Economically rational sample-size choice and irreproducibility

Oliver Braganza¹, *

¹ Institute for Experimental Epileptology and Cognition Research, University of Bonn, Germany

* oliver.braganza@ukbonn.de

Abstract

Several systematic studies have suggested that a large fraction of published research is not reproducible. One probable reason for low reproducibility is insufficient sample size, resulting in low power and low positive predictive value. It has been suggested that insufficient sample-size choice is driven by a combination of scientific competition and ‘positive publication bias’. Here we formalize this intuition in a simple model, in which scientists choose economically rational sample sizes, balancing the cost of experimentation with income from publication. Specifically, assuming that a scientist’s income derives only from ‘positive’ findings (positive publication bias) and that individual samples cost a fixed amount, allows to leverage basic statistical formulas into an economic optimality prediction. We find that if effects have i) low base probability, ii) small effect size or iii) low grant income per publication, then the rational (economically optimal) sample size is small. Furthermore, for plausible distributions of these parameters we find a robust emergence of a bimodal distribution of obtained statistical power and low overall reproducibility rates, both matching empirical findings. Overall, the model describes a simple mechanism explaining both the prevalence and the persistence of small sample sizes, and is well suited for empirical validation. It suggests economic rationality, or economic pressures, as a principal driver of irreproducibility.

Introduction

Systematic attempts at replicating published research have produced disquietingly low reproducibility rates, often below 50% [1–5]. A recent survey suggests that a vast majority of scientists believe we are currently in a ‘reproducibility crisis’ [6]. While the term ‘crisis’ is contested [7], the available evidence on reproducibility certainly raises questions. One likely reason for low reproducibility rates is insufficient sample size and resulting low statistical power and positive predictive value [8–12]. In the most prevalent scientific statistical framework, i.e. null-hypothesis-significance-testing, the statistical power of a study is the probability to detect a hypothesized effect with a given sample size. Insufficient power reduces the probability that a given hypothesis can be supported by statistical significance. Insufficient sample sizes therefore directly impair a scientist’s purported goal of providing evidence for a hypothesis. Additionally, small sample sizes imply low positive predictive value (PPV), i.e. a low probability that a given, statistically significant finding is indeed true [8–10]. Therefore small sample sizes undermine not only the purported goal of the individual researcher, but also the reliability of the scientific literature in general.
Despite this, there is substantial evidence that chosen sample sizes are overwhelmingly too small \([10–15]\). For instance in neuroscientific research, systematic evaluation of meta-analyses in various subfields yielded mean power estimates of 8 to 31\% \([10]\), substantially less than the generally aspired 80\%. Notably, these estimates should be considered optimistic. This is because they are based on effect size estimates from meta-analyses which are in turn likely to be inflated due to publication bias \([11,16]\). Remarkably, more prestigious journals appear to contain particularly small sample sizes \([11,17,18]\). Moreover, the scientific practice of choosing insufficient sample sizes appears to be extremely persistent, despite perennial calls for improvement since at least 1962 \([11,13,19]\).

Perhaps the most prominent explanation for this phenomenon is the competitive scientific environment \([6,20,21]\). Scientists must maximize the number and impact of publications they produce with scarce resources (time, funding) in order to secure further funding and often, by implication, their job. For instance Smaldino and McElreath have suggested that ‘efficient’ scientists may ‘farm’ significant (i.e. publishable) results with low sample sizes \([13]\). This suggests that sample-size choices may reflect an economic equilibrium or, in other words, that small sample sizes may be economically rational. Notably, economic equilibria may be enforced not only by rational choice but also through competitive selection mechanisms (see discussion) \([13,22,23]\). The existence of an economic equilibrium of small sample sizes would help to explain both the prevalence and the persistence of underpowering.

Recently, this economic argument has been formally explored in two related optimality models \([24,25]\). While similar to the present model in spirit and conclusion, these models contain some higher order parameters, creating challenges for empirical validation. Here, we present a simple model, well suited to empirical validation, in which observed sample sizes reflect an economic equilibrium. Scientists choose a sample size to maximize their profit by balancing the cost of experimentation with the income following from successful publications. For simplicity we assume only statistically significant ‘positive findings’ can be published and converted to funding, reflecting ‘positive publication bias’. The model predicts an (economically rational) equilibrium sample size (ESS), for a given base probability of true results (\(b\)), effect size (\(d\)), and mean grant income per publication (\(IF\)). We find that i) lower \(b\) leads to lower \(ESS\), ii) greater \(d\) and \(IF\) lead to larger \(ESS\). For plausible parameter distributions, the model predicts a bi-modal distribution of achieved power and reproducibility rates below 50\%, both in line with empirical findings.

**Materials and methods**

**Model**

Economically rational scientists choose sample sizes to maximize their \(Profit\) from science given by their \(Income\) from funding minus the \(Cost\) of experimentation (Eq.1). For simplicity we assume they receive funding only, if they publish and they can publish only positive results. Specifically,

\[
Profit(s, IF, d, b) = \frac{IF \times TPR(s, d, b)}{Income} - \frac{s}{Cost}
\]

where \(IF\) is a positive constant reflecting mean grant income per publication (Income Factor), \(TPR(s, d, b)\) is the total positive rate given a sample size (\(s\)), effect size (\(d\)) and base probability of true effects (\(b\)). The latter term (\(b\)) \([26]\) has also been called the ‘pre-study probability of a relationship being true (\(\hat{R}/(\hat{R} + 1)\))’ \([8]\). At the same time
scientists incur the cost of experimentation which is proportional to sample size \(s\). For simplicity we scale \(IF\) as the number of samples purchasable per publication such that the cost of experimentation reduces to \(s\). Accordingly, each sample pair costs one monetary (or temporal) unit. \(TPR(s, d, b)\) is the sum of false and true positive rates and can be calculated using basic statistical formulas \[8, 26\] (Eq. 2):

\[
TPR(s, d, b) = \frac{\alpha \times (1 - b)}{\text{false positive rate}} + \frac{(1 - \beta(s)) \times b}{\text{true positive rate}}
\]

where \(\alpha\) is the Type-1 and \(\beta(s)\) the Type-2 error and \((1 - \beta(s))\) is statistical power. The equilibrium sample size \((ESS)\) is the sample size at which \(Profit\) is maximal. Model code is added as supporting information.

Central assumptions

Our model relies on three central simplifying assumptions, which here shall first be made explicit and justified:

1. Economic equilibrium sample sizes are the result of profit maximization (i.e. optimization).
2. Due to positive-publication-bias scientists can publish only positive results, and receive income proportional to their publication rate.
3. Sample size is chosen for a set of parameters \((b, d, IF)\) which are externally given (e.g. by the research field).

The first assumption (profit maximization) can most simply be construed as rational choice in the economic sense but may also be the outcome of competitive selection \[13\]. For instance if funding is stochastic, scientists who choose profit-maximizing sample sizes would have an increased chance of survival. In contexts, where the cost of sampling is mainly researcher time, profit can similarly be interpreted as time. While rational choice would depend on private estimates of the parameters \((b, d, IF)\), competitive selection could operate through a process of cultural evolution, potentially combined with social learning \[13, 23\]. Importantly, rational choice and competitive selection are not mutually exclusive and potentially cooperative.

The second assumption (positive publication bias), though obviously oversimplified, seems justified as a coarse description of most competitive scientific fields \[27\]. Even if negative results are published, they may not achieve high impact and translate to funding.

The third assumption (optimization for given \(b, d, IF\)) implies that scientists have no agency over the base probability of a hypothesis being true \((b)\), the true effect size \((d)\) or the mean income following publication \((IF)\). Arguably, \(b\) and \(d\) are exogenously given by arising hypotheses and true effects while \(IF\) is likely to be an exogenous property of a research field. Accordingly, a scientific environment with a fixed or constrained combination of the three parameters can be thought of as a scientific niche. Note that this does not preclude the simultaneous occupation of multiple niches by individual scientists, for instance a high-IF/low-b niche and a high-b/low-IF niche. In combination with the first assumption this implies that scientists choose/learn/ are selected for specific sample sizes within niches (but may simultaneously occupy multiple niches). Note, that alternative models, in which choice of \(b\) is endogenized, describe similar results \[24, 25\].

| Parameter       | Description                                                                 | Range   |
|-----------------|-----------------------------------------------------------------------------|---------|
| base rate \((b)\) | base rate of true positive effects (also called pre-study                     | 0 - 1   |
|                 | probability of true effect)                                                 |         |
| effect size \((d)\) | cohen's d (effect normalized to standard deviation)                         | 0.1 - 1.5 |
| Income Factor \((IF)\) | number of sample pairs purchasable per publication                         | 100 - 1000 |

Table 1. Parameter space, Input parameters to the model.

Simulation

Simulations were performed in Python3.6 using the StatsModels toolbox [28]. Model code is shown as supporting information. Statistical power was calculated assuming independent, equally sized samples \((s)\) and a two-sided, unpaired t-test given effect size \(d\). Note, that this implies, \(IF\) should be interpreted as the number of sample pairs purchasable, and \(s\) indicates the size of one of the samples. We also calculated power using a one sample t-test, where \(IF\) represents the number of individual samples, and all results were robust. The Type-1 error \((\alpha)\) is assumed to be 0.05 throughout. Distributions in Fig. 3 were generated using the numpy.random module. The input distribution for \(d\) was of generated using a gamma distribution tuned to match empirical findings \([11]\) \((k = 3.5, \theta = 0.2)\). Input distributions of \(b\) and \(IF\) (Fig. 4) were generated using uniform or beta distributions with \(\alpha\) and \(\beta\) chosen from \(\alpha = (1.1, 10), \beta = (1.1, 10)\) \((IF\) values multiplied by 1000). Bimodal distributions were generated by mixing a low and high skewed beta distribution (with the above parameters) with weights \((0.5, 0.5, \text{bimodal})\) or weights \((0.9, 0.1, \text{low/ bimodal})\). From these distributions 1000 values were drawn at random and the ESS computed for each constellation. To compute the implied distribution of emergent power and positive predictive values, the corresponding values for each ESS were weighted by its TPR/ESS. This corrects for the fact that small ESS will allow to conduct more studies, but with smaller TPR (in effect the two nearly cancel each other, such that the weighting does not significantly affect the emergent distribution).

Results

The equilibrium sample size \((ESS)\)

We will now first illustrate the basic model behavior with an exemplary parameter set \((b = 0.2, 0.5; d = 0.5; IF = 200)\). The most important model feature is the robust emergence of an economically optimal, i.e. 'rational', equilibrium sample size \((ESS)\) at which Profit, i.e. the (indirect) Income from publications minus the Cost of experimentation, is maximal (Fig[1]). A scientist’s Income (Fig[1], blue & green curves) will be proportional to her publication rate, i.e. her total positive rate (eq[2]). An optimum sample size \((s)\) emerges because this rate must saturate close to the actual rate of true effects \((b)\). Specifically, with infinite sample size and resulting infinite power, the total positive rate approaches the rate of actually true effects \((b)\) plus a fraction of false positives \((\alpha \times (1 - b))\). The saturation and slope of the Income curve will thus depend on \(b\), \(IF\) and power, the latter of which is a function of sample size. Conversely, additional samples always cost more, implying that at some sample size additional Cost will outpace additional Income. Computing Profit for increasing sample sizes (Eq[1]) therefore reveals an optimal sample size at which Profit is maximal, termed the equilibrium sample size \((ESS; \text{Fig}[1B])\).

At very small sample sizes, insufficient power will prelude the detection of true positives, but income from false positives will never fall below \(\alpha \times IF\). Increasing sample size can then increase or decrease Profit, depending on the resulting increase in
Fig 1. Equilibrium Sample Size, Basic model behavior illustrated with $d = 0.5$, $IF = 200$. A) Illustrative income (blue, green for $b = 0.2, 0.5$, respectively) and cost (black) function with increasing sample size ($s$); MU: monetary units where one MU buys one sample B) Profit functions for $b = (0, 0.1, ..., 1)$. For any given $b$ the (ESS) is the sample size at which profit is maximal. C) Relation of the ESS to $b$ (black curve). Respective ESS for $b = 0.2$ and $0.5$ are indicated by blue and green lines. D) Statistical power of the ESS ($P(ESS)$) for the given $d$ and $IF$. E) Expected distribution of statistical power at ESS if $b$ is uniformly distributed.

statistically significant results. For instance if true effects are scarce ($b \leq 0.2$ for Fig 1), increasing power will only modestly increase income (Fig 1A, B, blue line), leading to sharply decreasing Profit. In the extreme (no true effects, $b = 0$) increasing sample size linearly increases Cost but the rate of statistically significant (publishable) findings remains constant at $\alpha$. The result is a range of small $b$ at which ESS remains at the minimal value ($s = 4$ in our model) (Fig 1C). While we set $s = 4$ as the minimal possible sample size, the minimal publishable sample size may vary by field conventions. The model suggests simply, that there will be an economic pressure toward the ESS. This economic pressure should be proportional to the peakedness of the Profit curve, i.e. the marginal decrease in Profit when slightly deviating from ESS. As $b$ increases from zero the peakedness decreases until the ESS begins to rapidly shift to larger values (between $b = 0.3$ and $0.4$ in our example). At larger values of $b$ peakedness increases again and the ESS begins to saturate. Note that adding a constant overhead cost or income per study will not affect the ESS. Such an overhead would shift the Cost curve (Fig 1A, black) as well as the Profit curves (Fig 1B) up or down, without altering the optimal sample size. Accordingly, we find that for a given $d$ and $IF$, hypotheses with smaller base probability, lead to smaller rational sample sizes.

Statistical power at ESS

We can now also explore the statistical power implied by the ESS (Fig 1D). It is most helpful to separate the resultant curve into three phases: i) a range of constant small power where ESS is minimal, ii) a small range of $b$ ($\approx 0.4 < b < 0.6$) where power rises steeply and iii) a range of large $b$ where ESS and power saturate. Unsurprisingly, where ESS is minimal, studies are also severely underpowered. Conversely, where ESS begins to saturate, studies become increasingly well powered. Notably, there is only a small range of $b$ where moderately powered studies should emerge. In other words, for most values of $b$, power should be either very low or very high. For instance, assuming a uniform distribution of $b$, i.e. scientific environments with all values of $b$ are equally frequent, we should expect a bi-modal distribution of power (Fig 1E). If $b$ is already bi-modally distributed, this prediction becomes even stronger. For instance scientific niches may be clustered around novelty driven research with small $b$ and confirmatory research with large $b$. Overall, power like ESS is positively related to $b$ with a distinctive three phase waveform.
Next, we tested the sensitivity of the $b$ to $ESS$ and $b$ to $power$ relationships for plausible ranges of $d$ and $IF$ (Fig. 2A). The $ESS$ for a given $b$ should depend both on effect size $d$ (via $power$) and $IF$ (via the relative cost of a sample). We reasoned that the majority of scientific research is likely to be conducted in the ranges of $d \in [0.2, 1]$ and $IF \in [50, 500]$ (see discussion). For small $d$ and $IF$ the range of small $b$, where $ESS$ and $power$ are minimal is expanded (Fig. 2A,B upper left panels). Conversely, both greater $d$ and $IF$ shift the inflection point at which larger sample sizes become profitable rightward. Accordingly, in this domain, above minimal sample sizes should be chosen even with small $b$ (Fig. 2A, lower right panels). When $d$ and/or $IF$ are large enough, $ESS$ leads to well powered studies across most values of $b$ (Fig. 2B, lower right panels). Accordingly the distinctive three-phase waveform is conserved throughout much of the plausible parameter space but breaks down towards its edges.

**Emergent power distributions for plausible input parameter distributions**

In real scientific settings a number of distributions of effect sizes $d$, income factors $IF$ and base probabilities $b$ are plausible. We therefore next investigated the emergent $power$ distributions for multiple distributions of input parameters (Fig. 3). We then calculated the $ESS$ and resultant $power$ for each random input parameter constellation (Fig. 3A). The distribution of effect sizes was modeled after empirical data [11] with the majority of effects in the medium to large range (Fig. 3B, see discussion). Since the true distribution of $IF$ is unknown, we modeled a range of distributions below $IF = 1000$. We reasoned that a single publication leading to funding for 1000 sample pairs was a conservative upper bound in view of published sample sizes [11, see discussion]. Within this range we probed a uniform distribution as well as low, medium and high distributions of $IF$. Since the true distribution of $b$ is similarly unknown, we first probed the uniform distribution (minimal assumption, Fig. 2C1-4) and a bimodal distribution (assuming a cluster of exploratory fields with low $b$ and confirmatory fields with high $b$, Fig. 2C5-11). Note, that in both these cases the mean $b$ is by definition around 0.5, i.e. as many hypotheses are true as are false. This is generally viewed as unrealistically high [8,13]. We therefore also probed two more realistic distributions of $b$, namely low (most values around 0.1, Fig. 2C9-12) and low/ bimodal (low mixed with a minor second mode with high $b$ (Fig. 2C13-16). The latter models a situation where most studies (90%) are exploratory and the remaining studies are confirmatory. We found the resulting bimodal distribution of $power$ to be robust throughout, with only the relative weights of the peaks changing. Next we investigated the mean reproducibility rates which could be expected for the resultant distributions. The positive predictive value ($PPV$) measures the probability that a positive finding is indeed true. It thus provides an upper bound on expected reproducibility rates (as the $power$ of reproduction studies approaches 100%, reproducibility rates will approach $PPV$). Note that the $PPV$ should be interpreted in light of the underlying $b$. For instance, for the first two distributions of $b$ (Fig. 2C1-11), the mean base probability is already 50%, so $PPV < 0.5$ would indicate performance worse than chance. For more realistic distributions of $b$ (Fig. 2C12-16) $PPV$ ranged from 0.26 (Fig. 2C10) to 0.4 (Fig. 2C16), comparable to reported reproducibility rates. Thus, for plausible parameter distributions, rational sample-size choice robustly leads to a bimodal distribution of statistical $power$ and expected reproducibility rates below 50%.
Fig 2. Effect of $d$ and IF on ESS, A) Each individual line depicts the ESS as a function of $b$ for a given combination of $d$ and IF. B) Statistical power resultant from the ESS in panel (A).

Discussion

Here, we describe a simple model in which sample-size choice is viewed as the result of competitive economic pressures rather than scientific deliberations (similar to [24,25]).
Fig 3. Distributions of statistical power for plausible input parameter distributions. Random input parameter constellations were drawn from a range of plausible, simulated distributions (grey, see methods). For each input parameter constellation the resultant ESS and power were calculated. A) Summary of model inputs and outputs and the probed distributions. B) Empirically matched distribution of effect sizes $d$ [1], used for all output distribution in C. C) Emergent power distributions and mean positive predictive values for each combination of $b$ and IF distributions.

The model formalizes the economic optimality of small sample size for a large range of empirically plausible parameters with minimal assumptions. Additionally, it makes several empirically testable predictions, including a bimodal distribution of observed statistical power. Given the simplicity of the model, the apparent similarity between its predictions and empirically observed patterns is remarkable.
Model predictions and empirical evidence

Our model predicts i) a correlation between base probability and sample size, ii) a correlation between effect size and sample size, iii) a correlation between mean grant income per publication and sample size. Moreover, for plausible parameter distributions the model predicts iv) a bimodal distribution of achieved statistical power and v) low overall reproducibility rates. For the purpose of discussion, it may be of particular interest to contrast our predictions, based on economically driven sample-size choice, to predictions derived from presumed scientifically driven sample-size choices. For instance scientifically driven sample-size choice might be expected to i) require larger samples for more unlikely findings, ii) require larger samples for smaller effects and iii) be independent of grant income. Moreover, scientifically driven sample sizes might be expected to iv) lead to a unimodal distribution of power around 80% and v) imply PPVs and reproducibility rates above 50%. Which sample sizes are scientifically ideal is of course a complex question in itself, and will depend not only on the cost of sampling but also on the scientific values of true and false positives as well as true and false negatives. Miller and Ulrich, [29] present a scientifically normative model of sample size choice, formalizing many of the above intuitions (however, importantly they do not account for the possibility that negative findings may not enter the published literature). Overall, the currently available empirical evidence appears more in line with the economically normative than the scientifically normative account.

ad i) The available evidence suggests that journals with high impact and purportedly more novel (or less likely) findings feature smaller sample sizes [11,17,18], in line with our prediction. This finding seems particularly puzzling given the increased editorial and scientific scrutiny such ‘high-impact’ publications receive. Accordingly, publication in a ‘high impact’ journal is generally considered a signal of quality and credibility [30]. From the perspective of an individual scientist, increasing sample size strictly increases the probability of being able to support her hypothesis (if she believes it is true) but does not alter the probability of rejecting it (if she expects it to be false). Similarly, a scientific optimality model assuming true and false positive publications have equal but opposite scientific value, suggests more unlikely findings merit larger power [29, see Fig5 therein]. All these considerations suggest high impact journals should contain larger sample sizes, highlighting a need for explanation.

ad ii) The available evidence suggests a negative correlation between effect size and sample size, seemingly contradicting our prediction [15,17,31]. However, the authors caution in the interpretation of this result due to the winner’s curse phenomenon [10,17,32]. This well documented phenomenon produces an negative correlation between sample size and estimated effect size even when a single hypothesis (i.e. single true effect size) is probed in multiple independent studies. It arises, because for small sample sizes only spuriously inflated effect sizes become statistically significant and enter the literature (also due to positive publication bias). Relating effect sizes from meta-analyses to original sample sizes by scientific subdiscipline may help to overcome this confound.

ad iii) We are unaware of evidence relating mean grant income per study to sample size. A study by Fortin and Currie [33] suggests diminishing returns in total impact for increasing awarded grant size. However, impact was assessed without reference to sample sizes. Furthermore, awarded grant size does not necessarily reflect mean grant income, since larger grants may be more competitive. Indeed, more competitive funding systems are likely to a) increase the underlying economic pressures and b) have additional adverse effects [34]. A feasible approach to test our prediction may be to relate mean grant income and mean sample size by scientific subdiscipline.

ad iv) The prediction of a bimodal distribution of power is well corroborated by evidence [10,14,15]. Particularly the lack of a mode around 80% power in our model, as
well as all empirical studies is notable. By comparison the scientific value driven model by Miller and Ulrich [29] suggests a single broad mode at intermediate levels of power.

ad v) The predicted low overall reproducibility rates are in line with empirical data for many fields. Two, now prominent, studies from the pharmaceutical industry suggested reproducibility rates of 11 and 22% [1,2] respectively. Academic studies from psychology and experimental economics found 36, 61 and 62% [3–5] respectively]. Our results suggest that differences in these numbers may be driven, for instance, by different base probabilities of hypotheses being true in the different fields.

The present model thus helps to explain a range of empirical phenomena and is amenable to closer empirical scrutiny in the future. Crucially, all in- and output parameters are in principle empirically verifiable. Future studies could, for instance, fit observed power distributions with the present model versus alternative formal models. This could directly generate predictions concerning input parameters which could in turn be empirically tested.

Niche optimization through competitive selection

A central assumption of this model is that sample size is optimized for a given set of parameters ($b, d, IF$). One way to interpret this is that scientists make rational sample size choices based on their estimates of these parameters for each hypothesis. As noted above, maximizing profit in this context need not be an end in itself but can also be seen as a strategy to secure scientific survival, given the uncertainty of both the scientific process as well as funding decisions. Alternatively, optimization may occur by selection mechanisms, where sample sizes are determined through a process of cultural evolution [13]. In this case one must however make the additional assumption, that parameters remain relatively constant within the scientific niche in which sample sizes are selected. In such a case researchers must only associate the scientific niche with a convention of sample size choice. These conventions could then undergo independent evolution in each niche. Such scientific niches may correspond to scientific subdisciplines and may indeed be identifiable on the basis of empirically consistent sample sizes. We did not address how scientists should distribute their efforts into multiple niches (e.g. exploratory research and confirmatory research). This question has been previously addressed in a related optimality model [24]. The authors suggest that, given prevailing incentives emphasizing novel research, the majority of efforts should be invested into research with low $b$. This is reflected in the present model by the low skewed distributions of $b$ ((Fig. 3C). Future evolutionary models could further investigate how mixed strategies of sample size choice perform when individual parameters vary within niches, or scientists are uncertain of the niche.

Input parameter range estimates

We probed the arising ESS for what we judged to be plausible ranges of the three input parameters ($b, d, IF$):

The base (or pre study) probability of true results is often assumed to be small ($b < 0.1$) for most fields [13]. This is in part because of a focus on novel research [24]. At the same time there is a small fraction of confirmatory studies, where substantial prior evidence indicates the hypothesis should be true, and $b$ should thus be large. We therefore chose to cover the full range of $b$ ($b \in [0, 1]$) in addition to some plausible distributions. In light of the considerations by [13] and [24], our distributions might be judged conservative in that real values of $b$ may be lower. Notably, models endogenizing choice over $b$ reach similar conclusions [21,25].

We probed a plausible range ($d \in [0.1, 1.5]$) and an empirically matched distribution of $d$ [11]. By comparison, in psychological research frequently cited reference points for
small, medium and large effect sizes are \( d = 0.2, 0.5 \) and 0.8, respectively.

Notably our empirically matched distribution (Fig. 3B) is based on published effect sizes, which are likely exaggerated due to the winner’s curse \([17]\). For instance \([3, 4]\) find that true effect sizes are on average only around 50 to 60% of originally published effect sizes. This again renders our estimates conservative, in that true values may be lower.

An empirical estimate of \( IF \) is perhaps most difficult, since the full cost per sample (time, wage, money) may be difficult to separate from other arising costs. Note that a constant overhead cost or income, which is independent of sample size, would not alter the optimal sample size. Nevertheless, we reasoned that plausible values for \( IF \) should be somewhere within the range of 10 to 1000. For instance, a typically reported sample size is 20 \([10, 11]\). \( IF \) must allow to cover the cost of the positive result plus however many unpublished additional samples were required to obtain it. A \( IF \) of 1000 would thus allow for up to 49 negative findings (or 980 unpublished samples). Given that science does not seem to provide substantial net profits, larger values for \( IF \) seem implausible.

Together, these considerations suggest that our predictions of \( power \) and expected reproducibility rates are more likely to be over- than under estimated. Of course, the forces affecting real sample size choices are (hopefully) not solely the economic ones investigated here. Specifically, scientific deliberations about appropriate sample size should at least play a partial role. Indeed, the model predicts the minimal sample size over a wide range of parameters. This could for instance be the minimal sample size accepted by statistical software. Above, we have suggested it is the minimal sample size deemed acceptable in a scientific discipline. This implies that discipline specific norms on minimal acceptable sample sizes reflect scientific deliberations and are enforced during the editorial and review process. Non-economic forces may be particularly relevant where the \( profit \) peak is broad.

Reproducibility

In our model low reproducibility rates appear purely as a result of the economic pressures on sample size. Many additional practices may increase the false positive rate for a given sample size such \([35–39]\). The economic pressures underlying our model must be expected to also promote such practices. Moreover, many of these practices are likely to become more relevant for many small studies. For instance flexible data analysis will increase the probability of false positives for each study. Moreover, in small studies substantial changes of effect size may result from minor changes in analysis (e.g. post-hoc exclusion of data points), thus increasing the relative power of biases. While substantial and mostly laudable efforts are being made to reduce such practices \([35, 40]\), our approach emphasizes that scientists may in fact have limited agency over sample size, given economic constraints. While the present model was geared toward establishing this argument with minimal assumptions, maximal clarity and maximal empirical verifiability, related models have explored the effects of various policy prescriptions given such economic constraints \([24, 25]\). For instance Campbell and Gustafson \([25]\) explore the effects of increasing requirements for statistical stringency as called for by a highly publicized recent proposal \([41]\). However, they find that this may dramatically lower publication rates, effectively increasing waste (unpublished research) and competitive pressure as well as reducing the rate of ‘breakthrough findings’. By contrast, Utzerath and Fernandez \([47]\) propose to directly address positive publication bias through dedicated funding programs and institutions, thereby realigning incentives while potentially decreasing waste and competitive pressure.
Relation to proxyeconomics

Our model is consistent with, and an individual instance of, proxyeconomics [23]. Proxyeconomics refers to any competitive societal system in which an abstract goal (here: scientific progress) is promoted using competition based on proxy measures (here: publications). In such cases, the measures or system may become corrupted due to an overoptimization toward the proxy measure [42–46]. As discussed above, such systems have the general potential to create a situation of limited individual agency and system-level lock-in [23]. The present model shows how the specific informational deficits of a proxy allow to create pattern predictions of the potentially emergent corruption. Specifically, an informational idiosyncrasy of the proxy (positive publication bias) leads to a number of predictions which can be i) empirically verified and ii) contrasted with alternative models (see above). A similar pattern prediction derived from positive publication bias is the winner’s curse [17]. Together, such pattern predictions provide concrete and compelling evidence for competition induced corruption of proxy measures and associated competitive systems.

Conclusion

Our model strengthens the argument that economic pressures may be a principle driver of insufficient sample sizes and irreproducibility. The underlying mechanism hinges on the combination of positive publication bias and competitive funding. Accordingly, any policy to address irreproducibility should either incorporate the arising economic forces or seek to change them [25,47].

Acknowledgments

This work was funded by VW-foundation under the 'Originalitätsverdacht' program (project: Proxyeconomics). Special thanks to Heinz Beck for making this project possible and to Jonathan Ewell for comments on the manuscript.

References

1. Begley CG, Ellis LM. Drug development: Raise standards for preclinical cancer research. Nature. 2012;483(7391):531–3. doi:10.1038/483531a.

2. Prinz F, Schlange T, Asadullah K. Believe it or not: how much can we rely on published data on potential drug targets? Nature reviews Drug discovery. 2011;10(9):712. doi:10.1038/nrd3439-c1.

3. Camerer CF, Dreber A, Forsell E, Ho TH, Huber J, Johannesson M, et al. Evaluating replicability of laboratory experiments in economics. Science. 2016;351(6280):1433–1436. doi:10.1126/science.aaf0918.

4. Camerer CF, Dreber A, Holzmeister F, Ho TH, Huber J, Johannesson M, et al. Evaluating the replicability of social science experiments in Nature and Science between 2010 and 2015. Nature Human Behaviour. 2018;2(9):637–644. doi:10.1038/s41562-018-0399-z.

5. Open Science Collaboration. Estimating the reproducibility of psychological science. Science. 2015;349(6251):aac4716–aac4716. doi:10.1126/science.aac4716.
6. Baker M. 1,500 scientists lift the lid on reproducibility. Nature. 2016;533(7604):452–454. doi:10.1038/533452a.

7. Fanelli D. Opinion: Is science really facing a reproducibility crisis, and do we need it to? Proceedings of the National Academy of Sciences of the United States of America. 2018;115(11):2628–2631. doi:10.1073/pnas.1708272114.

8. Ioannidis JPA. Why most published research findings are false. PLoS Medicine. 2005;4(6):e124. doi:10.1371/journal.pmed.0020124.

9. McElreath R, Smaldino PE. Replication, communication, and the population dynamics of scientific discovery. PLoS ONE. 2015;10(8).

10. Button KS, Ioannidis JPa, Mokrysz C, Nosek Ba, Flint J, Robinson ESJ, et al. Power failure: why small sample size undermines the reliability of neuroscience. Nature reviews Neuroscience. 2013;14(5):365–76. doi:10.1038/nrn3475.

11. Szucs D, Ioannidis JPA. Empirical assessment of published effect sizes and power in the recent cognitive neuroscience and psychology literature. PLOS Biology. 2017;15(3):e2000797. doi:10.1371/journal.pbio.2000797.

12. Lamberink HJ, Otte WM, Sinke MRT, Lakens D, Glasziou PP, Tijdink JK, et al. Statistical power of clinical trials increased while effect size remained stable: an empirical analysis of 136,212 clinical trials between 1975 and 2014. Journal of Clinical Epidemiology. 2018;102:123–128. doi:10.1016/J.JCLINEPI.2018.06.014.

13. Smaldino PE, McElreath R. The natural selection of bad science. Royal Society Open Science. 2016;3(9):160384. doi:10.1098/rsos.160384.

14. Nord CL, Valton V, Wood J, Roiser JP. Power-up: A Reanalysis of ‘Power Failure’ in Neuroscience Using Mixture Modeling. Journal of Neuroscience. 2017;37(34):8051–8061. doi:10.1523/JNEUROSCI.3592-16.2017.

15. Dumas-Mallet E, Button KS, Boraud T, Gonon F, Munafò MR. Low statistical power in biomedical science: a review of three human research domains. Royal Society Open Science. 2017;4(2):160254. doi:10.1098/rsos.160254.

16. Tsilidis KK, Panagiotou Oa, Sena ES, Aretouli E, Evangelou E, Howells DW, et al. Evaluation of excess significance bias in animal studies of neurological diseases. PLoS biology. 2013;11(7):e1001609. doi:10.1371/journal.pbio.1001609.

17. Brembs B, Button K, Munafò M. Deep impact: unintended consequences of journal rank. Frontiers in Human Neuroscience. 2013;7. doi:10.3389/fnhum.2013.00291.

18. Fraley RC, Vazire S. The N-Pact Factor: Evaluating the Quality of Empirical Journals with Respect to Sample Size and Statistical Power. PLoS ONE. 2014;9(10):e109019. doi:10.1371/journal.pone.0109019.

19. Cohen J. The statistical power of abnormal-social psychological research: A review. The Journal of Abnormal and Social Psychology. 1962;65(3):145–153. doi:10.1037/h0045186.

20. Fung FC, Casadevall A. Competitive science: is competition ruining science? Infection and immunity. 2015;83(4):1229–33. doi:10.1128/IAI.02939-14.

21. Edwards MA, Roy S. Academic Research in the 21st Century: Maintaining Scientific Integrity in a Climate of Perverse Incentives and Hypercompetition. Environmental Engineering Science. 2017;34(1):51–61. doi:10.1089/ees.2016.0223.
22. Axtell R, Kirman A, Couzin ID, Fricke D, Hens T, Hochberg ME, et al. Challenges of Integrating Complexity and Evolution into Economics. In: Wilson DS, Kirman A, editors. Complexity and Evolution: Toward a New Synthesis for Economics. MIT Press; 2016.

23. Braganza O. Proxyeconomics, An agent based model of Campbell’s law in competitive societal systems; 2018. Available from: http://arxiv.org/abs/1803.00345

24. Higginson AD, Munafò MR. Current Incentives for Scientists Lead to Underpowered Studies with Erroneous Conclusions. PLOS Biology. 2016;14(11):e2000995. doi:10.1371/journal.pbio.2000995.

25. Campbell H, Gustafson P. The World of Research Has Gone Berserk: Modeling the Consequences of Requiring “Greater Statistical Stringency” for Scientific Publication. The American Statistician. 2019;73(sup1):358–373. doi:10.1080/00031305.2018.1555101.

26. Smaldino PE. Measures of individual uncertainty for ecological models: Variance and entropy. Ecological Modelling. 2013;254:50–53. doi:10.1016/j.ecolmodel.2013.01.015.

27. Fanelli D. Negative results are disappearing from most disciplines and countries. Scientometrics. 2012;90(3):891–904. doi:10.1007/s11192-011-0494-7.

28. Seabold S, Perktold J. Statsmodels: Econometric and Statistical Modeling with Python. In: PROC. OF THE 9th PYTHON IN SCIENCE CONF; 2010. p. 57.

29. Miller J, Ulrich R. Optimizing Research Payoff. Perspectives on Psychological Science. 2016;11(5):664–691. doi:10.1177/1745691616649170.

30. Brembs B. Prestigious Science Journals Struggle to Reach Even Average Reliability. Frontiers in Human Neuroscience. 2018;12:37. doi:10.3389/fnhum.2018.00037.

31. Kühberger A, Fritz A, Scherndl T. Publication Bias in Psychology: A Diagnosis Based on the Correlation between Effect Size and Sample Size. PLoS ONE. 2014;9(9):e105825. doi:10.1371/journal.pone.0105825.

32. Esposito L, Drexler JF, Braganza O, Doberentz E, Grote A, Widman G, et al. Large-scale analysis of viral nucleic acid spectrum in temporal lobe epilepsy biopsies. Epilepsia. 2015;56(2):234–243. doi:10.1111/epi.12890.

33. Fortin JM, Currie DJ. Big Science vs. Little Science: How Scientific Impact Scales with Funding. PLoS ONE. 2013;8(6):e65263. doi:10.1371/journal.pone.0065263.

34. Gross K, Bergstrom CT. Contest models highlight inherent inefficiencies of scientific funding competitions. PLOS Biology. 2019;17(1):e3000065. doi:10.1371/journal.pbio.3000065.

35. Munafò MR, Nosek BA, Bishop DVM, Button KS, Chambers CD, Percie du Sert N, et al. A manifesto for reproducible science. Nature Human Behaviour. 2017;1(1):0021. doi:10.1038/s41562-016-0021.

36. Kerr NL. HARKing: hypothesizing after the results are known. Personality and social psychology review. 1998;2(3):196–217. doi:10.1207/s15327957pspr0203-4.
37. Eklund A, Nichols TE, Knutsson H. Cluster failure - Why fMRI inferences for spatial extent have inflated false-positive rates. Proceedings of the National Academy of Sciences. 2016;113(28):7900–7905. doi:10.1073/pnas.1602413113.

38. Simmons JP, Nelson LD, Simonsohn U. False-positive psychology - undisclosed flexibility in data collection and analysis allows presenting anything as significant. Psychological science. 2011;22(11):1359–66. doi:10.1177/0956797611417632.

39. Kriegeskorte N, Simmons WK, Bellgowan PSF, Baker CI. Circular analysis in systems neuroscience: the dangers of double dipping. Nature Neuroscience. 2009;12(5):535–540. doi:10.1038/nn.2303.

40. McNutt M. Journals unite for reproducibility. Science. 2014;346(6210):679–679. doi:10.1126/science.aaa1724.

41. Benjamin DJ, Berger JO, Johannesson M, Nosek BA, Wagenmakers EJ, Berk R, et al. Redefine statistical significance. Nature Human Behaviour. 2018;2(1):6–10. doi:10.1038/s41562-017-0189-z.

42. Campbell DT. Assessing the impact of planned social change. Evaluation and Program Planning. 1979;2(1):67–90. doi:10.1016/0149-7189(79)90048-X.

43. Goodhart CAE. Problems of Monetary Management: The UK Experience. In: Monetary Theory and Practice. London: Macmillan Education UK; 1984. p. 91–121. Available from: http://link.springer.com/10.1007/978-1-349-17295-5\_4.

44. Strathern M. 'Improving ratings': audit in the British University system. European Review Marilyn Strathern European Review Eur Rev. 1997;55(6):305–321. doi:10.1002/(SICI)1234-981X(199707)5:33.0.CO;2-4.

45. Manheim D, Garrabrant S. Categorizing Variants of Goodhart’s Law; 2018. Available from: https://arxiv.org/abs/1803.04585v3.

46. Fire M, Guestrin C. Over-Optimization of Academic Publishing Metrics: Observing Goodhart’s Law in Action; 2018. Available from: http://arxiv.org/abs/1809.07841.

47. Utzerath C, Fernández G. Shaping Science for Increasing Interdependence and Specialization. Trends in neurosciences. 2017;40(3):121–124. doi:10.1016/j.tins.2016.12.005.

Supporting information

Model Code

```python
import numpy as np
import statsmodels.stats.power as getpower

alpha = 0.05
def getESS(b, d, IF):
    """Calculate ESS for
    b: base rate of true hypotheses (between 0 and 1),
    d: Effect size (Cohen’s d),
    IF: Income factor (# of sample pairs purchasable per publication)"
    SS = np.arange(4,1000,2)
    Power = np.zeros(len(SS))
    falsePR = np.zeros(len(SS))
    truePR = np.zeros(len(SS))
    totalPR = np.zeros(len(SS))
    Income = np.zeros(len(SS))
    Profit = np.zeros(len(SS))
    ```
for i, s in enumerate(SS):
    # 1-sample t-test
    # analysis = getpower.TTestPower()
    # Power[i] = analysis.solve_power(effect_size=d, nobs=s, alpha=alpha,
    # power=None, alternative='two-sided')
    # 2-sample t-test
    analysis = getpower.TTestIndPower()
    Power[i] = analysis.solve_power(effect_size=d, nobs1=s, ratio=1.0, alpha=alpha,
    # power=None, alternative='two-sided')

falsePR[i] = alpha * (1-b)
truePR[i] = Power[i] + b
totalPR[i] = falsePR[i] + truePR[i]
Income[i] = totalPR[i] * (1 - s)

ESSidx = np.argmax(Profit)
SSSidx = np.abs(Power - 0.8).argmin()
PVRSS = truePR[ESSidx] / totalPR[ESSidx]
PPVESS = truePR[SSSidx] / totalPR[SSSidx]
PowerESS = Power[ESSidx]

... 

ESS = equilibrium sample size (sample size at which Profit is maximal)
SS = scientifically appropriate sample size (with power=80%)
TPRESS = total positive rate at ESS (describes published literature)
PPVESS = positive predictive value at ESS
PPVSS, positive predictive value at SSS
SS = vector of tested sample sizes
Profit = vector of profit for each tested sample size

return ESS, SSS, TPRESS, PPVESS, PowerESS, PPVSS, Income, SS, Profit