in the Chilean OMZ? In sediments with a high input of easily degradable biomass that fuel sulfate reduction, microbial sulfide production can overwhelm the nitrate pool and lead to sulfide poisoning of life in the seabed; sulfide-blackened dead *Thioploca* mats (nicknamed "*Thioploca nigra*") are a frequent occurrence on the Chilean shelf sediments (*9*). In the OMZ water column, the chemistry balance is tilted toward sulfide limitation. Comparison of the redox stoichiometries of the pelagic SUP05 group and benthic *Thioploca* lends plausibility to this scenario. Benthic *Thioploca* reduce nitrate to ammonia in order to oxidize sulfide as effectively as possible in a 1:1 ratio of nitrate and sulfide (*10*). The SUP05 populations favor a more parsimonious mode of sulfide oxidation by the reduction of nitrate to nitrite, with a sulfide/nitrate stoichiometry of 1:4 (see the figure). The dominant OMZ bacteria may have additional, as yet unexplored, mechanisms of coping with sulfide limitation.

As a caveat, such scenarios oversimplify the very complex nitrogen cycle; they neglect the highly active microbial cycling of ammonia in the oxycline (*11*). They also do not take into account anaerobic ammonia-oxidizing bacteria in the water column, which combine nitrite and ammonia to nitrogen gas (*5*). To trace the dynamics of sulfide oxidation and nitrate reduction processes and their microbial populations, Canfield *et al.* call for systematic seasonal studies.

The Chilean OMZ and continental shelf provide two examples for microbial sulfur and nitrogen cycling ecosystems that thrive in a highly dynamic balance and persist through annual or interannual oscillations in redox regime and water column stratification (*12*, *13*). With ocean temperatures and anthropogenic water column anoxia on the rise, nitrate-dependent microbial controls on sulfide concentrations will become increasingly relevant; in the near future, we will certainly hear more about these resilient microbial engines of the changing world oceans.

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GENETICS

The DNA Damage Road Map

Comparing maps of gene interactions offers insight into how yeast cells repair DNA damage.

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If you were on your way to a new country, you would pack a map to help you find the major cities, roads, and interesting places to explore. Recently, researchers have created similar maps to help them start unraveling the complex architecture of a cell. These maps are created by measuring genetic interactions, specifically the effect that a mutation in one gene has on the phenotype of a mutation in a second gene (see the figure). Using novel genetic tools for studying budding yeast (*1*) and automated technology, investigators can now systematically and rapidly measure these genetic interactions (epistasis) for all pairs in gene subsets of interest (about 400 to 800 genes). The resulting E-MAPs (epistasis miniarray profiles) (*2*) have helped chart interactions for a diverse array of cellular processes, including the early secretory pathway, chromosome function, signaling pathways, and RNA processing (*3*, *4*). These E-MAPs, however, have all been collected from cells grown under the same condition: in a rich growth medium. But just as a snowstorm can block some roads and force changes in traffic, changing environmental conditions can cause cells to rewire their genetic networks, necessitating the drawing of a new map. On page 1385 of this issue, Bandyo-

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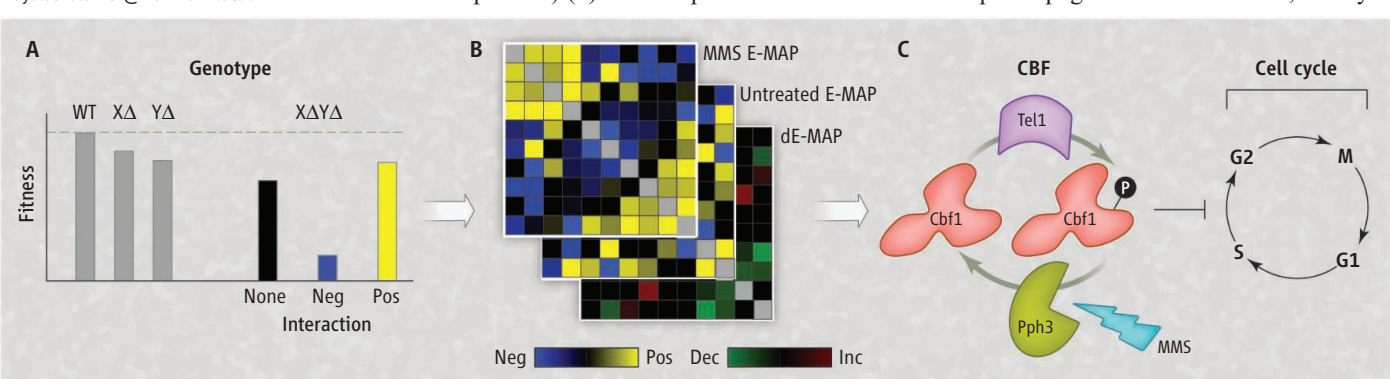

Compare and contrast. (**A**) E-MAPs are created by measuring the effect of gene mutations on a phenotype of interest such as fitness. By comparing wild-type (WT) strains to single mutations (XΔ, YΔ) and their combinations (XΔYΔ), investigators can identify mutation pairs that have no effect (black bar, right), a negative effect that is greater than expected (blue bar), or a positive effect that is less than expected (yellow bar). (**B**) By comparing E-MAPs of yeast cells grown under treated (MMS) and untreated conditions, researchers created a dE-MAP illustrating the change in interactions (increased or decreased) between the two conditions. (**C**) The dE-MAP highlighted the role of Tel1 and Pph3 in regulating Cbf1 activity in cell cycle checkpoints (right).

padhyay *et al*. (*5*) describe the creation of just such a condition-specific E-MAP and a novel method for analyzing it.

Yeast cells can grow under a myriad of conditions by changing their cellular wiring through the regulation of transcription, translation, protein modification, and degradation. To study an example of this changing landscape, Bandyopadhyay *et al*. (*5*) chose a subset of 418 yeast genes that includes all known signal transduction components and transcription factors, as well as DNA damage proteins and chromatin remodelers. Then, they created two E-MAPs showing how these genes interacted both under standard conditions ("untreated") and when treated with methyl methanesulfonate (MMS), a DNA-damaging agent (see the figure). A key idea underlying their analysis was to compare and contrast the two maps, thereby isolating interactions that are condition specific (see the figure). They used the differences in these interactions to create a third map, which they named the dE-MAP (differential epistasis mapping). The dE-MAP uncovers novel information on how a yeast cell deals with DNA damage. For example, two genes that encode proteins that repair DNA damage might not show any interaction in untreated cells but might show crucial interactions in yeast treated with MMS.

A bird's-eye view of the dE-MAP reveals that protein complexes tended to remain stable across the two conditions. The relationships between these complexes, however, were reprogrammed to assist the cell in dealing with stress. By highlighting these condition-dependent interactions, the dE-MAP allows the scientist interested in DNA damage to zoom in on the regulatory interactions between proteins that play a specific and major role in fighting the effects of MMS. There are hundreds of such stories in the data. One example that demonstrates the power of the approach involves a novel function that the authors found for the transcription factor CBF1 (centromere binding factor) in repressing cell cycle checkpoints (which ensure the fidelity of cell division). One of the advantages of having systematic interaction data are that, instead of examining only specific interactions, E-MAPs allow scientists to examine the "interaction profile" of a gene, or its pattern of interactions with all other genes in the map. This profile provides a rich fingerprint of the gene's function. Two genes with similar or related functions will have similar interaction profiles. In the past, this concept allowed the identification of several key gene complexes (*6*). The authors used this tool to reveal that CBF1's genetic interaction profile changed between the untreated and MMS growth conditions. Only in the MMS E-MAP is CBF1's activity highly correlated with the activity of two other genes, TEL1 (encoding a kinase) and PPH3 (encoding a phosphatase). Previous work had shown that Tel1 phosphorylates Cbf1, and the authors show that Pph3 regulates CBF1 by dephosphorylating it (see the figure).

With advances in automation and technology, researchers can now easily collect E-MAPs for many gene subsets and in many conditions. In fact, we are quickly nearing the day when all genetic interactions in yeast will be collected (*7*). The central challenge has become distilling biological insights from this rich data. This challenge can be met computationally (*8*–*11*) or by using careful experimental designs, as shown by Bandyopadhyay *et al*. More broadly, the dE-MAP approach provides an important reminder that most high-throughput interaction data provides just a snapshot representing a specific state. The new frontier is probing the dynamic interactions that enable cells to survive and thrive in varying environmental and genetic contexts. Experiments and analysis at this next, dynamic, level will give biologists truer insights into the ever-changing environment of a living cell.

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PLANT SCIENCE

Dynamic Metabolons

The assembly and disassembly of enzymes complexes may differentiate plant defense responses to insect attack and fungal infection.

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The metabolic activities of higher organisms are highly coordinated. At the cellular level, compartmentalization into organelles and substructures thereof optimizes the concentration of substrates targeted by enzymes. At the molecular level, further substrate concentration is gained by the formation of multienzyme complexes—so-called metabolons. The protein constituents of a metabolon are held together by noncovalent interactions and often stabilized by membrane anchoring. A metabolon allows the direct passage of a product from one enzymatic reaction to a consecutive enzyme in a metabolic pathway. Such channeling of intermediates limits their diffusion into the surrounding milieu, maintains separate pools of intermediates, facilitates fast turnover of labile or toxic intermediates, and may prevent undesired crosstalk between different metabolic pathways (*1*, *2*).

Coordinating metabolic pathways may involve dynamic shifts between the assembly and disassembly of metabolons or their interactions with proteins that modulate their output function. Such transient metabolons are called "functioning dependent structures," assembling in response to specific metabolic demands or abiotic and biotic challenges (*3*). For example, in humans, the six enzymes that constitute the purine nucleotide biosynthetic complex assemble upon depletion of purines. Phosphorylation of the metabolon by the CK2 kinase promotes its dissociation, whereas assembly can be initiated by phosphatases or kinase inhibitors (*4*). The transient complex of glycolytic enzymes that forms at the outer mitochondrial membrane in response to the respiratory demand for pyruvate is another example (*5*).

In plants, biosynthetic pathways that gen-

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The DNA Damage Road Map

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