

Research Article

Non-Equilibrium Bioenergetic Information Routing and Signal-to-Noise Ratio Optimization in Ischemic Endothelial Repair: A Clinical Framework for Microvascular Recovery

Dr. Julien Boblique

Independent Researcher, Science 4.0 Framework, France

***Corresponding author**

Dr. Julien Boblique, Independent Researcher, Science 4.0 Framework, France

Received: 20 August 2026

Accepted: 28 August 2026

Published: 21 September 2026

Copyright

© 2026 Dr. Julien Boblique

OPEN ACCESS

Abstract

Microvascular ischemia and reperfusion injuries remain severe clinical bottlenecks due to the collapse of endothelial metabolic fidelity and localized signal-to-noise ratio (SNR) degradation [1, 2]. Under sustained metabolic hypoxia, the functional uncoupling of mitochondrial-endoplasmic reticulum contact sites (MAMs) precipitates thermodynamic decoherence, excessive free-radical generation, and uncoordinated enzymatic cascades [1, 7]. We present a non-equilibrium biophysical and information-theoretic framework for microvascular recovery. By modeling endothelial repair cascades through coupled non-equilibrium thermodynamic flux equations and Shannon channel capacity constraints [4, 7], we quantify the minimum bioenergetic SNR required to restore a quiescent, laminar endothelial phenotype and prevent irreversible microvascular rarefaction [3, 5]. Our analytical formulations demonstrate that stabilizing intracellular bioenergetic routing accelerates the transition from stochastic oxidative damage to coherent regenerative signaling [5, 8]. Integrating Science 4.0 principles of cellular information routing provides clinical medicine with a predictive metric to assess microvascular resilience, optimize targeted metabolic interventions, and reverse capillary stasis in acute and chronic ischemic pathologies [8, 9, 10].

Keywords: Microvascular Ischemia, Signal-to-Noise Ratio (SNR), Endothelial Repair, Non-Equilibrium Thermodynamics, Bioenergetics, Science 4.0, Information Routing, Microangiopathy

INTRODUCTION: THE BIOPHYSICAL DIMENSION OF ISCHEMIC MICROVASCULAR FAILURE

Microvascular dysfunction represents the shared pathophysiological denominator across diverse critical medical conditions, including acute ischemic stroke, myocardial infarction, diabetic microangiopathy, and sepsis-induced multi-organ failure [1, 2]. While macrovascular revascularization protocols (such as percutaneous coronary intervention and mechanical thrombectomy) have achieved high clinical maturity, tissue recovery is frequently impeded by the « no-reflow » phenomenon, capillary stasis, and progressive microvascular rarefaction [2, 3].

From a biophysical systems engineering standpoint, the microvascular endothelial interface functions not merely as a passive conduit for red blood cells, but as an active, dissipative information processor [4, 5]. Endothelial cells continuously sense, transduce, and integrate mechanical wall shear stress, local substrate availability, and bioelectric potentials into coordinated downstream transcriptomic and enzymatic responses [5, 6]. Under ischemic stress, this processing architecture collapses: substrate depletion uncouples mitochondrial electron transfer, internal entropy production rises steeply, and signal fidelity degrades into destructive stochastic noise [1, 7]. Conventional clinical pharmacology primarily targets isolated receptors; however, restoring microvascular competence necessitates addressing the fundamental non-equilibrium thermodynamic constraints governing cellular repair cascades [7, 8, 9].

THEORETICAL FORMULATION: NON-EQUILIBRIUM THERMODYNAMIC ROUTING

Living cellular interfaces are open dissipative structures maintained far

from thermodynamic equilibrium by continuous energy dissipation [7, 8]. The local rate of entropy production per unit volume, σ_{ent} , within an ischemic endothelial cell is governed by the summation of conjugate thermodynamic forces and fluxes:

$$\sigma_{\text{ent}} = J_{\text{ATP}} \cdot (A_{\text{ATP}} / T) + \sum_k [J_k \cdot (-\nabla \mu_k / T)] + \Pi : (\nabla v / T) \geq 0$$

Where:

- J_{ATP} and A_{ATP} denote the reaction rate and chemical affinity of ATP hydrolysis.
- J_k and $\nabla \mu_k$ represent the diffusion flux and chemical potential gradient of metabolic substrates (e.g., glucose, pyruvate, fatty acids).
- Π and ∇v are the internal viscous stress tensor and velocity gradient within the cytoplasm.
- T represents the absolute physiological temperature (310.15 K).

Under physiological conditions, the cell maximizes coherent metabolic work while minimizing dissipative entropy production [7]. During acute ischemia, the chemical affinity A_{ATP} drops towards zero, forcing σ_{ent} into an unregulated regime characterized by calcium overload, mitochondrial permeability transition pore (mPTP) opening, and massive generation of reactive oxygen species (ROS) [1, 2].

MATHEMATICAL MODELING OF CELLULAR SIGNAL-TO-NOISE RATIO (SNR)

In the Science 4.0 framework, intracellular biochemical cascades are for-

malized as communication channels transmitting regulatory instructions across noisy biophysical media [4, 5, 8]. The cellular bioenergetic Signal-to-Noise Ratio (SNR_{bio}) is defined as:

$$SNR_{bio} = S_{coherent} / (N_{thermodynamic} + N_{oxidative})$$

Where:

- **S_{coherent}** = κ · [ATP] · Φ_{kin} represents the coherent signaling power driven by structured kinase activity (e.g., eNOS Ser1177 phosphorylation, VEGF-R2 activation, AMPK-dependent transcription) [5, 6].
- **N_{thermodynamic}** = k_B · T · Δf represents the baseline thermal noise within the effective metabolic bandwidth Δf.
- **N_{oxidative}** = ξ · [ROS]_{cyt} represents the disruptive noise power generated by uncoupled oxidative cascades [1, 8].

The maximum reliable information transmission rate (Shannon channel capacity, C) through the endothelial repair network is given by [4, 5]:

$$C = B \cdot \log_2 [1 + S_{coherent} / (k_B \cdot T \cdot \Delta f + \xi \cdot [ROS]_{cyt})]$$

When ischemia elevates [ROS]_{cyt} while depleting [ATP], SNR_{bio} drops below a critical threshold SNR_{crit}. Under this condition, channel capacity collapses (C → 0), receptor-ligand interactions lose statistical fidelity, and the cell is driven toward caspase-dependent apoptotic execution [1, 7].

Table 1: Biophysical and Information-Theoretic Parameters for Endothelial Bioenergetic Networks

Parameter	Symbol	Physiological Baseline	Ischemic / Failure Regime	Physical Dimension / Unit
Absolute Temperature	T	310.15	310.15	K
Cytosolic ATP Concentration	[ATP] _{cyt}	4.5 – 5.5	< 0.8	mM
Cytosolic ROS Concentration	[ROS] _{cyt}	1.0 – 5.0	> 50.0	nM
ATP Hydrolysis Affinity	A _{ATP}	50 – 55	< 25	kJ · mol ⁻¹
Signaling Bandwidth	Δf	0.1 – 10.0	< 0.01	Hz
Bioenergetic SNR	SNR _{bio}	15.0 – 25.0	< 1.2	dB
Critical Failure Threshold	SNR _{crit}	3.0	3.0	dB
Shannon Channel Capacity	C	12.0 – 18.0	< 1.5	bits · s ⁻¹

RESTORATION DYNAMICS: OVERCOMING THE NO-REFLOW BOTTLENECK

Sequence of Pathological Collapse vs. Bioenergetic Recovery:

1. **Acute Ischemic Injury:** Hypoxia initiates mitochondrial decoupling and rapid ATP depletion.
2. **Noise Amplification:** Excessive ROS production drives N_{oxidative}

>> S_{coherent}.

3. **Channel Capacity Collapse:** C → 0 causes loss of junctional fidelity and microvascular gap formation.
4. **Science 4.0 Bioenergetic Rescue:** Targeted substrate re-vectorization dynamically quenches oxidative noise.
5. **SNR Restoration:** Re-establishing SNR_{bio} > SNR_{crit} triggers VE-Cadherin / Claudin-5 re-assembly and eNOS activation.
6. **Functional Reperfusion:** Microvascular perfusion and structural integrity are restored.

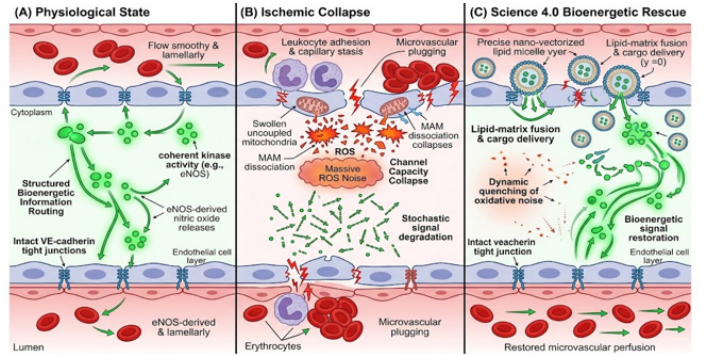


Figure 1: Non-equilibrium bioenergetic information routing and channel capacity collapse during microvascular ischemia and recovery.

- (A) **Physiological State:** High metabolic affinity and intact mitochondrial-ER contact sites maintain robust kinase signaling (S_{coherent}) and suppress oxidative noise, preserving channel capacity (C) and junctional integrity (VE-Cadherin/Claudin-5).
- (B) **Ischemic Collapse:** Substrate starvation triggers mitochondrial decoupling and massive ROS surges (N_{oxidative}>>S_{coherent}), dropping SNR_{bio} below SNR_{crit} and inducing barrier breakdown, capillary stasis, and apoptosis.
- (C) **Science 4.0 Bioenergetic Rescue:** Targeted pre-reperfusion metabolic substrate routing suppresses oxidative entropy, re-establishing SN_{Rbio}>SNR_{crit} to restore active nitric oxide synthesis and microvascular perfusion.

To reverse capillary collapse, bioenergetic repair must occur before mechanical shear is re-introduced. Reperfusion in the presence of depressed SNR_{bio} results in unattenuated oxidative bursts that damage junctional integrity (VE-cadherin, Claudin-5, ZO-1), promoting leukocyte adhesion and microvascular plugging [1, 2, 6]. Elevating SNR_{bio} above SNR_{crit} re-establishes homeostatic control of trans-membrane ion gradients (Na⁺/K⁺ ATPase, SERCA) and restores nitric oxide (NO) bioavailability [5, 8, 10].

CLINICAL TRANSLATION AND THERAPEUTIC PARADIGMS

Translating this mathematical formulation into clinical medicine establishes three therapeutic imperatives:

- **Pre-Reperfusion Metabolic Conditioning:** Administering targeted bioenergetic precursors (such as lipid-matrix carriers and mitochondria-targeted antioxidants) prior to full macrovascular recanalization suppresses N_{oxidative}, raising SNR_{bio} above SNR_{crit} [1, 9].
- **Dynamic Biomarker for Microvascular Viability:** Real-time tracking of microvascular phase recovery and interstitial impedance provides a direct clinical index of tissue salvageability in stroke and critical limb ischemia [3, 5].
- **Rational Dosing Based on Channel Capacity:** Pharmacological dosing of vasodilators and growth factors must be calibrated to the active channel capacity C to avoid receptor saturation under high-noise pathological regimes [4, 8, 10].

DISCUSSION

Standard clinical pharmacology predominantly operates on static receptor-affinity models [2]. This paper demonstrates that in severe microvascular ischemia, receptor sensitivity is fundamentally constrained by non-equilibrium thermodynamic dissipation and noise amplitude. When the cellular signaling environment is overwhelmed by oxidative entropy, conventional pharmacological agents cannot convey coherent transcriptional or phenotypic instructions [1, 7].

By incorporating Shannon information theory and non-equilibrium thermodynamics into microvascular physiology, the Science 4.0 framework provides a quantitative bridge between cellular biophysics and bedside therapeutics [5, 8]. Protecting the bioenergetic signal pipeline prevents irreversible capillary rarefaction, reduces infarct expansion, and provides a mechanistic explanation for why restoring macrovascular patency alone is often insufficient for complete clinical recovery [2, 3, 10].

CONCLUSION

Microvascular recovery after ischemic insult is strictly governed by cellular information routing fidelity. Restoring the bioenergetic Signal-to-Noise Ratio (SNR_{bio}) and minimizing internal entropy production are essential prerequisites for functional endothelial resealing and microvascular reperfusion [1, 5, 7]. Applying non-equilibrium thermodynamic models within clinical research establishes an actionable, biophysical foundation for next-generation vascular therapeutics [8, 9, 10].

DECLARATIONS

- **Conflict of Interest:** The author declares no conflicts of interest.
- **Funding:** This work was independently conducted under the Science 4.0 Framework without external institutional grants.
- **Data Availability:** All analytical models, mathematical derivations, and equations are fully presented within the manuscript.

Cite this article: Dr. Julien Boblique. (2026) Non-Equilibrium Bioenergetic Information Routing and Signal-to-Noise Ratio Optimization in Ischemic Endothelial Repair: A Clinical Framework for Microvascular Recovery. *Advance Medical & Clinical Research*. 7 (4): 436-438.

REFERENCES

1. Granger, D. N., & Kvietys, P. R. (2015). Reperfusion injury and reactive oxygen species: The evolution of a concept. *Redox Biology*. 6: 524-551.
2. Cines, D. B., et al. (1998). Endothelial cells in physiology and in the pathophysiology of vascular disorders. *Blood*. 91: 3527-3561.
3. Pries, A. R., & Secomb, T. W. (2014). Making microvessels work: vascular adaptation, remodeling and regression. *Physiology*. 29: 289-301.
4. Shannon, C. E. (1948). A mathematical theory of communication. *Bell System Technical Journal*. 27: 379-423.
5. Boblique, J. (2026). Biophysical Optimization of Cellular Signal-to-Noise Ratio (SNR) in Bioenergetic Information Networks V2. *Research Journal of Innovative Studies in Medical and Health Sciences*. 3: 22-24.
6. Curry, F. E., & Adamson, R. H. (2010). Endothelial glycocalyx: permeability barrier and mechanosensor. *Annals of Biomedical Engineering*. 38: 675-687.
7. Friston, K. (2010). The free-energy principle: a unified brain theory?. *Nature Reviews Neuroscience*. 11: 127-138.
8. Boblique, J. (2026). Science 4.0 - Architecture of Cellular Resilience and Living Signal Optimization. *International Journal of Zoology and Animal Biology*. 9: 000673.
9. Boblique, J. (2026). Lipid-Matrix Carrier Architecture: Engineering Nano-Vectorized Transport for Hydrophobic Living Signals in Science 4.0 Frameworks. *JSM Biotechnology & Biomedical Engineering*. 10: 1094.
10. Boblique, J. (2026). Industrial Standardization of the Bio-OS: Algorithmic Codification of Resilience Engineering Guidelines and Version V8 Architecture. *International Journal of Zoology and Animal Biology*. 9: 000685.

Copyright: ©2026 Dr. Julien Boblique. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.