Noise-plasticity correlations of gene expression in the multicellular organism

Arabidopsis thaliana

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18

19 **Abstract**

20 Gene expression levels exhibit stochastic variations among genetically identical
21 organisms under the same environmental conditions (called gene expression “noise” or
22 phenotype “fluctuation”). In yeast and *Escherichia coli*, positive correlations have been
23 found between such gene expression noise and “plasticity” with environmental
24 variations. To determine the universality of such correlations in both unicellular and
25 multicellular organisms, we focused on the relationships between gene expression
26 “noise” and “plasticity” in *Arabidopsis thaliana*, a multicellular model organism. In
27 recent studies on yeast and *E. coli*, only some gene groups with specific properties of
28 promoter architecture, average expression levels, and functions exhibited strong
29 noise-plasticity correlations. However, we found strong noise-plasticity correlations for
30 most gene groups in *Arabidopsis*; additionally, promoter architecture, functional
31 essentiality of genes, and circadian rhythm appeared to have only a weak influence on
32 the correlation strength. The differences in the characteristics of noise-plasticity

correlations may result from three-dimensional chromosomal structures and/or circadian rhythm.

Introduction

In many organisms, stochastic variations in gene expression have been observed among individuals in a genetically identical population under constant environmental conditions (Elowitz et al., 2002; Furusawa et al., 2005; Golding et al., 2005; Kaern et al., 2005; Newman et al., 2006; Chang et al., 2008; Konishi et al., 2008; Taniguchi et al., 2010; So et al., 2011; Silander et al., 2012; Woods, 2014). These variations, called “noise,” differ among genes with some genes being more prone to displaying this type of behavior. Recent investigations in *Escherichia coli* and the budding yeast *Saccharomyces cerevisiae* reported that the magnitude of expression noise shown by a gene can exhibit a positive correlation with “plasticity”, the variation in its expression levels due to mutation or environmental change (Sato et al., 2003; Blake et al., 2003; Landry et al., 2007; Choi and Kim, 2008, 2009; Tirosh and Barkai, 2008; Lehner,

2010; Lehner and Kaneko, 2011; Bajic and Poyatos, 2012; Singh, 2013). Such noise-plasticity correlations in gene expression levels reflect both a strategy and a mechanism for regulation of several gene groups. For example, in *E. coli* and yeast, some gene groups with specific properties of promoter architecture, average expression levels, and functions exhibit stronger noise-plasticity correlations (Tirosh and Barkai, 2008; Lehner, 2010; Bajic and Poyatos, 2012; Singh, 2013). Thus, the consideration of such noise-plasticity correlations in genes may provide insights into the survival strategies of various organisms.

The studies mentioned above in budding yeast and *E. coli* identified several aspects of gene expression noise-plasticity correlations that occur in unicellular organisms. In multicellular organisms, gene expression patterns in each cell are modified by intercellular interactions that are mediated through several signaling molecules. Recently, gene expression noise was shown to play important roles in sustaining pluripotency of embryonic stem cells, in cell fate decisions, and in cell differentiation in multicellular organisms (Mitsui et al., 2003; Kaneko, 2006; Kalmar et al., 2009; Ochiai et al., 2014). However, it remains to be elucidated whether gene

expression noise and plasticity at an individual level in multicellular organisms depend on similar characteristics to those in unicellular organisms. In this study, as a first step to the elucidation of the gene expression noise-plasticity relationships in multicellular organisms, we analyzed transcriptome data from the multicellular plant model, *Arabidopsis thaliana*, and compared the results to those of typical unicellular organisms, i.e., budding yeast and *E. coli*.

The physiological properties of *Arabidopsis* have been extensively investigated at both the whole plant level and the tissue level for different developmental stages and under various environmental conditions. To date, the genome sequence (The Arabidopsis Genome Initiative, 2000), the epigenomic status (Cokus et al., 2008; Chodavarapu et al., 2010; Roudier et al., 2011; Pascuzzi et al., 2014; Sequeira-Mendes et al., 2014), three-dimensional chromosome structures in the nucleus based on FISH and Hi-C analyses (Pecinka et al., 2004; Schubert et al., 2012, 2014; Feng et al., 2014; Grob et al., 2014; Wang et al., 2015), and extensive transcriptome data from DNA microarrays have been obtained from *Arabidopsis* and are available from public databases such as Gene Expression Omnibus (GEO) and Array Express. The

exhaustive analysis of these transcriptome data sets has provided insights into intermolecular relationships in stress responses (Maruyama-Nakashita et al., 2005; Kilian et al., 2007), the responses to hormone treatment (Nemhauser et al., 2006; Goda et al., 2008), and amino acid metabolism (Less and Galili, 2008; Wittenberg et al., 2012) in *Arabidopsis*.

Recently, the phenotypic plasticity of plants, from short-term plasticity such as changes in leaf angle, stomatal aperture, and photosynthetic rate to long-term plasticity such as developmental and cross-generational plasticity against short and long-term environmental variations, has been extensively investigated (Sultan, 2000; Valladares et al., 2007; Matesanz et al., 2010). Phenotypic variance has often been observed in plants with the same genome sets and grown under the same environmental conditions. Analyses of the gene expression noise that may be the origin of this phenotypic variation have been undertaken in rice and *Arabidopsis* (Nagano et al., 2012; Shen et al., 2012). In rice, these analyses indicated a significant relationship between gene expression noise and the functions of the genes (Nagano et al., 2012). In this paper, transcriptome data sets from *Arabidopsis* were used to search for correlations between

gene expression noise and short-term plasticity in several tissues, plants of different ages, and under different environmental conditions. Through the analysis of these transcriptome data sets, robust and significant noise-plasticity correlations were identified that were weakly influenced by the properties of the architecture of the promoter sequences, expression levels, and functional groups. These influences differed from those reported in budding yeast and *E. coli*.

Results

Gene expression level variations in different experimental data sets

The gene expression data sets from *Arabidopsis* were obtained from different tissues from plants of different ages and under variable growth conditions. Expression data for *Arabidopsis* genes were obtained from the Gene Expression Omnibus (GEO: <http://www.ncbi.nlm.nih.gov/geo/>). In this study, we analyzed well-documented experimental data sets from microarray analyses of 22,746 genes of *Arabidopsis* from the AtGenExpress project (<http://www.weigelworld.org/resources/microarray/AtGenExpress>). In particular, we

analyzed data sets involving control (non-treated wild type *Arabidopsis*, Columbia (Col-0)) data sets, and data sets from treated plants in which the number of time points multiplied by the number of replicates (data samples) of each data set was greater than 8. The names of the data sets, experiments, tissues used, ages (days-old), GEO accession numbers, and numbers of data of expression data sets are given in Table 1.

Name of data set	Name of experiment	Tissue	Day-old	GEO	# of data (control)	Reference
SS	Stress treatments	Shoot	18 days	GSE5620 - GSE5628	Replicates : 2 Time points : 9	Kilian et al., (2007)
SR	Stress treatments	Root	18 days	GSE5620 - GSE5628	Replicates : 2 Time points : 9	Kilian et al., (2007)
PS	Pathogen series: Pseudomonas half leaf injection	Leaf	28 days	GSE5685	Replicates : 2 Time points : 6	Dong X, Townsend H, Emmerson Z, Schildknecht B. (2007)
ER	Pathogen series: Response to <i>Erysiphe orontii</i> infection	Leaf	31 days	GSE5686	Replicates : 3 Time points : 8	Ausubel F, Dewdney J, Townsend H, Emmerson Z, Schildknecht B. (2007)
PH	Pathogen series: Response to <i>Phytophthora infestans</i>	Leaf	31 days	GSE5686	Replicates : 3 Time points : 3	Scheel D, Brunner F, Westphal L, Townsend H, Emmerson Z, Schildknecht B. (2007)
SU	Response to sulfate limitation	Root	10 days	GSE5686	Replicates : 2 Time points : 6	Maruyama et al., (2005)

Table 1. Names of data sets, names of experiments, tissues, ages, GEO accession numbers, and the number of replicates and time points of analyzed data sets.

The average expression level and average expression noise of each of 22,746 genes from non-treated (control or mock) conditions were obtained using different values in the different data sets (Supplementary Figure S1). Thus in the following arguments, the noise-plasticity relationships are estimated respectively for each data set.

Noise-plasticity correlations for *Arabidopsis* gene expression in experimental data sets

The noise-plasticity relationships of the 22,746 genes for each data set are plotted in Figure 1. Here, the noise (N) and plasticity (P) of genes for each data set (SS, SR, PS, ER, PH, and SU in Table 1), are named as N_{SS} , N_{SU} , ... P_{SS} , ..., and P_{SU} . The analysis identified significant correlations for all experimental data sets (p-values less than 10^{-4}). Thus, the noise-plasticity correlations for gene expression were robust and independent of the tissue, ages, growth conditions (see references in Table 1), or treatment.

Figure 1: Noise-plasticity scatter plots for 22,746 *Arabidopsis* genes from the SS, SR, PS, ER, PH, and SU data sets (Table 1). Here, the noise (N) and plasticity (P) of genes for each data set are named as N_{SS} , N_{SU} , ..., P_{SS} , ..., and P_{SU} . For all correlation coefficients (ρ), a p-value of less than 10^{-4} was obtained.

Promoter architecture dependency of noise-plasticity correlations

A recent study of budding yeast reported a detailed analysis of noise-plasticity correlations of gene groups with and without TATA promoters (Lehner, 2010). Here, the noise-plasticity correlations of gene groups with and without TATA promoters in

147 *Arabidopsis* were estimated for each experimental data set (Table 2) from the
 148 noise-plasticity scatter plots (Figure 2 and Supplementary Figure S2). The analysis
 149 indicated that significant noise-plasticity correlations were present in both gene groups
 150 although the correlation coefficient for the gene group with a TATA box was a little
 151 stronger.

		Data Sets						# of genes
Gene class		SS	SR	PS	ER	PH	SU	
Motif Search	TATA	0.801162547	0.812971334	0.741665995	0.877229303	0.638166501	0.713678059	1707
	non-TATA	0.70410144	0.705280889	0.643104428	0.805352193	0.507874562	0.646408494	10116
PlantProm	TATA	0.803969585	0.805952095	0.72483968	0.8693857	0.642596505	0.713802903	3347
	non-TATA	0.678331305	0.683013798	0.628029668	0.790042142	0.473164923	0.632156735	8476

153 Table 2: Noise-plasticity correlations for gene groups with and without TATA
 154 promoters from several data sets (Table 1). For all correlation coefficients, a p-value of
 155 less than 10^{-4} was obtained.

Figure 2: Noise-plasticity scatter plots for the SS data set (Table 1) showing gene groups with and without TATA promoters.

One of the purposes of this study was to compare *Arabidopsis* with previously analyzed unicellular organisms such as yeast and *E. coli*. Thus, we focused here on differences among gene groups with TATA and non-TATA promoters in the present arguments, although the TATA box is only one of the motifs involved in promoter activity in *Arabidopsis*. A comparative analysis of gene groups with other types of promoter architecture is currently in progress and will be reported in the future.

166

167 Dependency of mean expression level on noise-plasticity correlation

168 The noise-plasticity correlations of five gene groups, classified according to
169 average gene expression level under non-treated conditions (Higher, top 20% genes;
170 High, top 20~40% genes; Middle, top 40~60% genes; Low, top 60~80% genes; and
171 Lower, lowest 20% genes), were estimated for each experimental data set (Table 3(a))
172 from the noise-plasticity scatter plots (Figure 3 and Supplementary Figure S3). The
173 analysis indicated that significant noise-plasticity correlations were present in most of
174 the five gene groups. Moreover, the correlations became slightly weaker with the
175 increase in mean expression levels for the gene group (Table 3(a)). This effect was
176 greater in the gene group without TATA promoters than that with TATA promoters
177 (Table 3(b)(c)).

178 Notably, average noise levels also correlated negatively with expression levels
179 for each experimental data set (Table 3(d)). This result indicates that gene groups with
180 higher average noise levels exhibited higher noise-plasticity correlations.

(a)		Data Sets						# of genes
Gene class		SS	SR	PS	ER	PH	SU	
Expression levels	Lower	0.733124838	0.783632099	0.597850475	0.610751316	0.525722172	0.590437992	4549
	Low	0.751205906	0.654080518	0.636663247	0.776356386	0.5567612	0.599244736	4549
	Middle	0.563846317	0.603224613	0.514372871	0.677376384	0.402774327	0.446483382	4549
	high	0.550773716	0.583762052	0.427086984	0.65206279	0.353471737	0.437797905	4549
	higher	0.602178816	0.611146744	0.37501576	0.643502671	0.29192688	0.420520585	4550

(b)		Data Sets						# of genes
Gene class		SS	SR	PS	ER	PH	SU	
Expression levels (TATA)	Lower	0.760973941	0.688469671	0.683806494	0.81028254	0.568021725	0.568795428	269
	Low	0.767391945	0.683479579	0.632377748	0.827254237	0.608930353	0.539644141	254
	Middle	0.684286234	0.660382937	0.689429698	0.850152684	0.599622731	0.502088091	305
	high	0.716276983	0.69344424	0.658948087	0.843240439	0.614008526	0.480777249	295
	higher	0.787183283	0.742093661	0.647655171	0.832084328	0.528034686	0.313427815	584

(c)		Data Sets						# of genes
Gene class		SS	SR	PS	ER	PH	SU	
Expression levels (non-TATA)	Lower	0.837761235	0.746248624	0.740161065	0.874956806	0.565182476	0.575050951	609
	Low	0.728100781	0.67583862	0.679686766	0.871241636	0.499103193	0.613526895	1228
	Middle	0.567621274	0.54934547	0.569903096	0.789535519	0.380529313	0.430334001	2185
	high	0.599047866	0.546126369	0.506526437	0.71558567	0.379211437	0.416208194	2828
	higher	0.646805935	0.549960964	0.496327819	0.706405794	0.416916505	0.424672755	3266

(d) Noise		Data Sets						# of genes
Gene class		SS	SR	PS	ER	PH	SU	
Expression levels	Lower	0.833143589	0.775106015	0.871663739	1.183791487	0.906237011	0.807047097	4549
	Low	0.421476797	0.298163723	0.546898518	0.644063817	0.585149829	0.340627556	4549
	Middle	0.205919853	0.181029325	0.265538034	0.321443824	0.270158729	0.203542309	4549
	high	0.14762109	0.14011307	0.186279601	0.238927916	0.183552864	0.170186527	4549
	higher	0.118904418	0.121164766	0.163101715	0.219011572	0.150074919	0.148419355	4550

181

182 Table 3: (a) Noise-plasticity correlations among five gene groups classified by average

183 gene expression levels from several data sets (Table 1). (b)(c) Noise-plasticity

184 correlations of gene groups with and without TATA promoters belonging to gene

185 groups with different expression levels. For all correlation coefficients, a p-value of

186 less than 10^{-4} was obtained. (b) Noise strength of five gene groups classified by

187 average gene expression levels from several data sets.

188

189 Figure 3: Noise-plasticity scatter plots for the SS data set (Table 1) for the five gene
 190 groups classified by average gene expression level.

191

192 **Dependency of gene function on noise-plasticity correlations**

193 The noise-plasticity correlations of gene groups classified as “essential” genes
 194 (Meinke et al., 2008) were estimated for each experimental data set (Table 4(a)).
 195 Strong noise-plasticity correlations were obtained from most of the data sets except the
 196 PH data set. Next, the 22,746 genes were classified into the Gene Ontology (GO) Slim
 197 terms from TAIR; the noise-plasticity correlations were then estimated for each group.

198 Significant noise-plasticity correlations were found regardless of the nature of the gene
 199 group, and high correlation coefficients were always obtained for groups containing
 200 more than 1000 genes (Table 4(b) and Supplementary Table S1). However, low
 201 correlation coefficients were obtained in some small gene groups, e.g., the PH data set
 202 classified as “generation of precursor metabolites and energy.”

(a)		Data Sets						# of genes
Gene class		SS	SR	PS	ER	PH	SU	
Essential genes		0.594221533	0.620498722	0.611344186	0.779395159	0.310282866	0.561288897	481

(b)		Data Sets						# of genes
Gene class		SS	SR	PS	ER	PH	SU	
GO Slim biological process	multicellular organismal development	0.777901784	0.77590979	0.76517542	0.879061975	0.618875647	0.721621913	3408
	transport	0.806768388	0.779186949	0.719216124	0.861581653	0.615249087	0.68722564	3276
	signal transduction	0.820602108	0.792641264	0.692514902	0.891325264	0.693661654	0.761492046	1831
	cellular component organization	0.765876131	0.752584687	0.722483496	0.856916337	0.57692963	0.707008042	3456
	cellular process	0.798034579	0.782971878	0.751303878	0.877148094	0.634387429	0.732883121	12297
	DNA metabolic process	0.782529383	0.666095033	0.844019501	0.913947662	0.73702052	0.612254361	804
	RNA localization	0.736251896	0.459853141	0.749062176	0.689480405	0.407095538	0.582648256	67
	protein metabolic process	0.789746546	0.75550503	0.7378335	0.862661771	0.626479244	0.708425593	4183
	generation of precursor metabolites and energy	0.637920223	0.793310459	0.479428222	0.687023532	0.221118249	0.753399527	571
	transcription, DNA- dependent	0.808018159	0.796249517	0.780831718	0.900260213	0.703566562	0.763686382	2228
	metabolic process	0.80529708	0.78527943	0.757569657	0.879157491	0.640619377	0.734568262	11591
	response to abiotic stimulus	0.765058976	0.760153724	0.67062848	0.844872619	0.589955057	0.679993856	2682
	response to biotic stimulus	0.832086965	0.764543076	0.599308809	0.814099573	0.604496842	0.707391195	1374
	response to stress	0.821338172	0.778983491	0.698520265	0.867255788	0.643517632	0.710583396	3857

204 Table 4: (a) Noise-plasticity correlations among gene groups classified as essential

genes, and (b) those among gene groups classified by Gene Ontology (GO) terms (Biological processes) from several data sets (Table 1). For all correlation coefficients, p-values of less than 10^{-4} were obtained.

Genes exhibiting high responses to plant hormones [indole acetic acid (IAA), zeatin, gibberellic acid (GA), 1-aminocyclopropane-1-carboxylic acid (ACC), brassinolide (BL), abscisic acid (ABA) and methyl jasmonate (mJA)] were grouped and their noise-plasticity correlations estimated in each data set. Strong noise-plasticity correlations were obtained for all gene groups (Table 5).

Gene class		Data Sets						# of genes
		SS	SR	PS	ER	PH	SU	
Hormone response genes	IAA	0.895791776	0.897672319	0.802838469	0.893207293	0.723767073	0.862105274	4550
	Zeatin	0.825813936	0.848923607	0.677984814	0.793822528	0.566258366	0.778086978	4550
	GA	0.819367447	0.844356479	0.6676091	0.785805148	0.564767919	0.76607735	4550
	ABA	0.781056696	0.827645964	0.700394021	0.824830726	0.595547395	0.80895369	4550
	MJ	0.808847447	0.842218737	0.696383404	0.818964635	0.565759064	0.799685123	4550
	ACC	0.82858931	0.848031519	0.672945983	0.800435685	0.574560917	0.773563269	4550
	BL	0.816362997	0.849880114	0.684714359	0.8016745	0.577559444	0.771162878	4550

Table 5: Noise-plasticity correlations of the gene groups showing plant hormone responsiveness for several data sets (Table 1). For all correlation coefficients, p-values of less than 10^{-4} were obtained.

Relationship between circadian rhythms and noise-plasticity correlations

The 22,746 genes were assigned to five gene groups on the basis of the correlation between their expression level and circadian rhythms (Higher, top 20% genes; High, top 20~40% genes; Middle, top 40~60% genes; Low, top 60~80% genes; and Lower, lowest 20% genes). Correlation coefficients were then estimated for each experimental data set (Table 6) from the noise-plasticity scatter plots (Figure 4 and Supplementary Figure S4). This analysis indicated that significant noise-plasticity correlations were present in all gene groups. However, the gene groups with a stronger correlation between gene expression level and circadian rhythm tended to show weaker noise-plasticity correlation than other groups.

Gene class		Data Sets						# of genes
		SS	SR	PS	ER	PH	SU	
Correlations with circadian rhythm	Lower	0.920045389	0.891384101	0.860561377	0.937665389	0.795718454	0.893298791	4545
	Low	0.903607033	0.872385705	0.836301432	0.928875391	0.750849369	0.850201092	4544
	Middle	0.852512795	0.846553647	0.809667114	0.922343383	0.682079987	0.804015191	4544
	high	0.784579079	0.8002751	0.773660065	0.899409403	0.568273608	0.721750279	4544
	higher	0.684126264	0.70732506	0.727442656	0.776911284	0.474371623	0.619838995	4545

Table 6: Noise-plasticity correlations among five gene groups classified by the correlations between their expression levels and circadian rhythm for several data sets (Table 1). For all correlation coefficients, p-values of less than 10^{-4} were obtained.

233

234 Figure 4: Noise-plasticity scatter plots of the five gene groups classified by the
 235 correlation between their expression levels and circadian rhythms for the SS data set
 236 (Table 1).

237

238 Discussion

239 Recent studies in budding yeast identified several gene groups that exhibit strong
 240 noise-plasticity correlations and others that do not show such correlations. For example,
 241 gene groups in which each gene has a promoter with a TATA box show strong
 242 noise-plasticity correlation for expression levels; by contrast, those without a TATA

box do not show this correlation (Lehner, 2010). In the present study on *Arabidopsis*, the noise-plasticity correlations of groups containing genes with TATA promoters were similarly larger than those without TATA promoters. However, the difference in the strength of the noise-plasticity correlations in *Arabidopsis* was much smaller than found in budding yeast (Table 7).

In *E. coli*, only gene groups with higher mean expression levels exhibit significant correlations between expression noise and plasticity (Singh, 2013). In contrast, in *Arabidopsis*, strong noise-plasticity correlations were obtained for most gene groups, and gene groups with low mean expression levels exhibited particularly strong correlations (Table 3(a), Table 7). Moreover, the negative correlations between the noise-plasticity correlation coefficients and mean expression levels were greater for the gene group without TATA promoters in *Arabidopsis* (Table 3(b)(c)). On the other hand, little correlation between the noise-plasticity correlation coefficients and mean expression levels has been reported for both gene groups with and without TATA promoters in budding yeast (Lehner, 2010) (Table 7). Thus, the influence of mean expression level on noise-plasticity relationships might differ greatly from that in

259 unicellular organisms.

260 Furthermore, in budding yeast and *E. coli*, gene groups with essential functions
261 in cell growth and those with dosage-sensitive functions do not show strong
262 noise-plasticity correlations (Lehner, 2010; Singh, 2013). Indeed, the noise-plasticity
263 correlations for essential gene groups were weaker than those for all genes in
264 *Arabidopsis*. However, in *Arabidopsis*, stronger noise-plasticity correlations were
265 found for essential gene groups compared to budding yeast and *E. coli* (Table 4, Table
266 7), and were also found for most gene groups classified by GO Slim terms (Table 7,
267 and Supplementary Tables S1). Moreover, strong noise-plasticity correlations were
268 obtained for several gene groups exhibiting sensitivity to plant hormones (both growth
269 hormones and stress hormones). Thus, strong noise-plasticity correlations are expected
270 in most gene groups independent of their functional roles in *Arabidopsis*.

(a) Gene class	Yeast (Lehner 2010)		E. coli (Singh 2013)	Arabidopsis (SR)	
All genes	0.3		0.14	0.84	
TATA genes	0.62		*****	0.8	
non-TATA genes	0.16		*****	0.71	
Lower (expression level)	TATA	0.58	All	All	0.78
	nonTATA	0.19		TATA	0.69
				non-TATA	0.75
Low (expression level)	TATA	0.70	All	All	0.65
	nonTATA	0.24		TATA	0.68
				non-TATA	0.66
Middle (expression level)	TATA	0.68	All	All	0.60
	nonTATA	0.20		TATA	0.66
				non-TATA	0.55
High (expression level)	TATA	0.70	All	All	0.58
	nonTATA	0.28		TATA	0.69
				non-TATA	0.55
Higher (expression level)	TATA	0.61	All	All	0.61
	nonTATA	0.25		TATA	0.74
				non-TATA	0.55
Essential genes	0.15		-0.01	0.62	

271

(b) Gene class (GO slim)	Yeast (Lehner 2010)		Arabidopsis (SR)	
molecular_function	TATA	0.65	All	0.82
	nonTATA	0.18	TATA	0.81
			non-TATA	0.71
structural molecule activity	TATA	0.57	All	0.64
	nonTATA	-0.37	TATA	0.49
			non-TATA	0.46
transporter activity	TATA	0.46	All	0.81
	nonTATA	0.37	TATA	0.74
			non-TATA	0.74
protein binding	TATA	0.54	All	0.75
	nonTATA	0.1	TATA	0.84
			non-TATA	0.68
cell wall	TATA	0.20	All	0.82
	nonTATA	0.14	TATA	0.84
			non-TATA	0.73
nucleus	TATA	0.57	All	0.81
	nonTATA	0.14	TATA	0.80
			non-TATA	0.70
cytoplasm	TATA	0.57	All	0.78
	nonTATA	0.15	TATA	0.82
			non-TATA	0.67
mitochondrion	TATA	0.48	All	0.82
	nonTATA	0.32	TATA	0.84
			non-TATA	0.65
ribosome	TATA	0.30	All	0.60
	nonTATA	-0.29	TATA	0.61
			non-TATA	0.45

Gene class (GO slim)	Yeast (Lehner 2010)		Arabidopsis (SR)	
plasma membrane	TATA	0.51	All	0.77
	nonTATA	0.50	TATA	0.79
			non-TATA	0.70
generation of precursor metabolites and	TATA	0.24	All	0.79
	nonTATA	0.50	TATA	0.89
			non-TATA	0.76
transcription	TATA	0.76	All	0.80
	nonTATA	0.07	TATA	0.78
			non-TATA	0.70
transport	TATA	0.59	All	0.78
	nonTATA	0.25	TATA	0.79
			non-TATA	0.71
response to stress	TATA	0.68	All	0.78
	nonTATA	0.16	TATA	0.82
			non-TATA	0.72
signal transduction	TATA	0.62	All	0.79
	nonTATA	0.31	TATA	0.86
			non-TATA	0.72
biological_process	TATA	0.67	All	0.82
	nonTATA	0.28	TATA	0.81
			non-TATA	0.71
membrane	TATA	0.57	All	0.77
	nonTATA	0.29	TATA	0.78
			non-TATA	0.69
transferase activity	TATA	0.56	All	0.76
	nonTATA	0.12	TATA	0.79
			non-TATA	0.65

272

273 Table 7: (a) Comparison of noise-plasticity correlation strength for (a) all genes,

274 TATA and, non-TATA gene groups, gene groups with different expression levels among

275 budding yeast, *E. coli*, and *Arabidopsis*, and (b) for common GO Slim terms between
276 budding yeast and *Arabidopsis*. The results from the data set SR (Table 1) are typical
277 of those in *Arabidopsis*.

278

279 However, the strength of the correlation between gene expression level and
280 circadian rhythm did influence noise-plasticity relationships in *Arabidopsis*. Gene
281 groups with a high correlation with the circadian rhythm exhibited lower
282 noise-plasticity correlations than other gene groups. Thus, while the functional roles of
283 the genes did not influence noise-plasticity relationships, the correlation with circadian
284 rhythm did appear to be essential to this relationship in *Arabidopsis*.

285 There were some exceptions to general robustness of noise-plasticity correlations.
286 For example, noise-plasticity correlations for infection with *Phytophthora infestans*
287 (from PH data sets) tended to be weaker than those for the other treatment groups
288 (Table 2, Table 3). In the PH data set, gene groups that had high mean expression
289 levels and that were classified in the GO term “generation of precursor metabolites and
290 energy” exhibited comparatively weak noise-plasticity correlations for the pathogen

291 (Figure 5). This finding indicates that the strength of the noise-plasticity correlations
 292 depends on the properties of the treatment.

293
 294 Figure 5: Noise-plasticity relationship of the gene group with high mean expression
 295 levels and classified in the GO term “generation of precursor metabolites and energy.”
 296 This group exhibited weak noise-plasticity correlations for *Phytophthora infestans*.
 297 (PH, Table 1)

298

299 The results described in the present report suggest that the characteristics of
 300 noise-plasticity correlations in *Arabidopsis* differ from those in budding yeast and *E.*
 301 *coli*. In *Arabidopsis*, noise-plasticity correlations are essentially robust at different ages
 302 and in different tissues, and are only weakly influenced by promoter architecture, mean
 303 expression level, and circadian rhythm.

Multicellular organisms exhibit different circadian rhythms, cell differentiation patterns, and cell-cell interactions from primitive unicellular organisms such as yeast and *E. coli*. Moreover, multicellular organisms also show more complex higher order chromosome structures. For example, *Arabidopsis* chromosomes are considerably larger than those of the budding yeast: the genome size of the smallest chromosome of *Arabidopsis* (chromosome 4) is ~18 Mb (total genome size ~120 Mb) while that of the largest chromosome (chromosome 4) of budding yeast is 1.5 Mb (total genome size ~12 Mb). Thus, the *Arabidopsis* chromosomes are expected to contain more complex hierarchical structures. FISH and Hi-C analyses have identified topologically associated domain-like structures in *Arabidopsis* that are absent in budding yeast (Pecinka et al., 2004; Duan et al., 2010; Schubert et al., 2012, 2014; Feng et al., 2014; Grob et al., 2014; Wang et al., 2015).

Thus, we conjecture that gene regulation in *Arabidopsis* is more influenced by circadian rhythm-mediated global temporal regulation and by global structural complexities and transitions in chromosomes than by the local characteristics of the loci as in yeast and *E. coli*. This argument also suggests that noise-plasticity

relationships differ between unicellular and multicellular organisms. This prediction needs to be further tested using gene expression data from a wider range of organisms.

Materials and Methods

Data sources for gene classification

Data on promoter architectures, i.e., whether or not they include TATA boxes, were obtained from The *Arabidopsis* Gene Regulatory Information Server (AGRIS: <http://arabidopsis.med.ohio-state.edu/AtcisDB/corepromoters.html>). Here, two types of classification for promoter architecture are provided, namely, Motif Search and PlantProm. In these databases, not all genes are completely classified as to whether or not they include TATA boxes; 1707 and 3347 genes were classified as having TATA boxes and 10116 and 8474 genes were classified as without TATA boxes by Motif Search and PlantProm, respectively. In the present report, only classified genes were used for the analysis of noise-plasticity relationships of genes with and without TATA boxes.

In order to classify each gene, the complete Gene Ontology (GO) biological

classification list and GO Slim classification list were obtained from TAIR (<http://www.arabidopsis.org>). Data on “essential” genes were obtained from SeedGenes Project (Meinke et al., 2008; <http://www.seedgenes.org/GeneList>).

Definitions and estimations of gene expression noise and plasticity

The growth conditions and ages differed among the experimental data sets. Thus, for each data set, the noise-plasticity relationship was measured individually.

Recent gene expression analyses indicated that from *E. coli* to mammalian cells, the fluctuations in expression level for each gene tend to follow a log-normal distribution (Sato et al., 2003; Furusawa et al., 2005; Chang et al., 2008; Konishi et al., 2008). In this case, the log of the gene expression level is generally considered suitable for various statistical analyses since its distribution function is essentially Gaussian. Thus, expression noise and plasticity for each gene are defined and estimated using the deviations among $\log_2$ [microarray signal intensity] as described in an earlier study (Sato et al., 2003). These estimations reveal that the values for noise and plasticity have no dimensions and are not influenced by gene specific characteristic scales such

352 as average expression levels.

353 The expression noise for each gene is defined as the stochastic variation among
 354 samples of $\log_2$ intensities under non-treated conditions (control data, “Mock”
 355 condition data, etc.). For two or more sets of data for microarray signal intensities
 356 obtained under the same conditions at the same time point t , $C_i(t)$ ($i = 1, 2$, or 3
 357 indicates sample index), the expression noise for each gene is estimated by the time
 358 average of standard deviations among the sample data, $Std\{ \}_{i}$, as $N =$
 359 $\langle Std\{\log_2 C_i(t)\}_i \rangle_t$ where $\langle \rangle_t$ indicates the average over t (Fig. 6(a)). In addition,
 360 the average expression levels of each gene under non-treated conditions are defined as
 361 $A = \langle \langle \log_2 C_i(t) \rangle_i \rangle_t$ where $\langle \rangle_i$ indicates the average over i .

362 The expression plasticity (P) for each gene is defined by the absolute variation
 363 between sample averages of $\log_2$ intensities under stress and non-treated (control or
 364 Mock) conditions, $\langle \log_2 T_i(t) \rangle_i$ and $\langle \log_2 C_i(t) \rangle_i$, where $T_i(t)$ indicates the i -th
 365 sample of the microarray signal intensity under a treated condition at time t . The
 366 plasticity is estimated as the time average of absolute deviations between the sample
 367 average of $\log_2$ intensities of the treated and non-treated conditions measured as $P =$

368 $\langle |\langle \log_2 T_i(t) \rangle_i - \langle \log_2 C_i(t) \rangle_i| \rangle_t$ where $\langle \rangle_i$ indicates the average over i (Fig. 6(b)).

370 Figure 6: Illustrations of the definitions of (a) noise N , and (b) plasticity P .

371

372 The noise (N) and plasticity (P) of genes for each data set are named as N_{ds} and

373 P_{ds} , such as N_{SS} , N_{SU} , ... P_{SS} and P_{SU} . Note that the data sets SS and SR involve the data

374 of 8 stress treatments (cold, osmotic shock, salt, drought, genomic, UV, wound, and

375 heat stresses). Thus, P_{SS} and P_{SR} are estimated as the average of P among these

376 treatments.

378 Selection of hormone-response genes

379 A microarray analysis data set on plant hormone responses is available in

380 AtGenExpress and was used here to identify plant hormone-related gene groups. The

same 22,746 genes as in Table 1 were used here; two samples of three time points data were obtained for control and each hormone applied (IAA, zeatin, GA, ACC, BL, ABA, and mJA) (Goda et al., 2008).

The hormone response (R) for each gene is defined by the absolute variation between sample averages of $\log_2$ intensities under hormone-treated and non-treated conditions, $\langle \log_2 A_i(t) \rangle_i$ and $\langle \log_2 C_i(t) \rangle_i$, where $A_i(t)$ indicates the i -th sample of the microarray signal intensity under a treatment condition at time t . The hormone response is estimated as the time average of absolute deviations between the sample average of $\log_2$ intensities in the treated and non-treated conditions measured as $R = \langle |\langle \log_2 A_i(t) \rangle_i - \langle \log_2 C_i(t) \rangle_i| \rangle_t$, where $\langle \rangle_i$ and $\langle \rangle_t$ indicate the average over i and time point t . For each hormone, genes with the top 20% for R were selected as hormone-response genes (more than 90% of selected genes for each hormone treatment hold $R > 1$).

Definitions of correlation between gene expression levels and circadian rhythm

For each data set, the correlation between each gene expression level and

397 circadian rhythm was defined as the maximum value among the absolute values of
398 Pearson correlation coefficients between the expression levels of the gene and one of
399 the clock-associated genes in the control conditions. Here, *CCA1*, *LHY1*, *PRR9*, *PRR7*,
400 *PRR5*, *TOC1*, *LUX*, *ELF4*, and *ELF3* were chosen as clock-associated genes since they
401 are known to constitute the core regulatory network of the circadian rhythm in
402 *Arabidopsis* (Nakamichi, 2011).

403

404 **Correlation estimations**

405 The correlations among several values were estimated using Spearman
406 correlation coefficients. The statistical analyses were performed using R
407 (<http://www.r-project.org>).

408

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Author Contributions

A.A. and A.J.N. conceived the project. K.H. and A.A. performed the data analysis, and
A.A. and A.J.N. wrote the manuscript.

References

Bajic D., Poyatos J. F. (2012) Balancing noise and plasticity in eukaryotic gene

429 expression. BMC Genom. 343: 1-11. doi:10.1186/1471-2164-13-343

430

431 Blake W. J., Kaern M., Cantor C. R., Collins J. J. (2003) Noise in eukaryotic gene

432 expression. Nature, 422: 633-637. doi:10.1038/nature01546

433

434 Chang H. H., Hemberg M., Barahona M., Ingber D. E., Huang S. (2008)

435 Transcriptome-wide noise controls lineage choice in mammalian progenitor cells.

436 Nature 453: 544-547. doi: 10.1038/nature06965

437

438 Chodavarapu R. K., Fen S., Bernatavichute Y. V., Chen P.-Y. et al. (2010) Relationship

439 between nucleosome positioning and DNA methylation. Nature 466: 388–392.

440 doi:10.1038/nature09147

441

442 Choi J. K., Kim Y. J. (2008) Epigenetic regulation and the variability of gene

443 expression. Nat. Genet. 40: 141-147. doi: 10.1038/ng.2007.58

444

445 Choi J. K., Kim Y. J. (2009) Intrinsic variability of gene expression encoded in
446 nucleosome positioning sequences. *Nat. Genet.* 41: 498–503. doi: 10.1038/ng.319.
447

448 Cokus S. J. et al. (2008) Shotgun bisulphite sequencing of the *Arabidopsis* genome
449 reveals DNA methylation patterning. *Nature* 452: 215–219. doi: 10.1038/nature06745
450

451 Duan Z., Andronescu M., Schutz K., McIlwain S., et al. (2010) A three-dimensional
452 model of the yeast genome. *Nature* 465: 363–367. doi: 10.1038/nature08973
453

454 Elowitz M. B., Levine A. J., Siggia E. D., Swain P. S. (2002) Stochastic gene
455 expression in a single cell. *Science* 297: 1183–1186. doi: 10.1126/science.1070919
456

457 Feng S, Cokus S. J., Schubert V., Zhai J. et al. (2014) Genome-wide Hi-C analyses in
458 wild-type and mutants reveal high-resolution chromatin interactions in *Arabidopsis*.
459 *Mol. Cell* 55: 694–707. doi: 10.1016/j.molcel.2014.07.008
460

461 Furusawa C., Suzuki S., Kashiwagi A, Yomo T., Kaneko K. (2005) Ubiquity of
462 log-normal distributions in intra-cellular reaction dynamics. BIOPHYSICS 1: 25-31.
463 doi: 10.2142/biophysics.1.25

464

465 Goda H., Sasaki E., Akiyama K., Maruyama-Nakashita A., et al. (2008) The
466 AtGenExpress hormone and chemical treatment data set: experimental design, data
467 evaluation, model data analysis and data access. Plant J. 55: 526-42. doi:
468 10.1111/j.0960-7412.2008.03510.x.

469

470 Golding I., Paulsson J., Zawilski S. M., Cox E. C. (2005) Real-time kinetics of gene
471 activity in individual bacteria. Cell 123: 1025–1036. doi: 10.1016/j.cell.2005.09.031

472

473 Grob S., Schmid M. W., Grossniklaus U. (2014) Hi-C analysis in Arabidopsis identifies
474 the KNOT, a structure with similarities to the flamenco locus of Drosophila. Mol. Cell
475 55: 678-693. doi: 10.1016/j.molcel.2014.07.009

476

477 Kaern M., Elston T. C., Blake W. J., Collins J. J. (2005) Stochasticity in gene
478 expression: from theories to phenotypes. *Nat. Rev. Genet.* 6: 451–464.
479 doi:10.1038/nrg1615

480

481 Kalmar T., Lim C., Hayward P., Munoz-Desclazo S. et al. (2009) Regulated
482 fluctuations in Nanog expression mediate cell fate decisions in embryonic stem cells.
483 *PLoS Biol.* 7: e1000149. doi: 10.1371/journal.pbio.1000149

484

485 Kaneko K. (2006) *Life: An Introduction to Complex Systems Biology*. Springer Berlin,
486 Heidelberg.

487

488 Kilian J., Whitehead D., Horak J., Wanke D. et al. (2007) The AtGenExpress global
489 stress expression data set: protocols, evaluation and model data analysis of UV-B light,
490 drought and cold stress responses. *Plant J.* 50: 347-63. doi:
491 10.1111/j.1365-313X.2007.03052.x

492

- 493 Konishi T., Konishi F., Takasaki S., Inoue K., et al. (2008) Coincidence between
494 transcriptome analyses on different microarray platforms using a parametric
495 framework. PLoS ONE 3: e3555. doi: 10.1371/journal.pone.0003555
496
- 497 Landry C. R., Lemos B., Rifkin S. A., Dickinson W. J., Hartl D. L. (2007) Genetic
498 properties influencing the evolvability of gene expression. Science 317: 118–121. doi:
499 10.1126/science.1140247
500
- 501 Lehner B. (2010) Conflict between noise and plasticity in yeast. PLoS Genet. 6:
502 e1001185. doi:10.1371/journal.pgen.1001185
503
- 504 Lehner B., Kaneko K. (2011) Fluctuation and response in biology. Cell. Mol. Life Sci.
505 68: 1005–1010. doi: 10.1007/s00018-010-0589-y
506
- 507 Less H., Galili G. (2008) Principal transcriptional programs regulating plant amino
508 acid metabolism in response to abiotic stresses. Plant Physiol. 147: 316–330. doi:

509 <http://dx.doi.org/10.1104/pp.108.115733>

510

511 Maruyama-Nakashita A., Nakamura Y., Watanabe-Takahashi A., Inoue E. et al. (2005)

512 Identification of a novel cis-acting element conferring sulfur deficiency response in

513 *Arabidopsis* roots. *Plant J.* 42:305-314. doi: 10.1111/j.1365-313X.2005.02363.x

514

515 Matesanz, S., Gianoli, E., & Valladares, F. (2010). Global change and the evolution of

516 phenotypic plasticity in plants. *Annals of the New York Academy of Sciences*,

517 1206:35-55. doi: 10.1111/j.1749-6632.2010.05704.x

518

519

520 Meinke D, Muralla R, Sweeney C, Dickerman A (2008) Identifying essential genes in

521 *Arabidopsis thaliana*. *Trends Plant Sci.*13: 483-491. doi:10.1016/j.tplants.2008.06.003

522

523 Mitsui K., Tokuzawa T., Itoh H., Segawa K. et al. (2003) The homeoprotein Nanog is

524 required for maintenance of pluripotency in mouse epiblast and ES cells. *Cell* 113:

525 631–642. doi: 10.1016/S0092-8674(03)00393-3

526

527 Nagano A. J., Sato Y., Mihara M., Antonio B. A. et al. (2012) Deciphering and

528 prediction of transcriptome dynamics under fluctuating field conditions. *Cell* 151:

529 1358–1369. doi: <http://dx.doi.org/10.1016/j.cell.2012.10.048>

530

531 Nakamichi N. (2011) Molecular mechanisms underlying the *Arabidopsis* circadian

532 clock. *Plant Cell Physiol.* 52: 1709-1718. doi: 10.1093/pcp/pcr118

533

534 Nemhauser J. L., Hong F. X. and Chory J. (2006) Different plant hormones regulate

535 similar processes through largely nonoverlapping transcriptional responses. *Cell*, 126,

536 467–475. doi: 10.1016/j.cell.2006.05.050

537

538 Newman J. R., Ghaemmaghami S., Ihmels J., Breslow D. K. et al. (2006) Single-cell

539 proteomic analysis of *S. cerevisiae* reveals the architecture of biological noise. *Nature*

540 441: 840-846. doi:10.1038/nature04785

541

542 Ochiai H., Sugawara T., Sakuma T., Yamamoto T. (2014) Stochastic promoter
543 activation affects Nanog expression variability in mouse embryonic stem cells.
544 Scientific Reports 4: 7125. doi:10.1038/srep07125

545

546 Pascuzzi P. E., Flores-Vergara M. A., Lee T.-J., Sosinski B. et al. (2014) In vivo
547 mapping of Arabidopsis scaffold/matrix attachment regions reveals link to
548 nucleosome-disfavoring poly(dA:dT) tracts. Plant Cell 26: 102-120. doi:
549 <http://dx.doi.org/10.1105/tpc.113.121194>

550

551 Pecinka A, Schubert V., Meister A., Kreth G. et al. (2004) Chromosome territory
552 arrangement and homologous pairing in nuclei of Arabidopsis thaliana are
553 predominantly random except for NOR-bearing chromosomes. Chromosoma 113:
554 258-269. doi: 10.1007/s00412-004-0316-2

555

556 Roudier F., Ahmed I., Berard C., Sarazin A. et al. (2011) Integrative epigenomic

557 mapping defines four main chromatin states in Arabidopsis. EMBO J. 30: 1928–1938.

558 doi: 10.1038/emboj.2011.103

559

560 Sato K., Ito Y., Yomo T., Kaneko K. (2003) On the relation between fluctuation and

561 response in biological systems. Proc. Natl. Acad. Sci. USA 100:14086–14090. doi:

562 10.1073/pnas.2334996100

563

564 Schubert V., Berr A., Meister A. (2012) Interphase chromatin organisation in

565 Arabidopsis nuclei: constraints versus randomness. Chromosoma 121:369-387. doi:

566 10.1007/s00412-012-0367-8

567

568 Schubert V., Rudnik R., Schubert I. (2014) Chromatin associations in Arabidopsis

569 interphase nuclei. Front. Genet. 5: 389 1-11. doi: 10.3389/fgene.2014.00389

570

571 Sequeira-Mendes J., Araguez I, Peiro R, Mendez-Giraldez R. et al. (2014) The

572 functional topography of the Arabidopsis genome is organized in a reduced number of

573 linear motifs of chromatin states. *Plant Cell* 26: 2351-2366. doi:
574 <http://dx.doi.org/10.1105/tpc.114.124578>
575
576 Shen X., Pettersson M., Rönnegård L., Carlborg Ö. (2012) Inheritance beyond plain
577 heritability: variance-controlling genes in *Arabidopsis thaliana*. *PLoS Genet.* 8: e
578 1002839. doi: 10.1371/journal.pgen.1002839
579
580 Silander O. K., Nikolic N., Zaslaver A., Bren A., Kikoin I., et al. (2012) A
581 genome-wide analysis of promoter-mediated phenotypic noise in *Escherichia coli*.
582 *PLoS Genet.* 8: e1002443. doi: 10.1371/journal.pgen.1002443
583
584 Singh G. P. (2013) Coupling between noise and plasticity in *E. coli*. *G3(Bethesda)* 3:
585 2115-2120. doi: 10.1534/g3.113.008540.
586
587 So L. H., Ghosh A., Zong C., Sepulveda L. A., Segev R., et al. (2011) General
588 properties of transcriptional time series in *Escherichia coli*. *Nat. Genet.* 43: 554–560.

589 doi:10.1038/ng.821

590

591 Sultan S. E. (2000). Phenotypic plasticity for plant development, function and life

592 history. Trends Plant Sci. 5: 537-542. doi:10.1016/S1360-1385(00)01797-0

593

594 Taniguchi Y., Choi P. J., Li G. W., Chen H., Babu M., et al. (2010) Quantifying E. coli

595 proteome and transcriptome with single-molecule sensitivity in single cells. Science

596 329: 533-538. DOI: 10.1126/science.1188308

597

598 The Arabidopsis Genome Initiative (2000) Analysis of the genome sequence of the

599 flowering plant Arabidopsis thaliana. Nature 408: 796-815. doi:10.1038/35048692

600

601 Tirosh I., Barkai N. (2008) Two strategies for gene regulation by promoter

602 nucleosomes. Genome Res. 18: 1084-1091. doi: 10.1101/gr.076059.108

603

604 Valladares, F., Gianoli, E., & Gómez, J. M. (2007). Ecological limits to plant

605 phenotypic plasticity. New Phytologist, 176: 749-763. doi:
606 10.1111/j.1469-8137.2007.02275.x
607
608 Wang C., Liu C., Roqueiro D., Grimm D. et al. (2015) Genome-wide analysis of local
609 chromatin packing in *Arabidopsis thaliana*. Genome Res. 25: 246-256. doi:
610 10.1101/gr.170332.113
611
612 Wittenberg T A., Tzin V., Angelovici R., Less H., Galili G. (2012) Deciphering
613 energy-associated gene networks operating in the response of *Arabidopsis* plants to
614 stress and nutritional cues. Plant J. 70: 954–966. doi:
615 10.1111/j.1365-313X.2012.04926.x
616
617 Woods H. A. (2014) Mosaic physiology from developmental noise: within-organism
618 physiological diversity as an alternative to phenotypic plasticity and phenotypic
619 flexibility. J. Exp. Biol. 217: 35-45. 10.1242/jeb.089