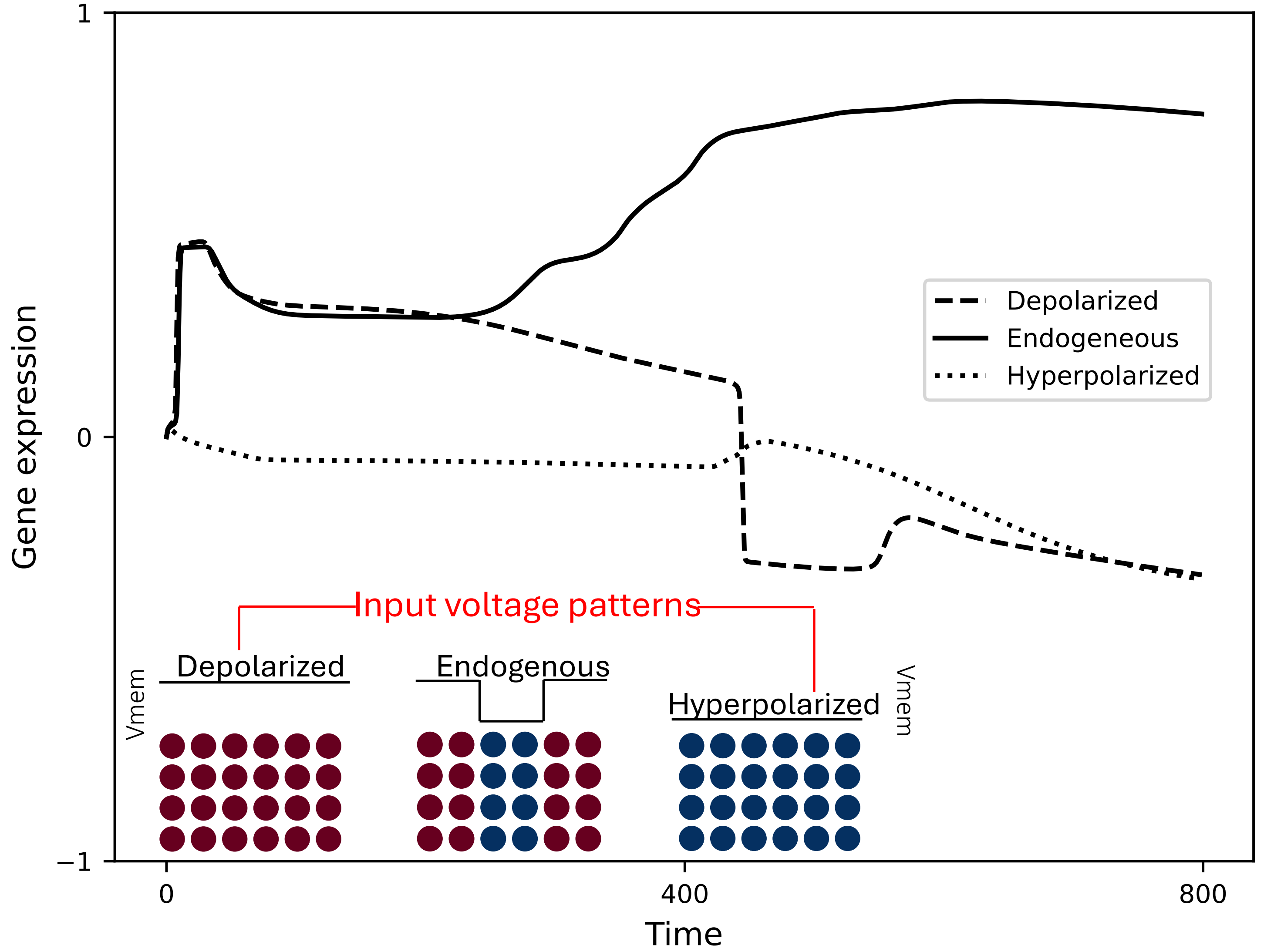
A minimal bioelectric-genetic network model can demonstrate how spatial bioelectric information can be integrated into gene activity





Manicka, S., et al. (2023). "Information integration during bioelectric regulation of morphogenesis of the embryonic frog brain." iScience **26**(12).

Genes activate only for the “correct” (endogenous) bioelectric input patterns

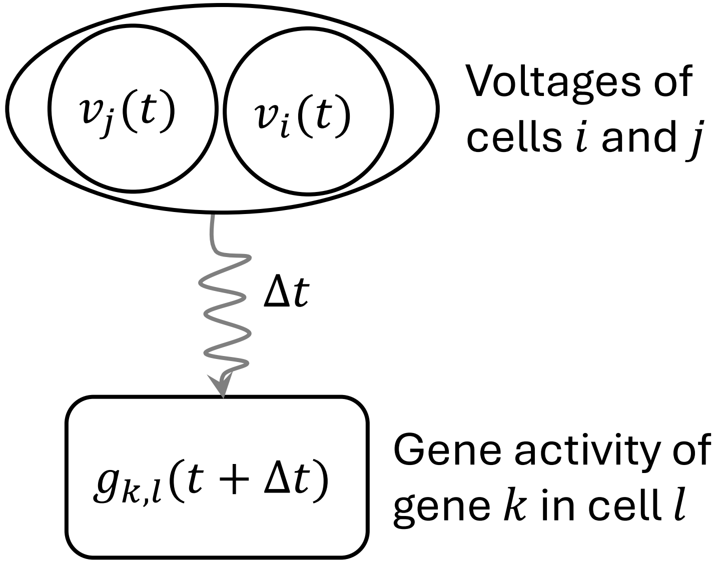


Manicka, S., et al. (2023). "Information integration during bioelectric regulation of morphogenesis of the embryonic frog brain." iScience **26**(12).

Characterizing collective behavior using higher-order spatiotemporal causal influence analysis

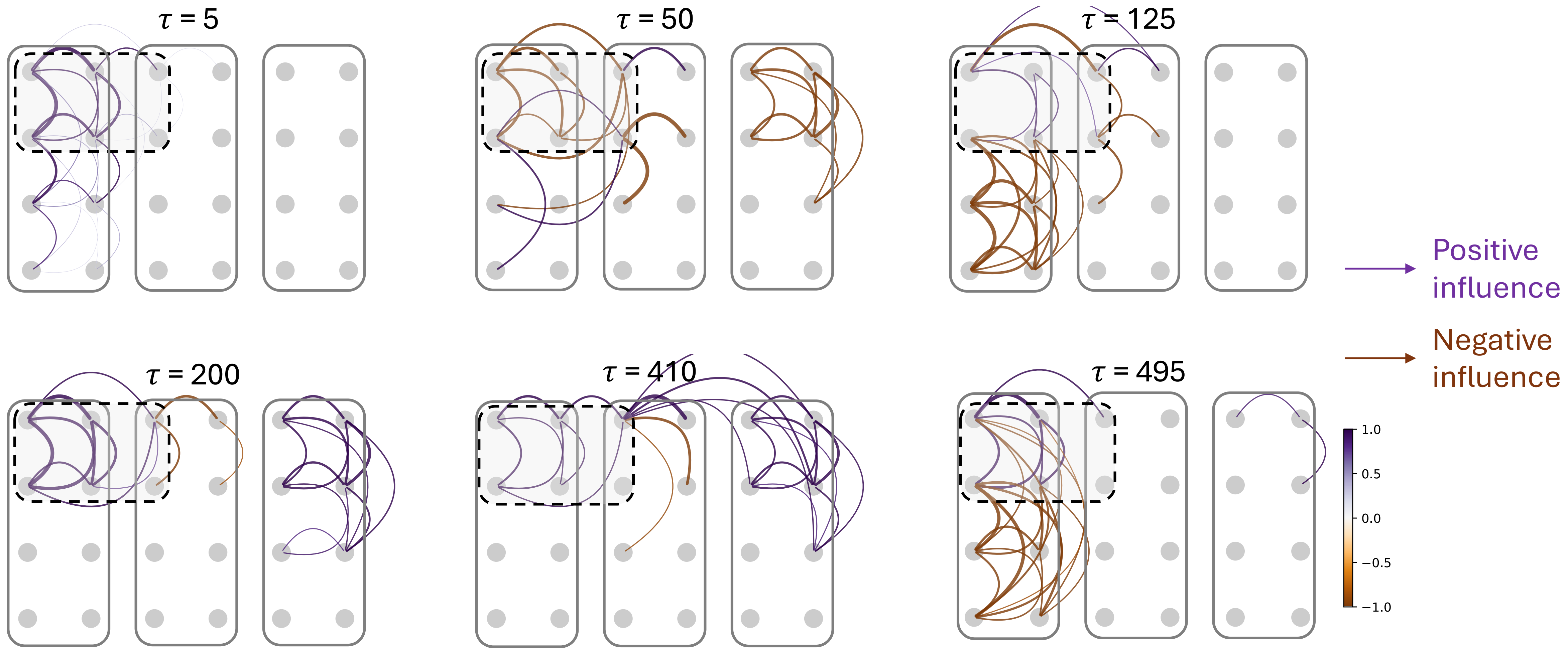
Second-order causal influence

$$\left[\frac{\partial}{\partial V_j(t)}\left(\frac{\partial g_{k,l}(t+\tau)}{\partial V_i(t)}\right)\right]$$



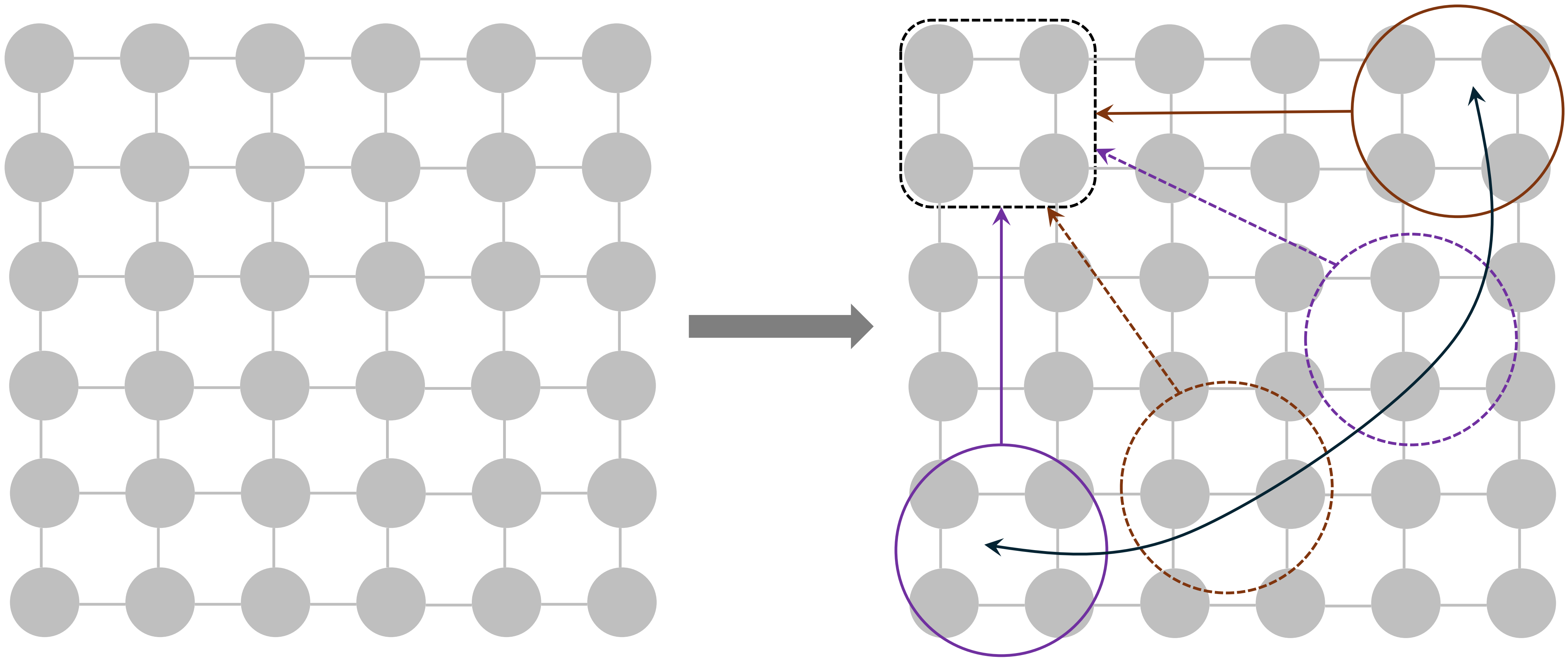
Manicka, S., et al. (2023). "Information integration during bioelectric regulation of morphogenesis of the embryonic frog brain." iScience **26**(12).

Second order bioelectric-genetic causal relations temporally segregate into positive and negative regions across space



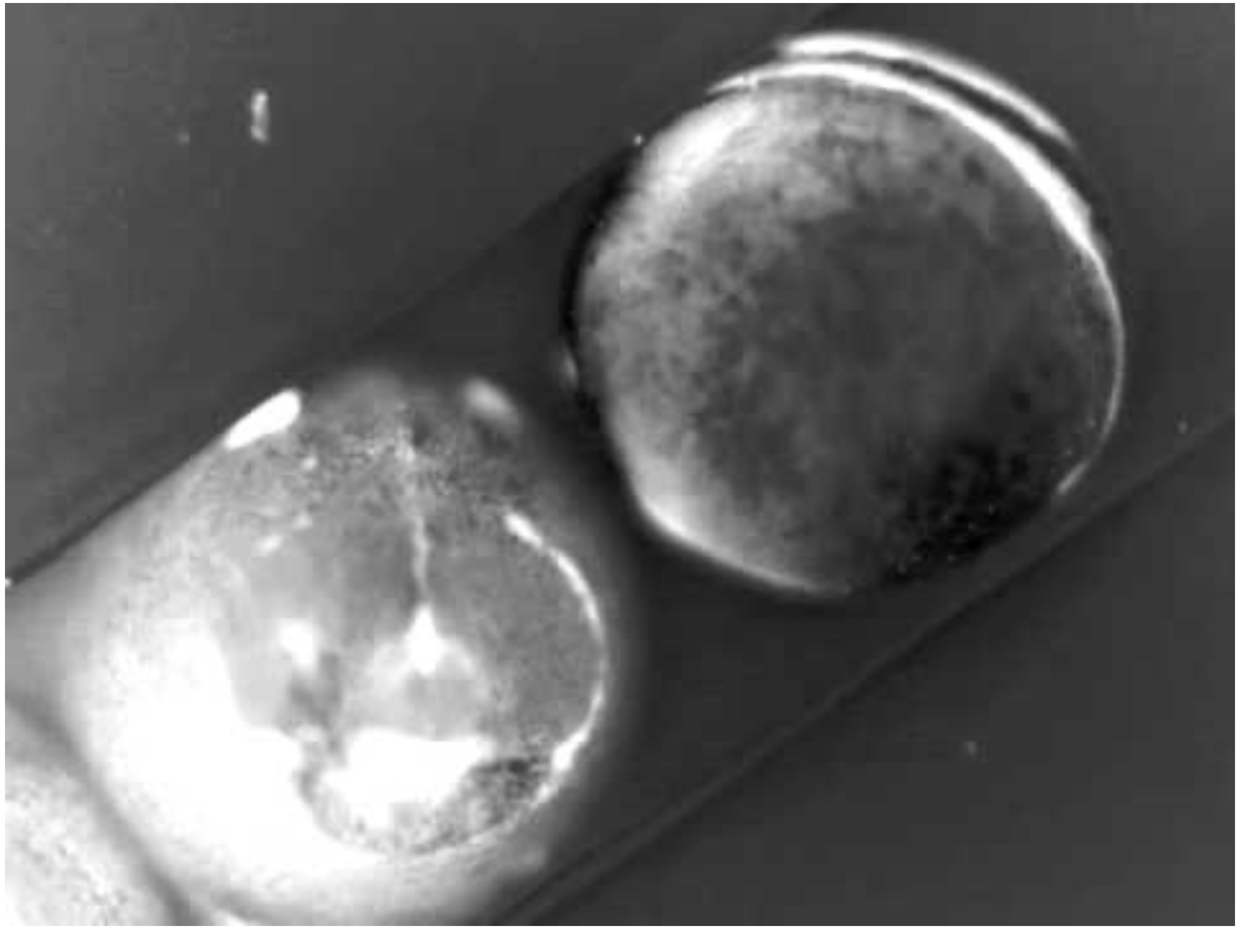
Manicka, S., et al. (2023). "Information integration during bioelectric regulation of morphogenesis of the embryonic frog brain." iScience **26**(12).

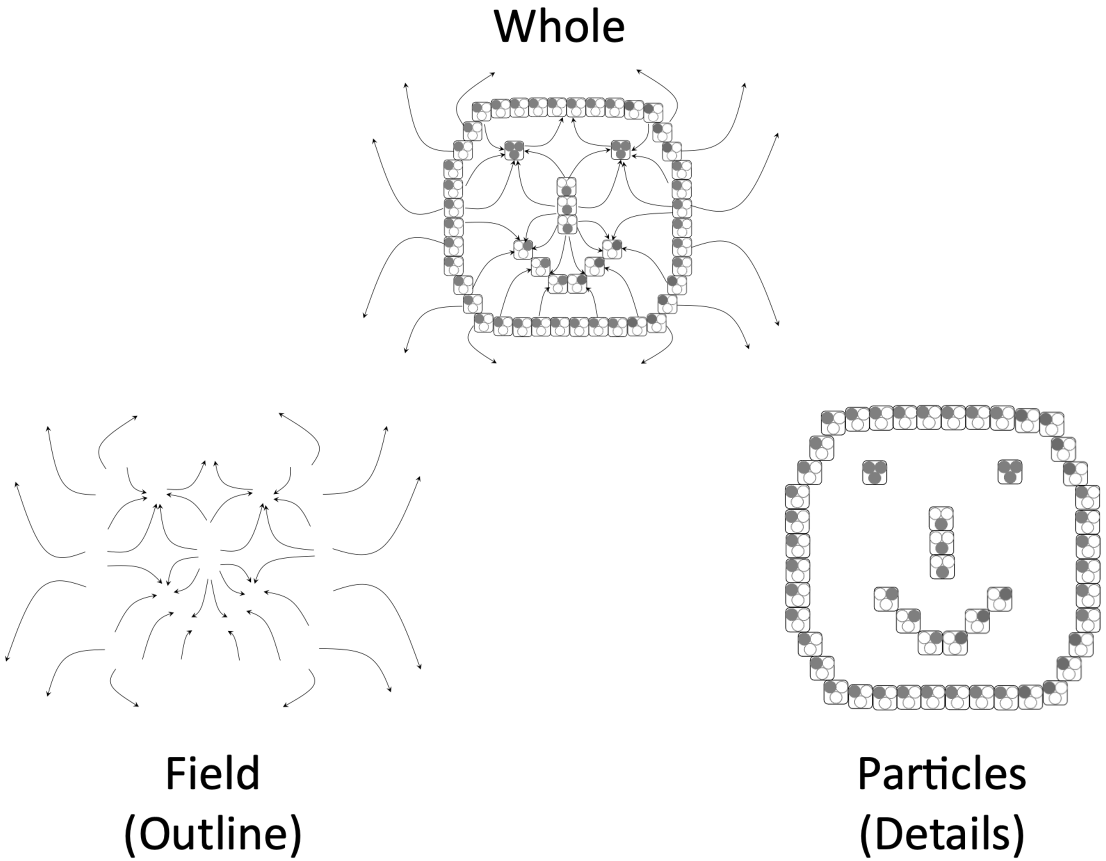
Macroscale pattern of collective behavior



Example 3:
Electric field mediated morphogenesis

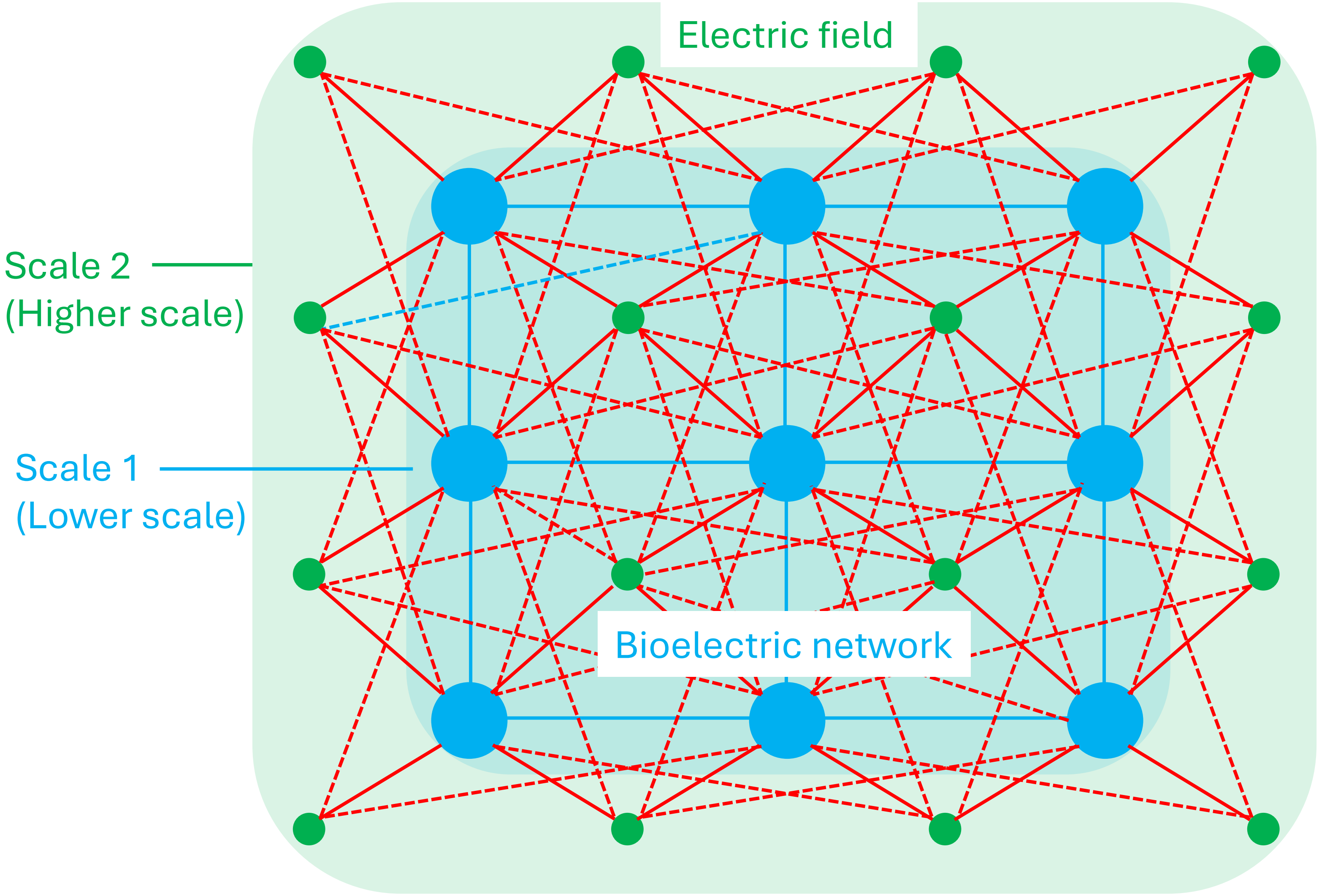
How might electric field mediate the development of bioelectric prepatterns like the vertebral face in embryos?

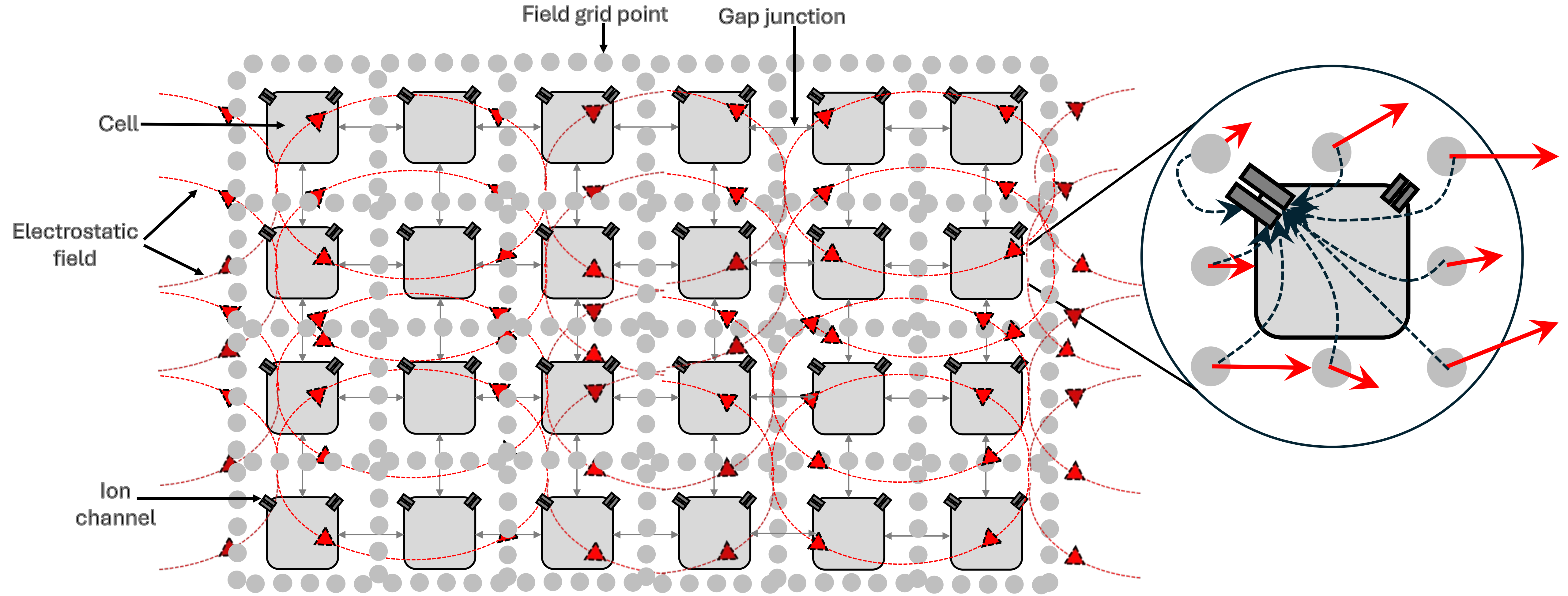




Vandenberg, L. N., et al. (2011). "V-ATPase-dependent ectodermal voltage and pH regionalization are required for craniofacial morphogenesis." Dev Dyn **240**(8): 1889-1904.

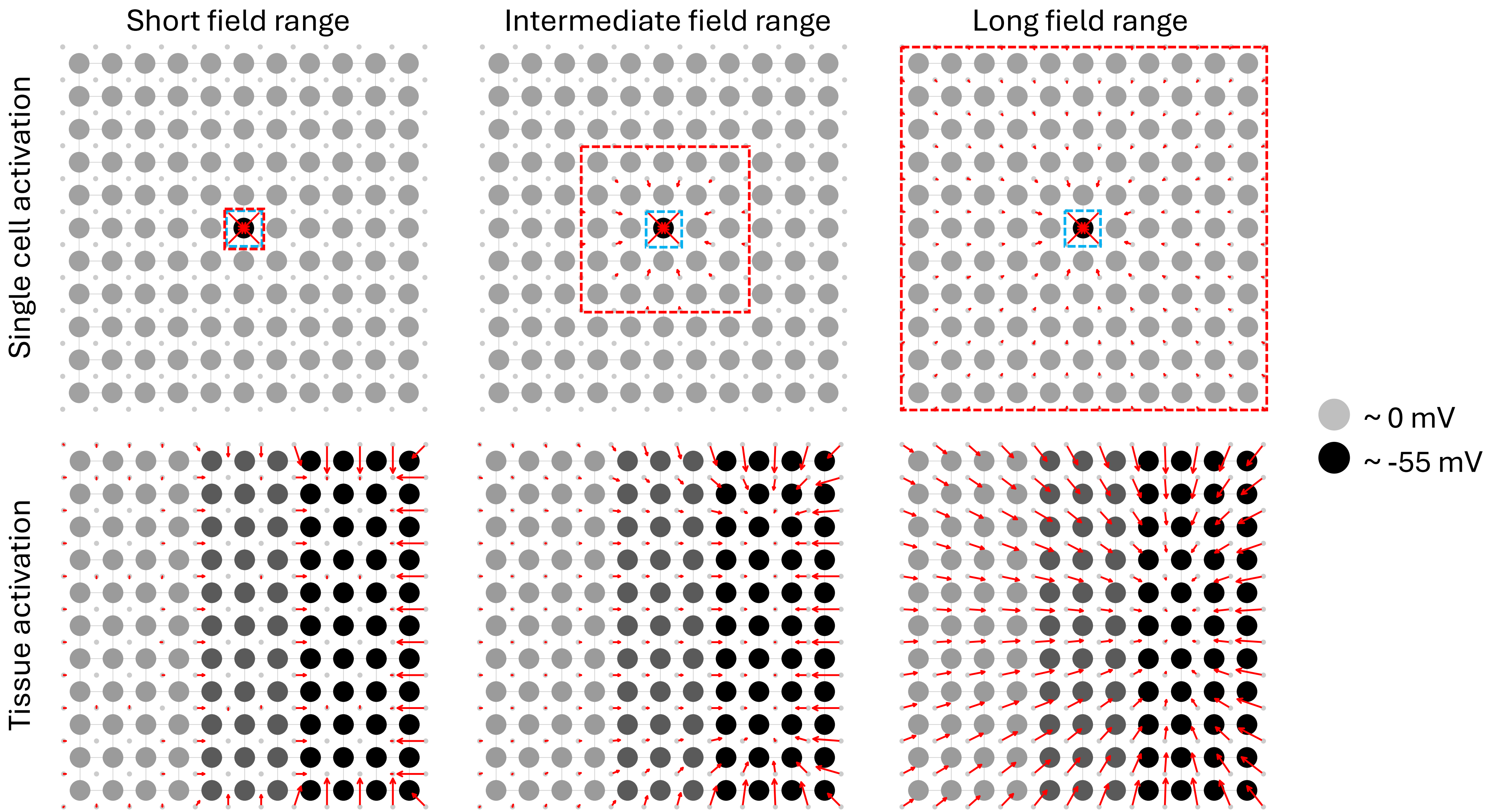
A minimal bioelectric-field network model can demonstrate vertebrate face prepattern development





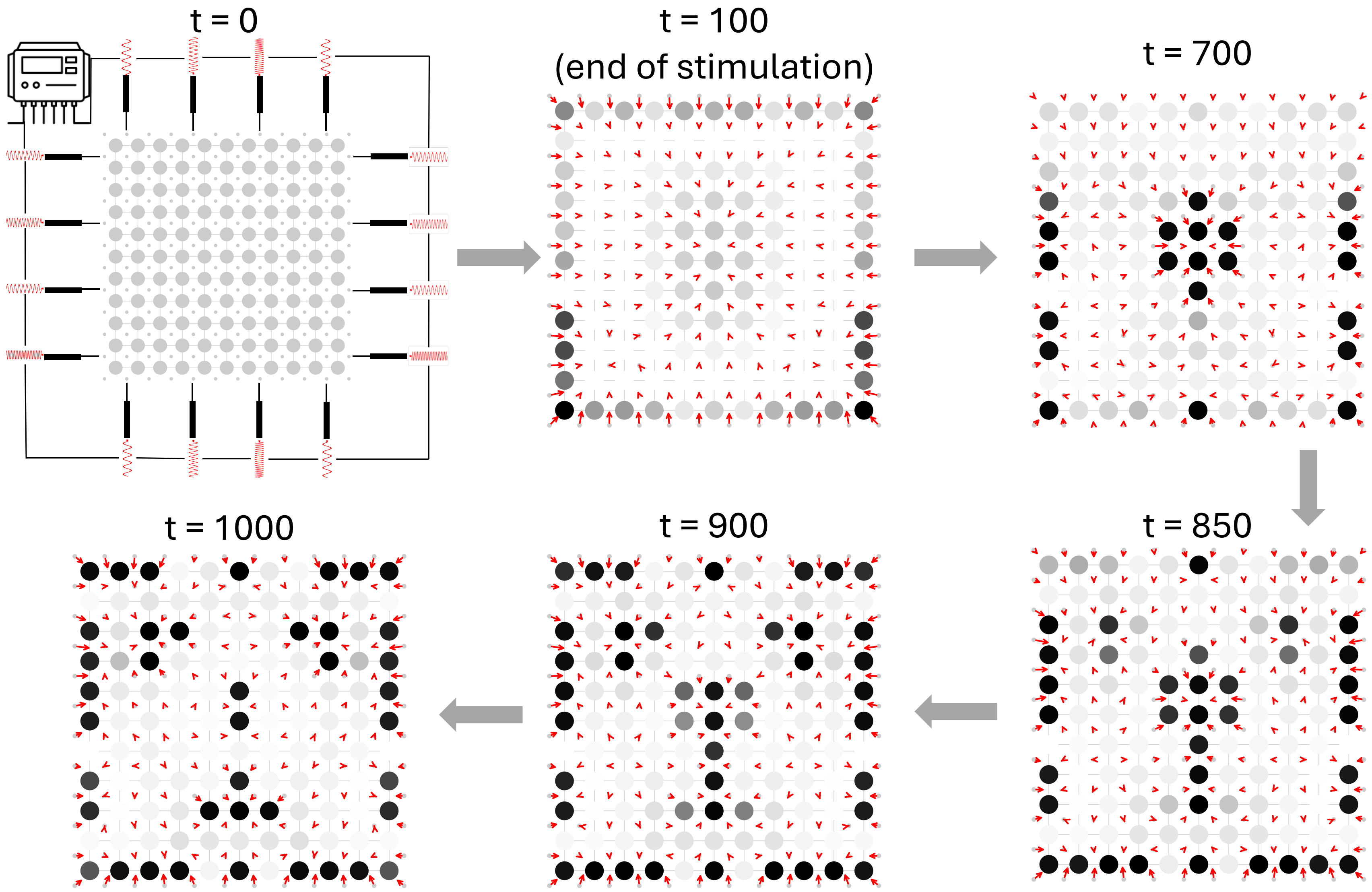
(Manuscript in preparation)

Force field profiles depend on field range and voltage pattern

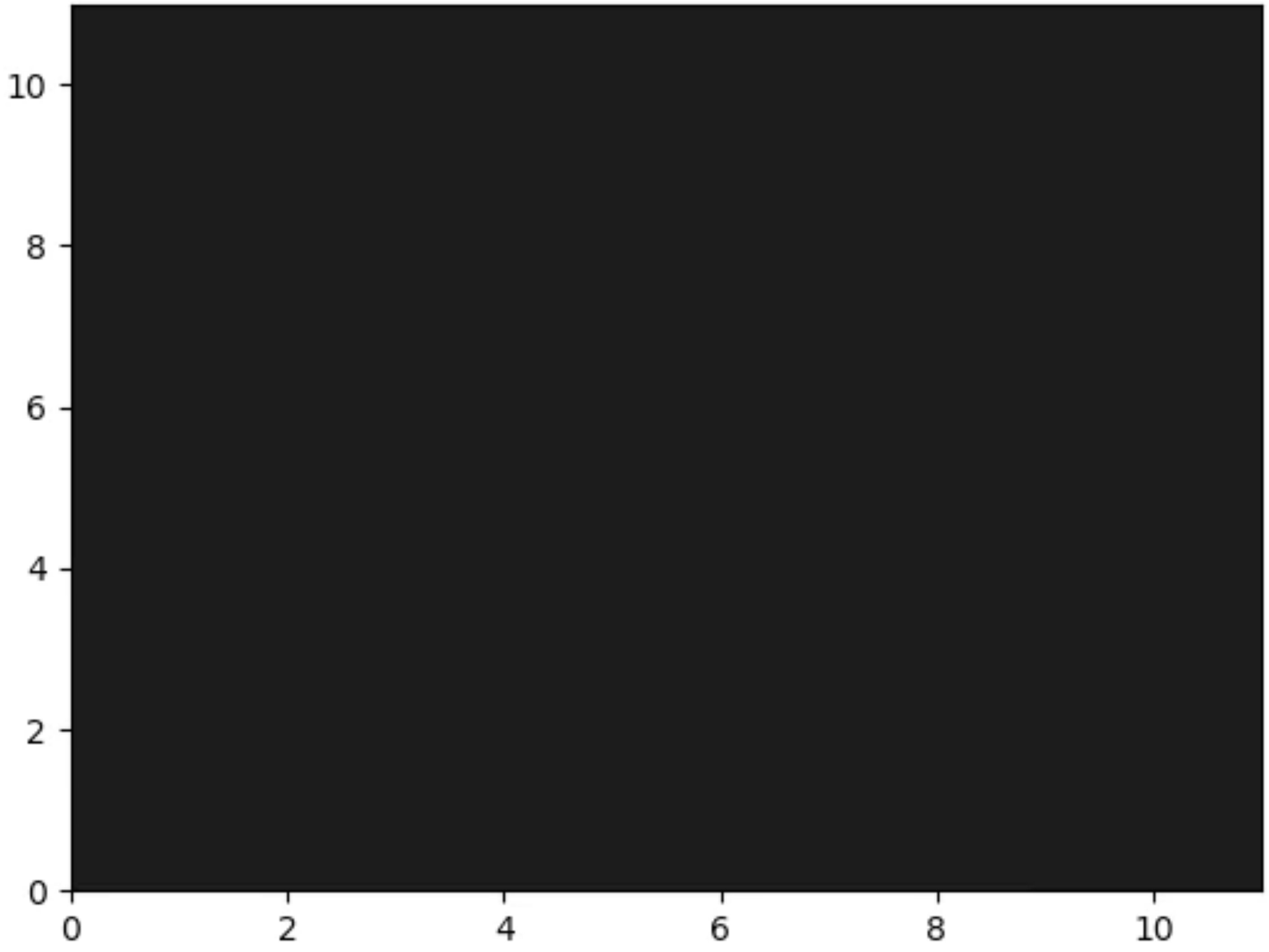


(Manuscript in preparation)

Model develops the face pattern following a transient field stimulation of just the boundary of the tissue



(Manuscript in preparation)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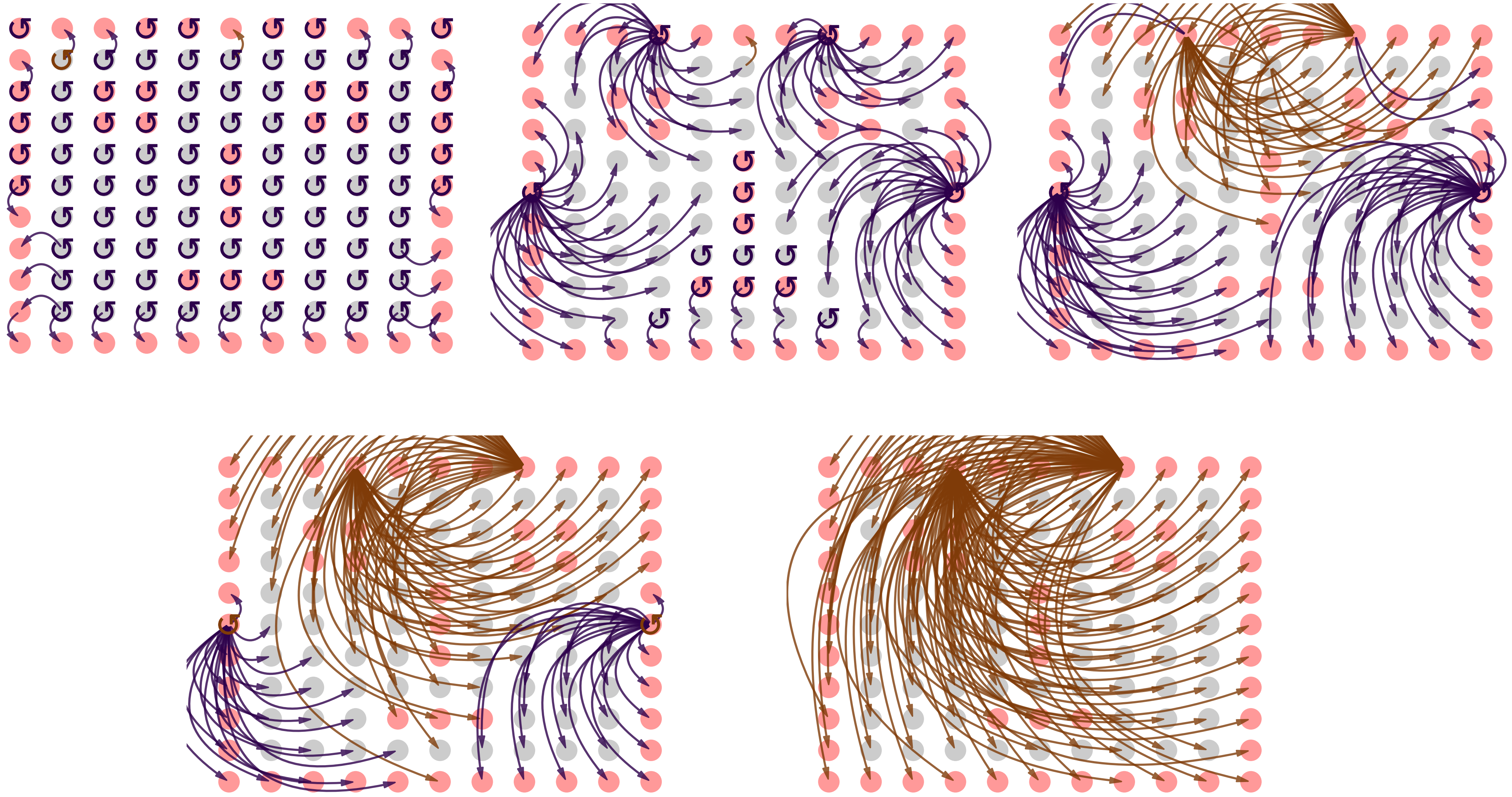
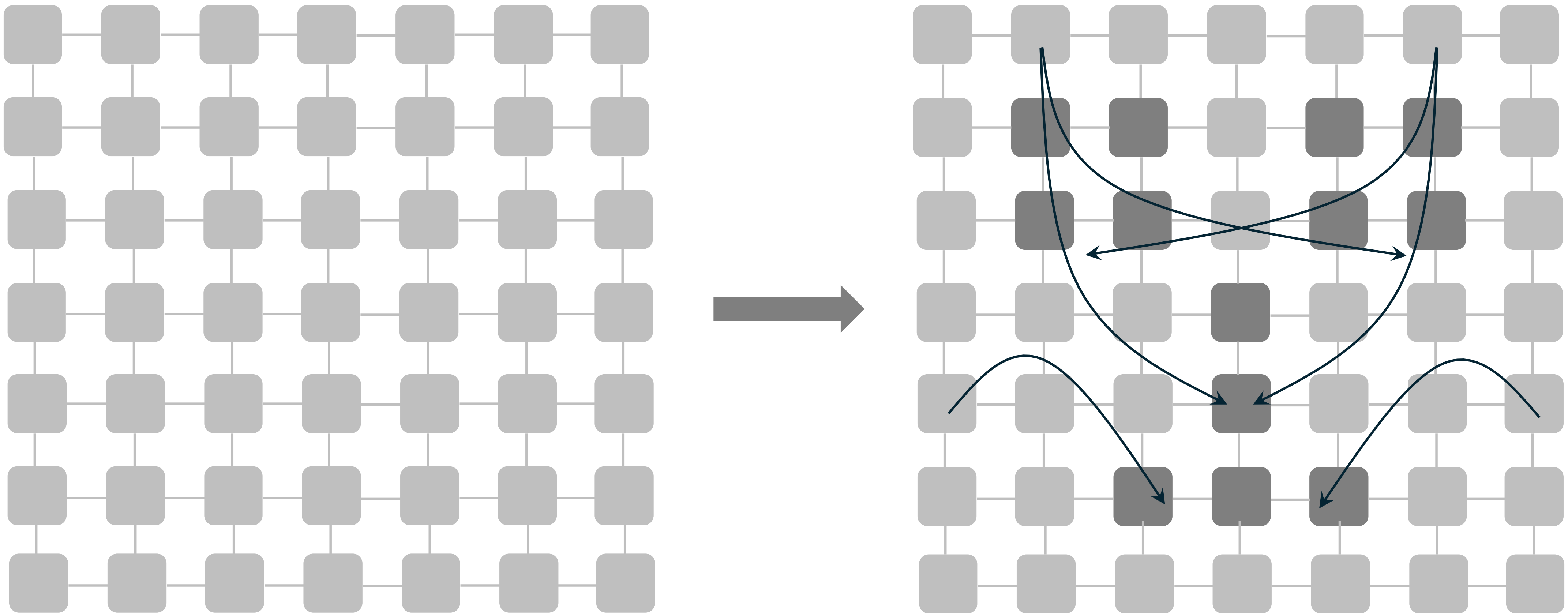
Intercellular causal influence patterns reveals a mechanism where the boundary shepherds patterning of the bulk



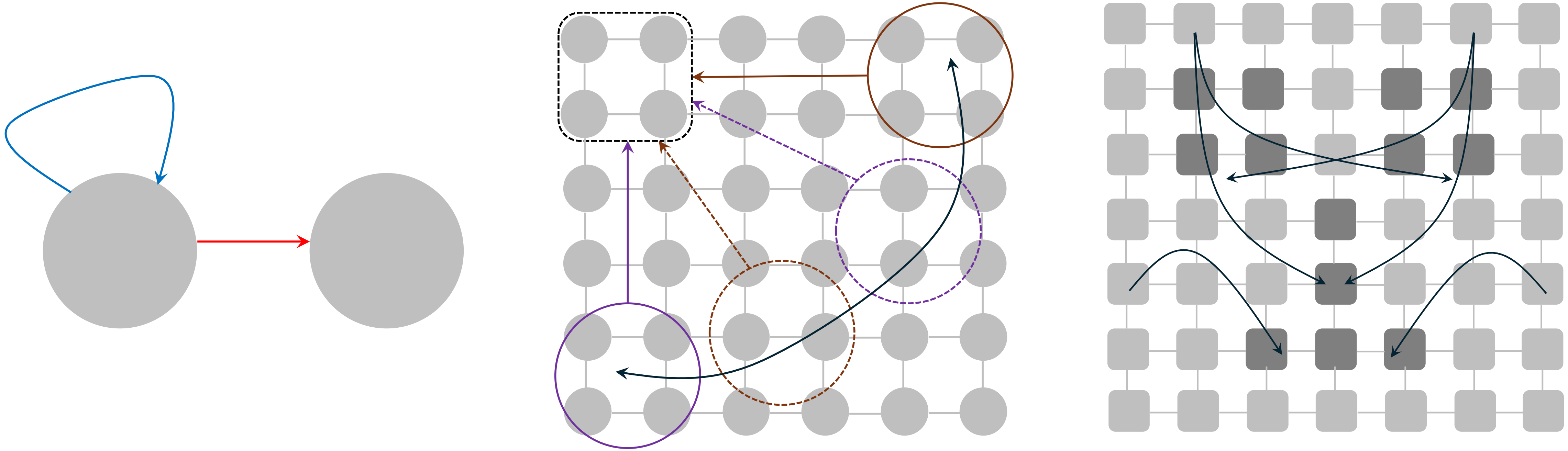
(Manuscript in preparation)

Macroscale pattern of collective behavior



Summary

One way to understand collective behavior is by characterizing the pattern of how the subunits of a collective *causally* integrate and segregate across spatiotemporal scales



But…

- The structure of the causal influence network depends on the state of the underlying network, so can only be interpreted for a specific simulation
- Expensive to compute, so unscalable (in its current form)

Acknowledgements

Emerald Gate

Vaibhav Pai

Michael Levin