## Murburn concept explains why oxygen is acutely needed to sustain life

Murburn concept (from "mured burning", signifying a restricted uncontrolled oxidative process) provides a tangible rationale why oxygen is so quintessential for immediate maintenance of life-order. It postulates that oxygen-centered diffusible reactive species (DRS, like superoxide radical) are formed in cells, whose reaction potential and electrical activity are obligatorily needed for catalysis, electron-transfer and other core cellular functions. Therefore, murburn concept mandates that cells must have murzymes, proteins that generate and/or recruit DRS. This thesis contrasts prevailing classical perceptions which consider DRS as undesirable and toxic/waste products of metabolism. (Murburn concept is also relevant for anaerobic organisms, wherein DRS centered on other elements are formed.)

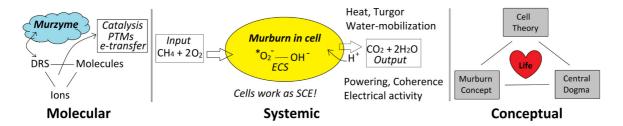


Fig. 1. In the left panel, molecular interactions involved in murburn concept are shown. A murzyme may use (generate/modulate/stabilize/utilize) DRS, which may enter into interactive equilibriums with diverse or select molecules and ions in milieu, giving rise to catalytic electron or moiety transfers, including posttranslational modifications (PTMs) of auto or hetero proteins. The central panel shows the overall systemic or macroscopic physiological overview of ECS-initiated murburn in cells leading to their functioning as SCEs. Methane (CH4) is considered as an example of nutrient input. One of its murburn products (CO2) is a voidable gas and the other product (water, H2O) is also the solvent. Owing to colligative effects, the latter is spontaneously mobilized to move out, thereby retaining cellular composition in a dynamic fashion. Physically, these processes also generate heat and turgor. Chemically, the transient DRS enable electrical activity, power otherwise non-spontaneous reactions and enable seamless coherence. The conceptual importance of murburn concept as a founding principle of life is shown in the right panel. While the vitally deterministic central dogma allows for topology/affinity based selectivity, the inevitable stochastic (based in chanced events) murburn processes complement with other parameters needed to support life.

Murburn concept founds cellular activities in simple frameworks of thermodynamics, and establishes the continuum of the laws of physics in biology. Its conceptualization was necessitated by the inadequacy or redundancy or non-demonstrability of some classical ideas like electron transport chains, membrane-based ion pumps, chemiosmosis, proton motive force, self-assembled rotary molecular machineries, etc. Most of these erstwhile acclaimed ideas gained footing when the details of organelles' architecture, biomolecules' structures and distributions, etc. were not adequately explored. Despite volumes of diverse incompatible information made available later, inertial mindsets maintained a 'status quo'. The aesthetic perspective that "Reactions occurring outside proteins' active sites via DRS would be too chaotic for maintaining the order of life!" also prevented the consideration that DRS could be useful in physiology. However, with the global recognition of NO (nitric oxide) as a molecular messenger a few decades back, this stigma is gradually wearing off and DRS



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are being seen in better light. In this emerging scenario, murburn models afford us a pan-systemically relevant and predictable framework of cellular functioning, with a fresh approach.

Of the fundamental forces, cells can only use electromagnetic force to do useful work. Therefore, moving electrons or moieties amongst cellular components forms the core drive of physiology. Murburn concept explains that cellular powering initiated by redox proteins bring about effective charge separation (ECS), and this is facilitated by oxygen (owing to the formation of oxygen-centered DRS). Admitting this tangible, probable and ascertainable aspect of reality can explain direct observations with redox proteins like: substrate diversities; atypical reaction and dose-response profiles; unusual and variable activations, inhibitions and ratios of reactants-products; trans-membrane potential fluctuations; etc. Unrestricted interactive equilibriums involving the DRS lead to chemico-physical changes and rearrangement of cellular contents, thereby also impacting posttranslational modifications (PTMs). Murburn concept deems that ECS in cells ultimately enables them to do useful work as simple chemical engines (SCE). Such works of life include: powering, seamless networking of cellular components, maintenance of constituents' concentrations, sensing and response to stimuli, etc. A significant number of murzymes have been identified to function in key cellular routines like respiration (synthesis of ATP, the cellular energy currency), heat generation, photosynthesis, electrophysiology, processing of unfamiliar/unwanted molecules, visual perception and signal relay, etc. This makes murburn concept a primordial and fundamental principle for understanding the evolution and sustenance of cellular life. Currently, it is understood to complement the central dogma (which controls the long-term cellular activities by flow of information via "DNA  $\rightarrow$  mRNA  $\rightarrow$  protein" and selective catalysis thereof). Murburn concept is the only standing theorization which explains why oxygen is so acutely required and how cyanide can kill quickly at mg/Kg dosages. As murburn concept poses unparalleled and profound impact on biomedical pursuits, its recognition as a paradigm-shift idea and pillar of life is inevitable.

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## **Publication**

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