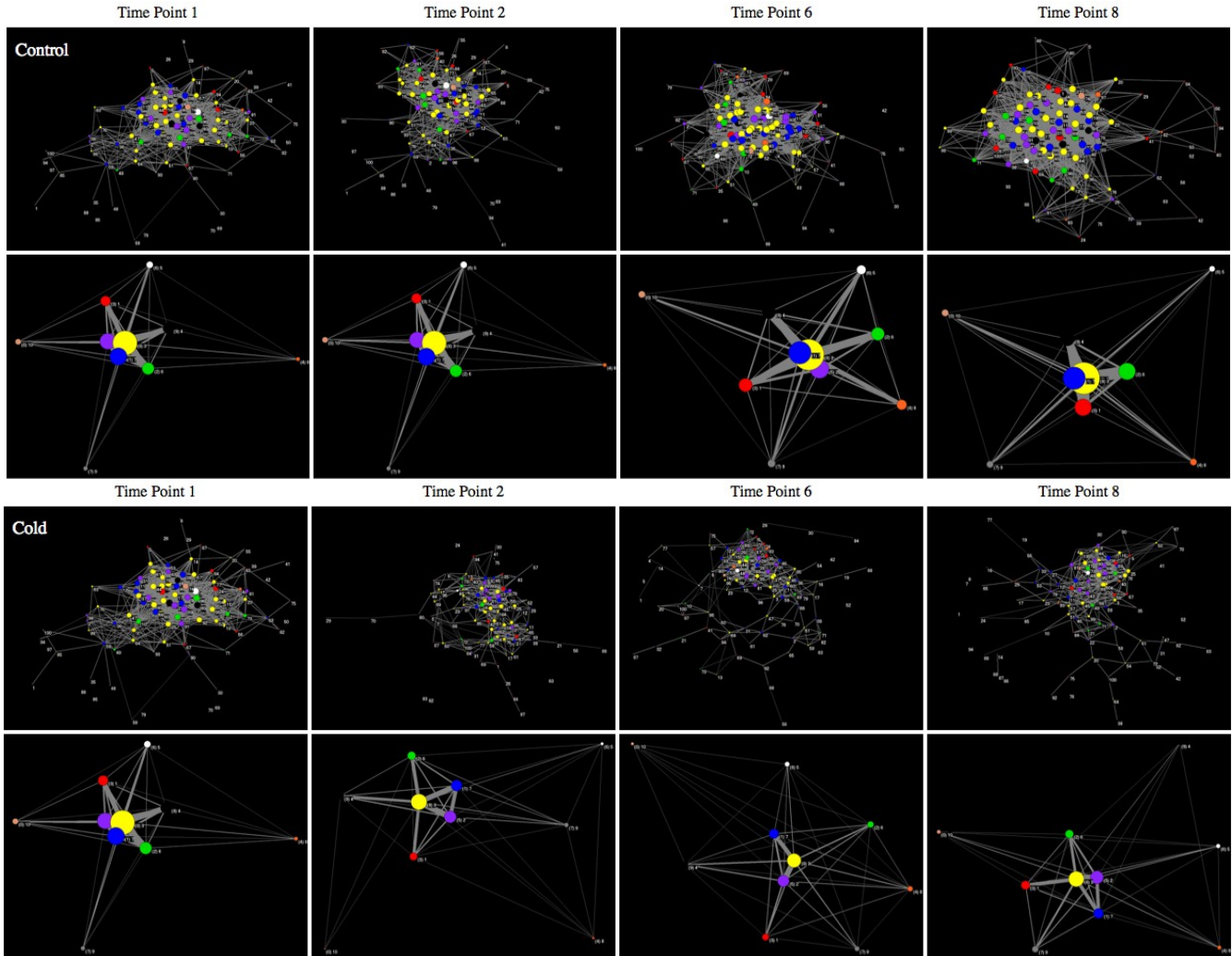


Supplementary Information

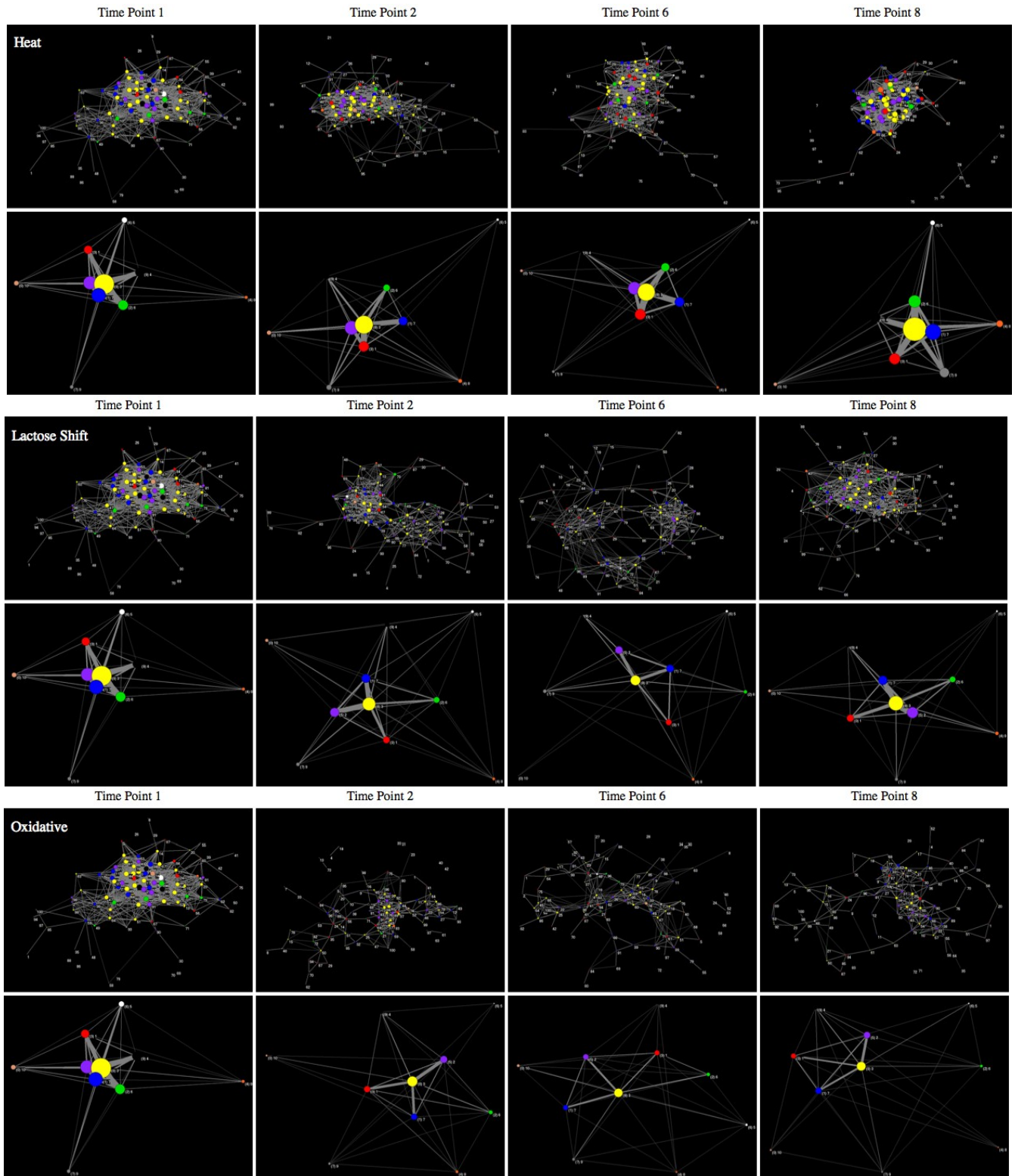
Stress induces biphasic-rewiring and modularization patterns in the metabolomic networks of *Escherichia coli*

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and Gustavo Caetano-Anollés

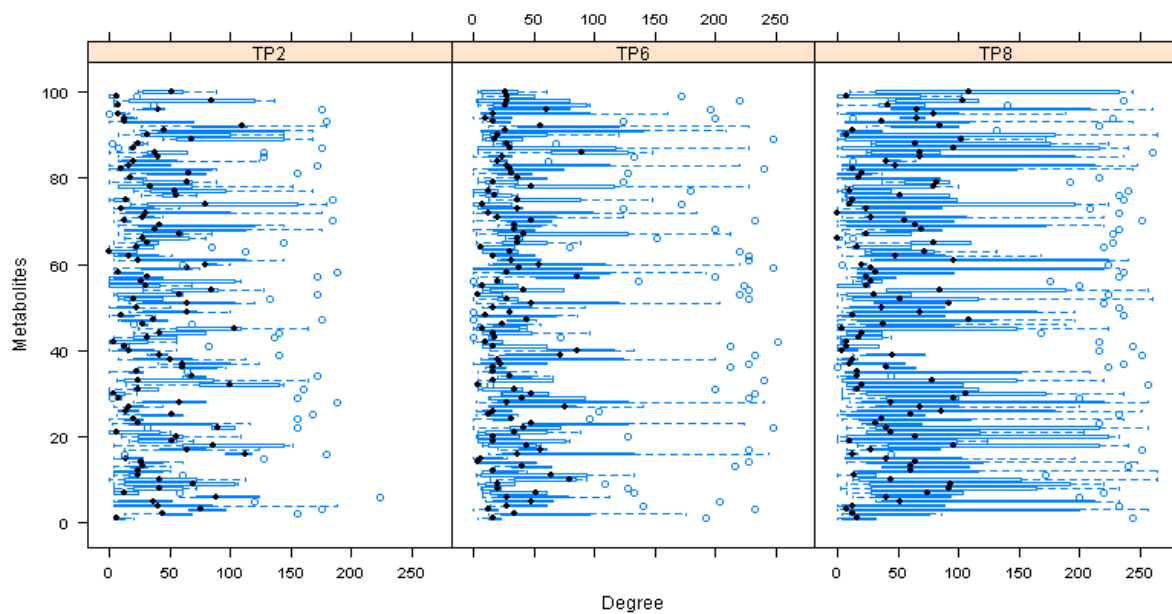
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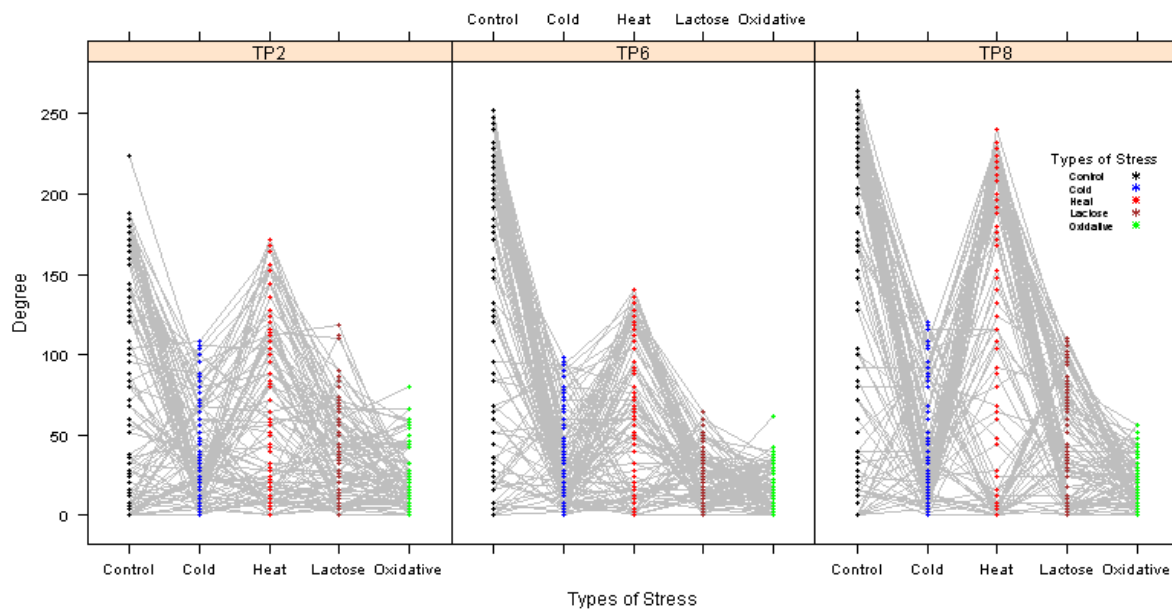
SI Figure 1. Timeline of metabolomic networks (top) and reduced derivatives (bottom) showing biphasic-rewiring patterns in response to stress perturbations. A force-directed algorithm places nodes that are more connected with shorter paths in the center of the graphs [T.M.J. Fruchterman and E.M. Reingold, "Graph drawing by force-directed placement," *Software – Practice & Experience* (Wiley), 21 (11), 1129–1164, 1991]. Nodes are colored according to pathway maps in KEGG: yellow, hubs; blue, carbohydrate; green, energy; red, lipid; orange, nucleotide; purple, amino acid; brown, glycan; white, cofactors/vitamins; grey, secondary metabolites and xenobiotics; and black, miscellaneous. Vertex size is proportional to connectivity.



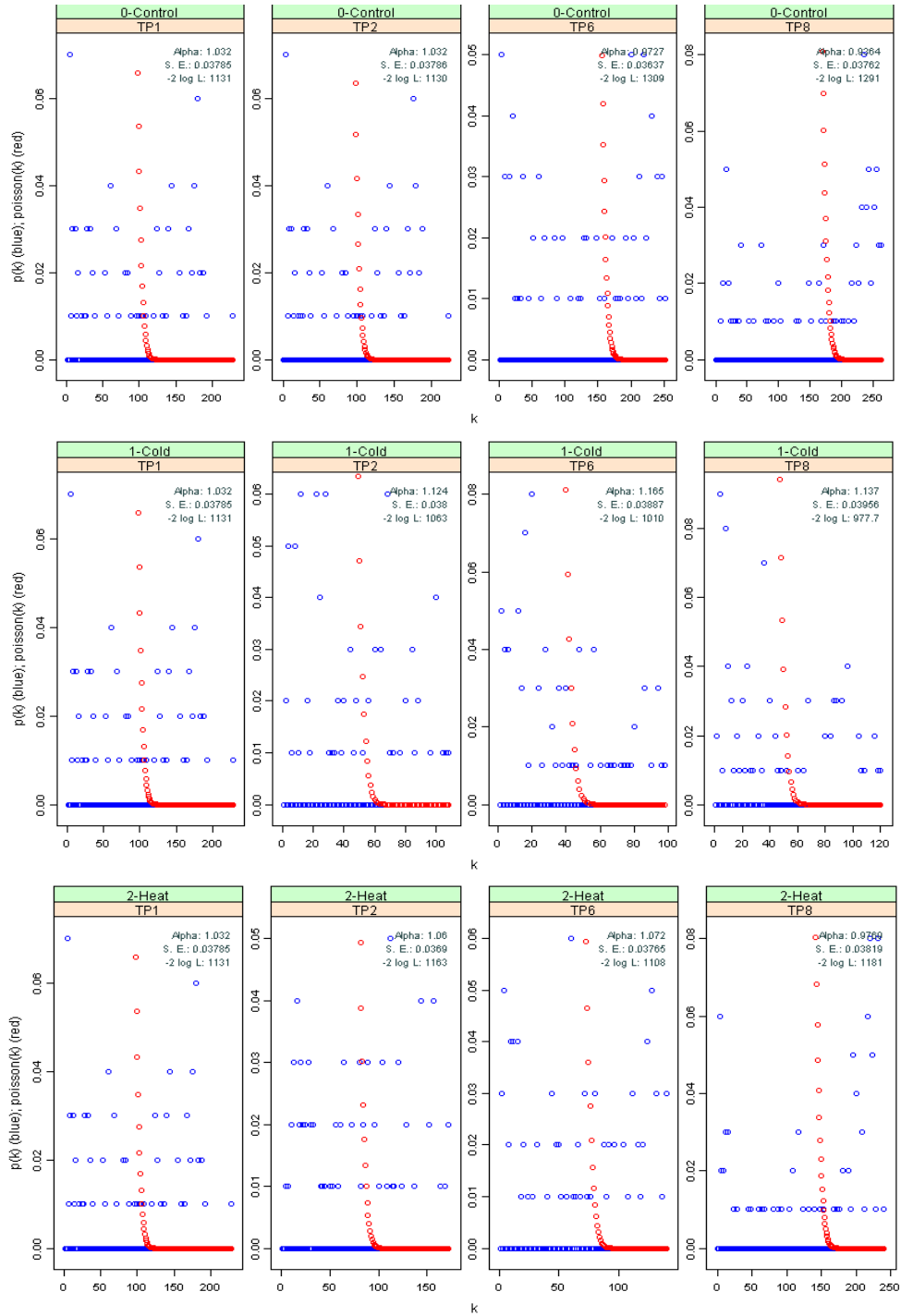
SI Figure 1. (continued)



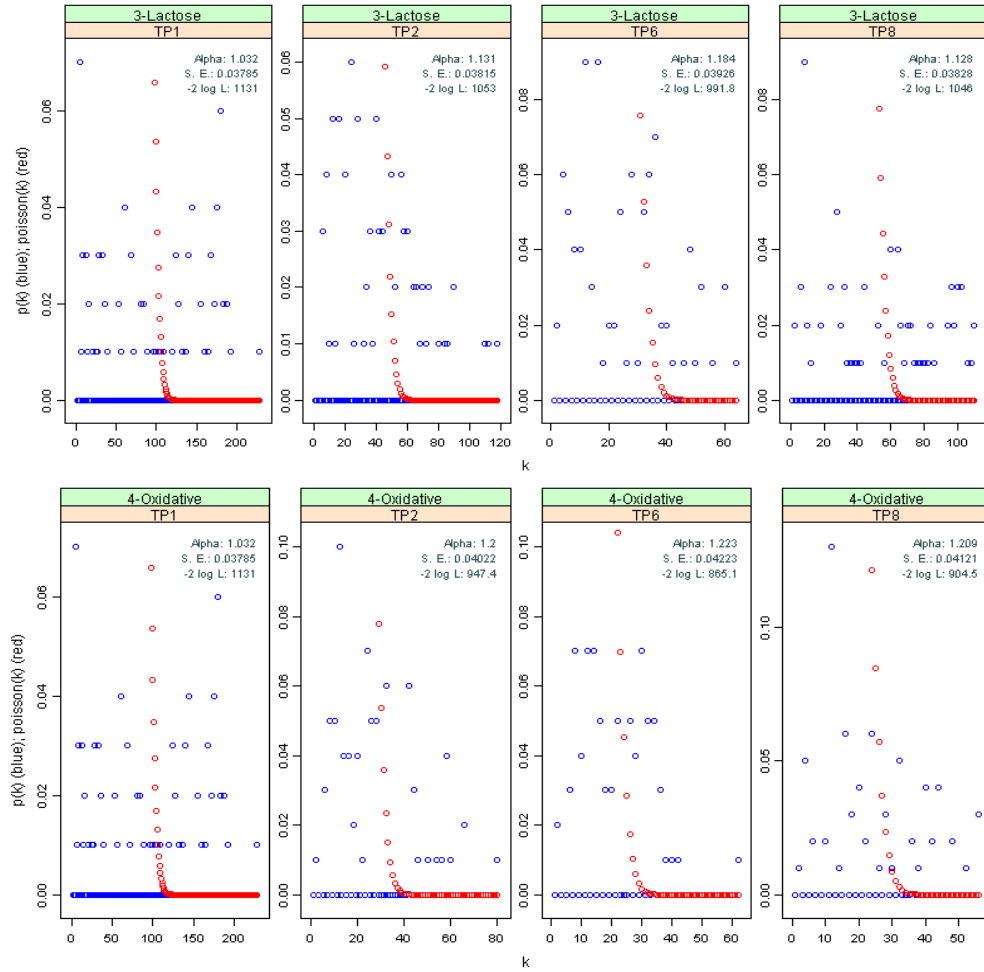
SI Figure 2. Boxplot of metabolite connectivities for metabolomics networks of individual time points.



SI Figure 3. Connectivity of metabolites in metabolomics networks measured as vertex degrees for all time points of bacterial responses to different stress perturbations and control.



SI Figure 4. $P(k)$ versus k (blue) and Poisson (red) plots showing marked departures from scale-free behavior. Scale-freeness of the networks was probed using R and the the power.law.fit method [A. Clauset, C.R Shalizi, and M.E.J Newman, "Power-law distributions in empirical data," SIAM Review 51,661–703, 2009; M.E.J. Newman, "Power laws, Pareto distributions and Zipf's law," Contemporary Physics, 46, 323-351, 2005]. The method gives the maximum likelihood scaling-exponent or alpha-values



SI Figure 4. (continued)

SI TABLE I. BIOLOGICAL ENDPOINTS

Stress	Optical density (600 nm) at time point ^a			
	1	2 (0 min)	6 (40 min)	8 (90 min)
Control	0.507±0.015	0.602±0.013	0.907±0.016	1.422±0.015
Cold	0.506±0.009	0.61± 0.012	0.647±0.009	0.683±0.029
Heat	0.503±0.012	0.593±0.012	0.700±0.021	0.757±0.031
Diauxie	0.56±0.079	0.633±0.060	0.690±0.029	1.053±0.227
Oxidative	0.49±0.043	0.6430.009	0.673±0.012	0.943±0.040

^aThe moment of stress corresponds to time point 2.