Life After Earth

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Abstract

A recent study reported that there is evidence life may have originated prior to the formation of the Earth. That conclusion was based on a regression analysis of a certain data set involving evolution of functional genome size across major phyla. Here it is shown that if measurement errors and “confidence” intervals are taken into account, then the regression analysis of the same data set leads to conclusions that allow for life to have appeared after the formation of the Earth.

1 Introduction

Recently, Sharon and Gordon (2013) - hereafter SG - reported an analysis of data on the evolution of genetic complexity during the history of life on Earth. As a measure of genetic complexity SG use the functional genome size of major phylogenetic lineages, whose logarithms become the $y$-axis values of their data set, with the estimated dates of the transitions where these lineages first originated being the $x$-axis values. They performed regression on the data (on $y$ vs. $x$), and proposed that the $x$-intercept of the fit provides an estimate for the age of life.

The work was criticized on many levels, ranging from the manner in which the data was produced, to the way in which the data was analyzed. A fundamental problem is the paucity of data over the first 2 billion years or so of Earth’s history, resulting in large uncertainties in functional genome size at specific times. For instance, for prokaryotes, the size of the functional genome is guessed from the smallest present-day prokaryote genome. Exactly when this genome size evolved is a matter of conjecture; although an approximate date can be estimated from molecular clock type evolution rates based on more recent organisms, as some reviewers have pointed out (see, for instance, Sharov 2006), rates of increase of functional genome size could have been very different in the distant past. Fitting the data

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with an extrapolation based on a single, fixed rate of increase could lead to possibly incorrect conclusions. Likewise, the use of only coding regions of the genome as a measure of genome complexity has been pointed out as a potential problem, as non-coding regions could play a regulatory role and the associated complexity is unaccounted for when only coding regions are measured. Thus estimating genome complexity of extinct organisms based on an uncertain estimate of functional genome size of present-day organisms could be doubly flawed.

In addition to all of the above criticisms, there are additional concerns over the statistical analysis in SG. First, and foremost, is the way in which the regression fit is used to extrapolate far beyond the range of \( x \) values appearing in the data. It is well known that extrapolation can lead to misleading conclusions (Perrin 1904), and so, any conclusions regarding the age of life, based on extrapolation, should be considered with extreme caution. A second aspect of the SG regression fit is that it does not incorporate “confidence” intervals. Here, the term “confidence” is used loosely; the interval actually computed in this study is the prediction interval (see below). The inclusion of such intervals can lessen the misleading impacts of extrapolation, because prediction intervals generally widen as one moves away from the mean of the data. Then, the \( x \)-intercept is accompanied by a relatively wide range of values, all of which are equally likely values for the age of the life. In other words, inclusion of prediction intervals can further mitigate misleading conclusions. Another limitation of the SG regression analysis is that it does not account for uncertainty in the dates at which the transitions occurred (i.e., the \( x \)-values of the data), also known as measurement errors. As explained here, measurement errors generally reduce the slope of the regression fit, and consequently increase the value of the \( x \)-intercept. As such, measurement errors lead to overestimates for the age of life.

In this paper, a simple measurement error model is developed, and rudimentary prediction intervals are produced. First, an attempt is made to estimate the measurement errors, and then, it is shown that a measurement error model of the data leads to conclusions that are consistent with life having formed around 4.5-billion years ago. In short, we find that when the regression analysis includes prediction intervals and incorporates measurement errors, then the data used by SG provide no evidence to support the claim that life must have formed prior to the formation of the Earth.

2 Regression Effect

Consider a scatterplot of \( y \) vs. \( x \), displaying some amount of association between the two variables (e.g., Figure 1). It is well known that as the spread of the data increases, the slope of a least-squares fit approaches zero. This effect is known by a variety of names, including the regression effect (Bland and Altman 1994). It is demonstrated in Figure 1, where the black circles have less scatter than the red circles. The straight lines are the ordinary least-squares fits to respective data. It can be seen that increasing scatter leads to lower values of the slope. (In this particular case, the red circles have been generated by adding error to the \( x \)-values of the black circles.)
The mathematics underlying the regression effect is straightforward. It is easy to show

\[
\frac{\hat{y}(x) - \bar{y}}{s_y} = r \left( \frac{x - \bar{x}}{s_x} \right),
\]

where \(\hat{y}(x)\) is the predicted/fitted value, \(\bar{x}\) and \(\bar{y}\) are the sample mean of \(x\) and \(y\), respectively, and \(s_x, s_y\) are their sample standard deviations. The quantity \(r\) is Pearson’s correlation coefficient, and it measures the amount of scatter on the scatterplot. As \(r\) approaches zero (from either side), the predicted value \(\hat{y}(x)\) tends to the sample mean of \(y\). Indeed, this “regression to the mean” is the reason why the least-squares fit is called regression (Galton 1886). In summary, as the amount of scatter in the scatterplot of \(y\) vs. \(x\) increases, the least-square fit converges to a horizontal line with slope zero, and y-intercept equal to \(\bar{y}\).

3 Regression Dilution

The aforementioned scatter may be due to errors in \(x\), in \(y\), or both. In the most common form of regression, the predictor \(x\) is assumed to be error-free, and only the response is assumed to be subject to errors. Measurement error models (Buonaccorsi 2010; Fuller 1987) are designed to allow for both \(x\) and \(y\) to be subject to errors. Consequently, as expected from the previous example, measurement errors tend to “flatten” the least-squares line - a phenomenon called “regression dilution” (Buonaccorsi 2010; Fuller 1987). Moreover, if the measurement errors can be estimated, then one can undo the dilution.

A simple measurement error model is as follows: Let \((X_i, Y_i), i = 1, ..., a\), denote the true, error-free, values of two continuous random variables, satisfying the relation

\[
Y_i = \alpha^* + \beta^* X_i .
\]

The corresponding observed values \((x_i, y_i)\) can then be written as

\[
x_i = X_i + \omega_i , \quad y_i = Y_i + \epsilon_i ,
\]
where \( \omega_i \) and \( \epsilon_i \) are the measurement error in \( X \) and the error in \( Y \), respectively. For simplicity, it is assumed that both are normally distributed with zero mean, and variances given by \( \sigma_w^2 \) and \( \sigma_{\epsilon}^2 \). I.e., \( \omega_i \sim N(0, \sigma_w^2) \) and \( \epsilon_i \sim N(0, \sigma_{\epsilon}^2) \). In the functional model the \( X \) is assumed fixed (non-random), but in the structural model \( X \) is assumed to be a random variable (Buonaccorsi 2010; Fuller 1987). In the former, the \( a \) values of \( X_i \) are assumed to be fixed quantities, while in the latter they are considered to be a random sample taken from a population (or a distribution). The latter is adopted here, because it is more appropriate for the problem at hand. Again, for simplicity, one assumes \( X_i \sim N(\mu, \sigma_b^2) \). \[1\]

If one mistakenly ignores measurement errors (in \( X \)), and instead performs regression on \((x_i, y_i)\), i.e.,

\[
y_i = \alpha + \beta x_i + \epsilon_i ,
\]

then it can be shown that the least-squares estimate of the regression slope and y-intercept are given by (Fuller 1987; Draper and Smith 1998)

\[
\beta = \beta^*/\lambda , \quad \alpha = \bar{y} - (\beta^*/\lambda) \bar{x} ,
\]

with

\[
\lambda = 1 + \frac{\sigma_w^2}{\sigma_b^2} .
\]

Given that \( \lambda > 1 \), it follows that \( \beta < \beta^* \), i.e., the slope is “diluted” relative to the slope that would have been obtained if measurement errors were zero. Said differently, measurement errors tend to “flatten” the least-squares fit, and therefore, lead to an overestimate of the \( x \)-intercept. In the framework of SG, then, measurement errors lead to an overestimate for the age of life. In a measurement error model of SG’s data, the corrected \( x \)-intercept \( \bar{x} - \bar{y}/(\beta \lambda) \) estimates the age of life.

Equation (5) implies that one can correct this effect, by simply multiplying the observed regression coefficient \( \beta \) by \( \lambda \). In other words, the quantity \((\beta \lambda)\) is an estimator of \( \beta^* \). Similarly, the least square estimate of \( \alpha \) is \((\bar{y} - (\beta \lambda) \bar{x})\). In order to make these corrections, however, one must estimate \( \lambda \).

Frost and Thompson (2000) discuss six methods for estimating \( \lambda \), and the corresponding variance. One of the simpler methods examined there identifies \( \lambda \) as the inverse of the intraclass correlation coefficient (also known as the reliability ratio). One advantage of that estimator is that its variance has a simple expression:

\[
\frac{(\lambda^2 - 1)^2}{a} .
\]

Although in the next section an attempt is made to estimate \( \lambda \) itself, the main focus of the study is to consider the “inverse problem” of finding a range of \( \lambda \) values which lead to \( x \)-intercepts consistent with 4.5 billion years as the age of life.

\[1\] The subscripts “b” and “w” are motivated by “between-group” and “within-group” variances - language common to the analysis of variance formulation of regression (Montgomery 2009).
It is not necessary to find a specific $\lambda$ value which leads to an $x$-intercept of 4.5 billion years. A regression fit whose prediction interval includes an $x$-intercept of 4.5 billion years is sufficient, in the sense that it does not contradict the null hypothesis that life began after the formation of the Earth. To that end, we supplement all of the above estimates with prediction intervals. In order to construct such an interval, one must compute the variance for the corrected regression slope, a quantity which has been derived by Frost and Thompson (2000):

$$V[(\beta \lambda)] = \lambda^2 V[\beta] + \frac{1}{a}(\beta^2 + V[\beta])(\lambda^2 - 1)^2. \quad (8)$$

where Eq. (7) has been used.

There is an ambiguity in whether the appropriate interval for this problem is a confidence interval or a prediction interval (Ryan 1997). The former is designed to cover the true conditional mean of $y$, given $x$, a certain percentage of time, e.g., 95%. The latter is designed to cover a single prediction of $y$, a certain percentage of time. By construction, the prediction interval is wider than the confidence interval. Here, a prediction interval is considered, because our interest is in the $x$-intercept, which corresponds to a single prediction of $y$. The choice between the two intervals is of secondary importance. What is more important than the choice of the two intervals is that some interval must be considered.

The construction of prediction intervals in measurement error models is itself a complex issue and is considered by Buonaccorsi (1995). One relatively simple 95% prediction interval is given by $\hat{y}(x) \pm 1.96\sigma_{pe}$, where $\sigma_{pe}$ is the variance of the prediction error, given by

$$\sigma_{pe}^2 = \sigma_e^2 + \frac{\sigma_{w}^2}{a} + (X - \bar{X})^2 V[\beta \lambda] + [(\beta \lambda)^2 + V[\beta \lambda]] \sigma_b^2, \quad (9)$$

where $V[(\beta \lambda)]$ is given by Eq. 8, and $\sigma_e^2$ is estimated by the variance of the residuals. This is the expression derived in Buonaccorsi (1995) for the special case where the value of $X$ at which the prediction is made is a known (non-random) quantity. The first three terms on the right-hand side of Eq. (9) are the variance of the prediction error in the error-free case (Draper and Smith 1998); the last term is the result of measurement errors.

### 4 Estimating Measurement Errors

One may wonder what is a typical value of $\lambda$ for the data at hand. For that, $\sigma_b$ and $\sigma_w$ must be estimated. To that end, consider a situation where each $X_i$ is measured $n$ times. Denoting the resulting data as $x_{ij}, i = 1, ..., a, j = 1, ..., n$, it is known that unbiased estimates of $\sigma_b^2$ and $\sigma_w^2$ are

$$\left(\frac{s_b^2}{n} - \frac{s_w^2}{n}\right), \ s_w^2, \quad (10)$$

respectively, with $s_b^2$ and $s_w^2$ defined as

$$s_b^2 = \frac{n}{a-1} \sum_{i=1}^{a} (\bar{x_i} - \bar{x})^2, \quad s_w^2 = \frac{1}{a(n-1)} \sum_{i,j} (x_{ij} - \bar{x}_i)^2. \quad (11)$$
where an overline denotes averaging over the index with a dot (Montgomery 2009). For large \( n \), the quantity \( s_b^2/n \) converges to the sample variance of the \( X_i \), i.e., \( s_X^2 = \frac{1}{n-1} \sum_{i=1}^{n} (X_i - \overline{X})^2 \), which in turn can be estimated with the sample variance of the \( x_i \). For the data at hand, then, \( s_b^2/n \sim 1.86 \) billion years. In the large-\( n \) limit, the term \( s_w^2/n \) converges to zero, because in that limit \( s_w^2 \) itself converges to the constant \( \sigma_w^2 \). Therefore, asymptotically, \( \sigma_b \sim \sqrt{1.86} \sim 1.36 \).

The within-group standard deviation \( s_w \) reflects the spread in values or uncertainty of the dates of appearance of the respective functional genomes (e.g., prokaryote, eukaryote, worms, fish, mammals) used in the data analysis. While the statistical analysis presented here assumes that the \( a \) measurements all have common variance (i.e., homoscedastic), in reality the uncertainty in the time of appearance of a functional genome increases from present to past. Thus the largest errors or uncertainties are found in the oldest functional genome considered. As an example of dating uncertainty, while the earliest mammals are believed to have arisen about 225 million years ago based on early fossils (Rose 2006), molecular clock studies based on genomes place mammalian origins around 100 million years ago (Dawkins 2005). There is thus an uncertainty of the order of 100 million years or more in setting the time of the mammalian functional genome. The origin of eukaryotes has been identified to lie in the time interval between 2.3 billion and 1.8 billion years ago, thus with an uncertainty of 250 million years around the mean estimate of 2.05 billion years ago (Seilacher, Bose, and Pfluger 1998). Early fossil evidence for prokaryotes in lava beds has been dated to a time around 3.5 billion years ago (Furnes et al. 2004); however, it is unclear exactly when the functional genome size reached the present-day minimum value of around \( 5 \times 10^5 \); the uncertainty in this time value could easily be of the order of 1 billion years.

Within-group standard deviations in the dates at which respective functional genome sizes were attained therefore have an order of magnitude spread in range of values, from 100 million to 1000 million years, with most standard deviation values being of the order of a few hundred million years. In a homoscedastic model of the type assumed in the present article, we will use as a rough (weighted) estimate a value of \( s_w \sim 500 \) million years.

Therefore, with \( \sigma_b \sim 1.36 \) billion and \( \sigma_w \sim 0.5 \) billion, we have \( \lambda \sim 1.14 \). For uncertainties around 100 million years, \( \lambda \) is around 1.00, and it is around 1.54 if uncertainty is around 1 billion years.

5 Life

The above formulas for the prediction interval depend on the quantity \( \lambda \). Here, we examine the range of \( \lambda \) values which lead to conclusions consistent with the hypothesis that life did not begin prior to the formation of the Earth.

Figure 2 shows all of the results. The black line shows the ordinary least-square fit to the data. It is the \( x \)-intercept of this line, i.e., about 9.5 billion years, which led SG to conclude that life must have begun prior to the formation of the Earth (i.e., about 4.5 billion
years ago). The region between the black, dashed lines is the 95% prediction interval for the ordinary least squares fit. According to this prediction interval (without taking measurement errors into account) life may have originated as early as 7 billion years ago.

The results based on the above measurement error model are shown in red. The value of $\lambda$ for this fit is 1.14 - the value estimated in the previous section. Note that the resulting prediction interval includes 4.5 billion. In other words, if $\lambda$ is about 1.14, then the results of the analysis do not reject the hypothesis that life began after the formation of the Earth. Even a $\lambda$ as small as 1.1 leads to results (not shown here) consistent with 4.5 billion years as the age of life.

Although, a proper interpretation of prediction intervals correctly draws all focus away from the “center” of the interval, it is possible to arrange for the corrected fit itself to have an $x$-intercept of 4.5. The result is not shown here, but the corresponding value of $\lambda$ is about 2.7. Values of $\lambda$ in the 1.1 to 2.7 range are not uncommon; Frost and Thompson (2000) even consider $\lambda$ values as large as 5. More importantly, that range includes the $\lambda$ values estimated in the previous section.

6 Conclusion and Discussion

Recently, Sharov and Gordon (2013) presented an argument to support the claim that life must have originated prior to 4.5 billion years ago, i.e., prior to the formation of the Earth. Here we have shown that an analysis of the same data allows for life to have been formed.
more recently than 4.5 billion years ago, when one takes into account measurement errors and prediction intervals. Although, we do not estimate the measurement errors, we demonstrate that the range of such errors is within the acceptable range. In short, the data analyzed by SG provide no evidence to reject the hypothesis that life formed after the formation of the Earth.

The original conclusion of Sharov and Gordon (2013) is a consequence of an incomplete analysis. Although the analysis presented here is more complete, many improvements are possible. For instance, nonlinear fits can estimated, and more refined measurement error models can be developed. The inference component of our analysis - i.e., the 1.96 appearing in the prediction interval - can also be improved upon; the prediction intervals computed here are only an approximation. This was sufficient because the main goal of the paper has been to introduce measurement error models and to illustrate the importance of producing interval estimates (as opposed to point estimates) of the $x$-intercept. In short, many aspects of the above formulation are simplistic, approximate, or even controversial. As such, they offer avenues of further research. One aspect, however, that is incontrovertible is that measurement errors lead to biased (i.e., over- ) estimates for the age of life, and that the bias can be corrected/removed. Another unquestionable issue is that all estimates should be accompanied by some measure of uncertainty (e.g., prediction intervals), because without such measures, the conclusions will not be statistically sound.

These two recommendations - that measurement error models and interval estimates should be employed - are the main lessons of the current paper. The details of the measurement model and/or how the interval estimates are generated are of secondary importance because they affect our conclusions only in degree, not in kind. However, this analysis can be improved in a number of ways. The assumption of homoscedasticity can be relaxed, the $\sigma_w$ and the $\sigma_b$ can be estimated without the large-$n$ assumption, nonlinear fits can be examined, and one can even compute a prediction for the $x$-intercept itself. Lastly, for a more reliable conclusion data sets considerably larger than used by SG can be employed as genome size data is readily available for many major transitions along the tree of life (see, e.g., http://commons.wikimedia.org/wiki/File:Tree_of_life_with_genome_size.svg).

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