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Correction: Proportionality between variances in gene expression induced by noise and mutation: consequence of evolutionary robustness

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Although the simulation data as well as the conclusion on the proportionality between $V_{ip}(i)$ and $V_g(i)$ in the work [1] is correct, interpretation of some data therein should be corrected. As the sampling number ($L = 200$) to measure the average gene expression level is not large enough, there is a bias in the estimate in $V_g(i)$. Finiteness in the number of sampling L will generally cause a bias of the order of $V_{ip}(i)/L$, in the estimate of the variance $V_g(i)$. The too good proportionality between $V_{ip}(i)$ and $V_g(i)$ for large σ, shown in Figure two (a)(b) of [1] (especially for small $V_g(i)$), is due to this artifact. Accordingly, the sharp peak at $\sim 1/L = 1/200$ in Figure three of [1] is due to this insufficiency by the sample number.

Still, the proportionality between the two variances $V_{ip}(i)$ and $V_g(i)$, albeit not so sharp, holds, as already observed in the region with larger $V_g(i)$ in [1]. We have simulated the model with a larger number of samples, i.e., $N = L = 1000$. As is shown in Figure 1, the proportionality is well discernible, where the proportion coefficient $V_g(i)/V_{ip}(i)$ decreased with the increase in the noise level σ, which was already observed in the broad peak beyond $1/L$ in Figure three of [1]. This broad peak beyond $1/L$ in Figure three of [1] was found to be sharper as N was increased, from 200 to 1000. This peak indeed corresponds to the proportion coefficient extracted from Figure 1 in the present Correction. As the noise level σ was increased, the peak position $\rho = V_g(i)/V_{ip}(i)$ decreased. Hence for larger σ, larger L is needed to get reliable estimate in the proportion coefficient. As for Figure five and Figure six of [1], the sharp proportionality for $V_g(i) \lesssim 0.001$ is due to the above bias, while the discussion therein concerns with the approach of $V_g(i)$ to $V_{ip}(i)$ at larger $V_g(i)$, which is not affected by the bias here.

To sum up, the main claim of [1], i.e., proportionality between $V_{ip}(i)$ and $V_g(i)$ is valid, but the value of the proportion coefficient $\rho = V_g(i)/V_{ip}(i)$ should be corrected. It decreases with the noise level, in contrast to the discussion in [1] for large σ. Major factor on this proportionality is attributed to the correlation of each variance with the average value $\overline{Sign(x(i))}$: In other words, a state with an intermediate expression level (i.e., smaller $|\overline{Sign(x(i))}|$) can be more easily switched on or off, both by noise and also by mutation, and hence the variances generally increase as $|\overline{Sign(x(i))}|$ approaches 0. Still, some

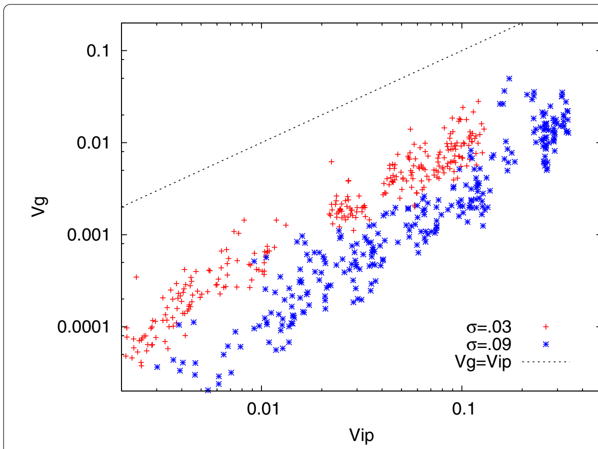

Figure 1 Relationship between $V_g(i)$ and $V_{ip}(i)$. As described in the Method section of [1], $V_{ip}(i)$ was computed as the variance of the distribution of $Sign(x_i)$ over L runs for an identical genotype, while $V_g(i)$ was computed as a variance of the distribution of $(\overline{Sign(x_i)})$ over N individuals, where $\overline{Sign(x_i)}$ was the mean over L runs. Here we adopted $N = L = 1000$, instead of 200 in [1]. $\sigma = 0.09$ (blue *) and 0.03 (red +). The plot of ($V_g(i)$ and $V_{ip}(i)$) for all genes i over 55-65th generations, where we have plotted only those genes with $V_g(i) > .0002$, as the those with smaller than that may have little accuracy in estimating $V_g(i)$.

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correlation between $V_{ip}(i)$ and $V_g(i)$ remains even after removing this correlation through $\overline{Sign(x(i))}$.

I regret any inconvenience that misintepretation of the data with an insufficient sample size may have caused.

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References

1. Kaneko K: **Proportionality between variances in gene expression induced by noise and mutation: consequence of evolutionary robustness.** *BMC Evol Biol* 2011, **11:**27.

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