
Biochemistry related items

**Effect of O$_2$ on Metabolism Evolution**


**#1 Effect of O$_2$ on Metabolism Evolution**


- Pre-oxygen earth - >2.5 billion years
  - Electron donors: $\text{H}_2$, $\text{H}_2\text{S}$, CH$_4$
  - Acceptors: $\text{CO}_2$, $\text{SO}_4^{2-}$, $\text{NO}_3^-$ ($\text{N}_2$)
  - Selling electrons cheap!

- Post-oxygen earth - <2.2 billion years
  - O$_2$ is an exceptionally good (but dangerous) electron acceptor - new possibilities for energy generation
  - Fewer reductants become available; metabolism expands - oxygen becomes a “favorite” direct and indirect participant
  - Anoxic bugs become marginalized
Effect of O\textsubscript{2} on Metabolism Evolution

- The Effect of Oxygen on Biochemical Networks and the Evolution of Complex Life
- Jason Raymond and Daniel Segrè

Tapping the “KEGG” [www.genome.jp/kegg/kegg2.html]

Raymond and Segrè chose 10-100 random “seed” metabolites in KEGG KBytes Encyclopedia of Genes and knocked in a set of KEGG pathways to make self-sustained, oxygen requiring metabolites. Only clusters of similar networks were found. Oxygen was required for the largest and most interconnected networks, thus oxygen seems to have led to a great bloom of new metabolism. Oxygen requiring reactions seem to have evolved independently after the prokaryote/eukaryote split. New pathways maked antibiotics, steroids and other complex metabolites possible.

Tapping the “KEGG” [www.genome.jp/kegg/kegg2.html]

Metabolism’s Greatest Hits

<table>
<thead>
<tr>
<th>Compound</th>
<th>Total reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP</td>
<td>457</td>
</tr>
<tr>
<td>NAD+</td>
<td>614</td>
</tr>
<tr>
<td>O2</td>
<td>728</td>
</tr>
<tr>
<td>CoA</td>
<td>954</td>
</tr>
<tr>
<td>O2</td>
<td>996</td>
</tr>
<tr>
<td>NH\textsubscript{3}</td>
<td>282</td>
</tr>
<tr>
<td>S-adenosyl methionine</td>
<td>224</td>
</tr>
<tr>
<td>Pyruvate</td>
<td>149</td>
</tr>
<tr>
<td>2-oxoglutarate</td>
<td>142</td>
</tr>
</tbody>
</table>

Fig. 2. The effect of oxygen on KEGG’s metabolic “backbone” (pruned as a pruned version of the full network, with 1861 metabolites and 2652 possible reactions; see SOM for detailed description). Blue nodes and edges represent metabolites and reactions, respectively, that are present in anoxic metabolic networks. Red nodes and edges are used to represent metabolic networks whose presence is dependent on oxygen availability. Green edges correspond to reactions that are found only in the anoxic network but use at least one anoxic metabolite, representing replacement or remodeling of anoxic pathways to take advantage of oxygen, as in thiamin and B12 biosynthesis.
Fig. 1. The effect of various metabolites (legend at right) on the total number of reactions in ecosystem-level metabolic networks, as computed with the network expansion algorithm. Each point represents two consecutively generated networks: the first network, whose size is the abscissa value, is generated from a randomly chosen set of seed metabolites, and the second network, whose size is the ordinate value, is generated from that same seed set amended with the addition of one of the nine metabolites shown in the legend. Points are colored based on the amended metabolite, shown in the legend. All networks occupy four broadly similar groups (bold lines and roman numerals) and subgroups (H, higher; L, lower) that result from often very different but chemically interconvertible seed sets. Only networks that include O2 as a metabolite are able to transition into group IV (dashed line), with other transitions being determined by the availability of key metabolites.

Adding O2 to networks greatly expands the possibilities compared to other important metabolites.

Fig. 4. Increase in total number of reactions catalyzed by individual genomes after the inclusion of O2 in a network originally seeded with N2, H2S, CO2, and the cofactors pyridoxal phosphate, ATP/ADP, THF, and NAD+/H. Horizontal bars represent the percent increase in oxic versus anoxic network size on a genome-by-genome basis, colored according to the growth mode of the organism (colors are consistent with those in Fig. 3). The inset superimposes this data on a species tree for these organisms, showing that adaptation to O2 has occurred throughout the tree of life. Also shown are the three-letter KEGG binomen abbreviations used in the inset and in Fig. 3. Enzymes specific to the oxic network expansion observed in strict anaerobes are detailed in SOM and table S3.

Life gets complicated!

#2 Regrowing Beta Cells from spleen pieces? A reconsideration

- Science 24 March 2006: Vol. 311, no. 5768, p. 1669

- S. KOPAMA ET AL., SCIENCE 302, 1229 (2003) report that injected spleen cells with adjuvant (complete Freund’s adjuvant (CFA)) can regenerate islets in diabetic mice and cure them. Very exciting result!
New Data Dispute

This week in Science, however, it seems that the adjuvant alone is enough to get regeneration (Science 24 March 2006: Vol. 311. no. 5768, pp. 1774 - 1775) and the beta cells are NOT from stem cells in spleen. ~25% cure