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Ultradian Metabolic Oscillation of *Saccharomyces cerevisiae*: A metabolic Synchronizer and Regulation Mechanism.

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Biological oscillations are intrinsic to all living systems and play a significant role in the regulation of the activities of biological systems [1], but in most cases knowledge concerning the underlying processes that dictate the time base, synchronization, and regulation of systems remains rudimentary. Clocks, one of autonomous biological oscillations, are universal and fundamental to living organisms and are the basis of temporal control of metabolism and behavior [2]. The majority of research has focused on the daily clock (circadian clock) that is found in the entire range of organisms from cyanobacteria to humans.

We have previously reported that autonomous metabolic oscillation of *Saccharomyces cerevisiae* occurs during continuous aerobic culture [3-5]. The oscillation period was approximately 45 min in glucose- or ethanol-grown culture (therefore, that is called ultradian oscillation). Autonomous ultradian metabolic oscillation is independent of cell cycle, glycolysis, or environmental triggering, and can be characterized on cyclic changes of many metabolites and factors (Fig. 1). Recent studies have confirmed that the ultradian metabolic oscillation is under ultradian clock control and is not directly linked with mitochondria energy generation [6,7].

To understand the regulation mechanism of the ultradian metabolic oscillation we have investigated the synchronization factor, which must be emitted and sensed by the cell, because the integrated respiratory oscillation output arises from the metabolism of individuals in the population [5]. Recently, we demonstrated that periodic production of H_2S from inorganic sulfate by sulfite reductase in the sulfate assimilation pathway results in population synchrony *via* periodic inhibition of respiratory activity [8-10], and periodic depletion of cystein and/or glutathione, which is involved in the detoxification of toxic materials originating from respiration, may cause periodic H_2S production [10-12]. Analysis of gene expression using cDNA microarray and cellular pool of metabolites suggested that periodic transcriptional activation of genes, which are related to carbon/sulfur and antioxidant metabolism, took place during autonomous metabolic oscillation [13].

Based on our previous reports with dynamic transcriptional regulation during ultradian oscillations [3-13], we propose a novel physiological role of H_2S as a redox regulator as well as population synchronizer in yeast *S. cerevisiae* (Fig. 2).

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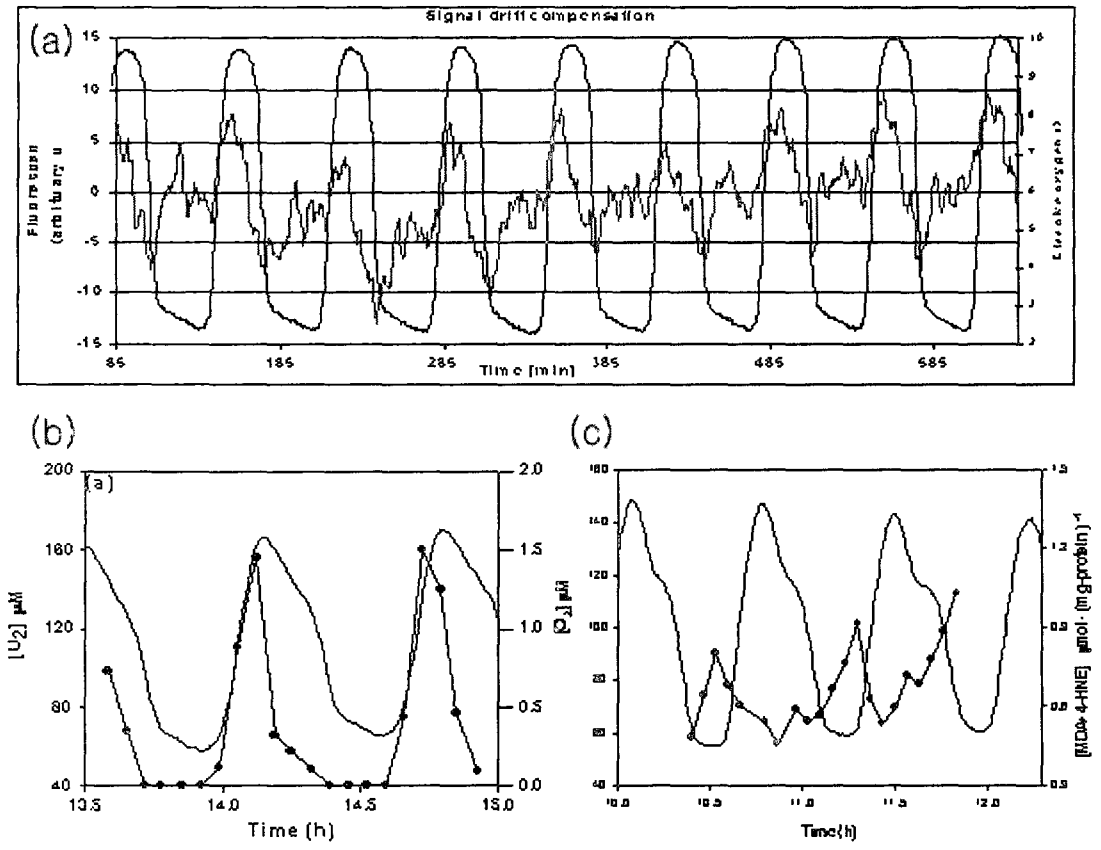

Fig. 1. Autonomous ultradian respiratory oscillation during continuous culture of *S. cerevisiae*. Oscillation profiles of NAD(P)H as cellular redox state (upper panel), H2S concentration (left in lower panel) and intracellular level of lipid peroxides (right in lower panel).

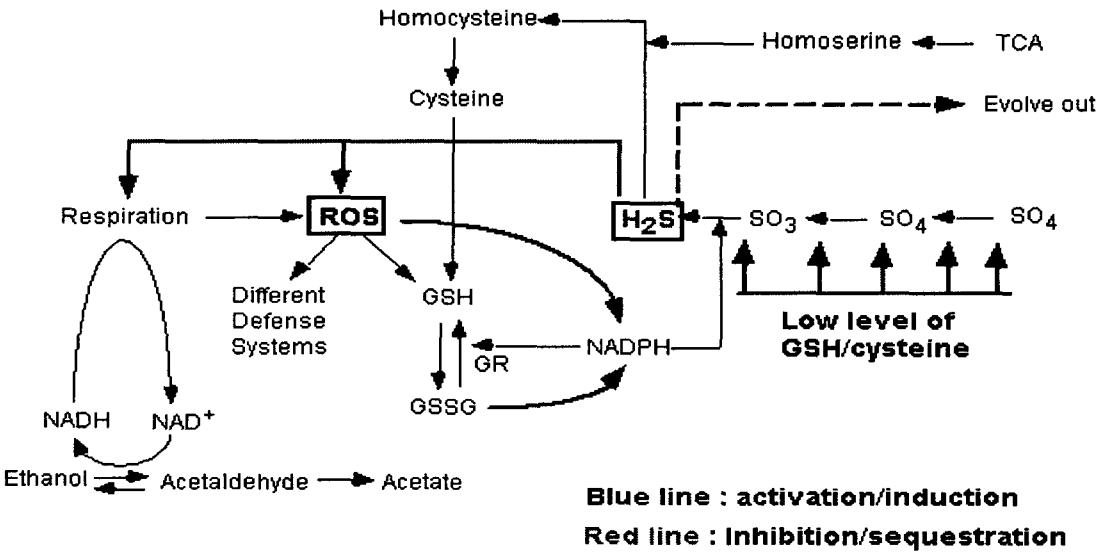

Fig. 2. Proposed regulation model of autonomous ultradian metabolic oscillation in *S.cerevisiae*