Обеспечивают ли стандартные животные
воспроизводимый результат?

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Кризис воспроизводимости в био-медицинских исследованиях

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Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

Summary

There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power and bias, the number of other studies on the same question, and, importantly, the ratio of true to no relationships among the relationships probed in each scientific field. In this framework, a research finding

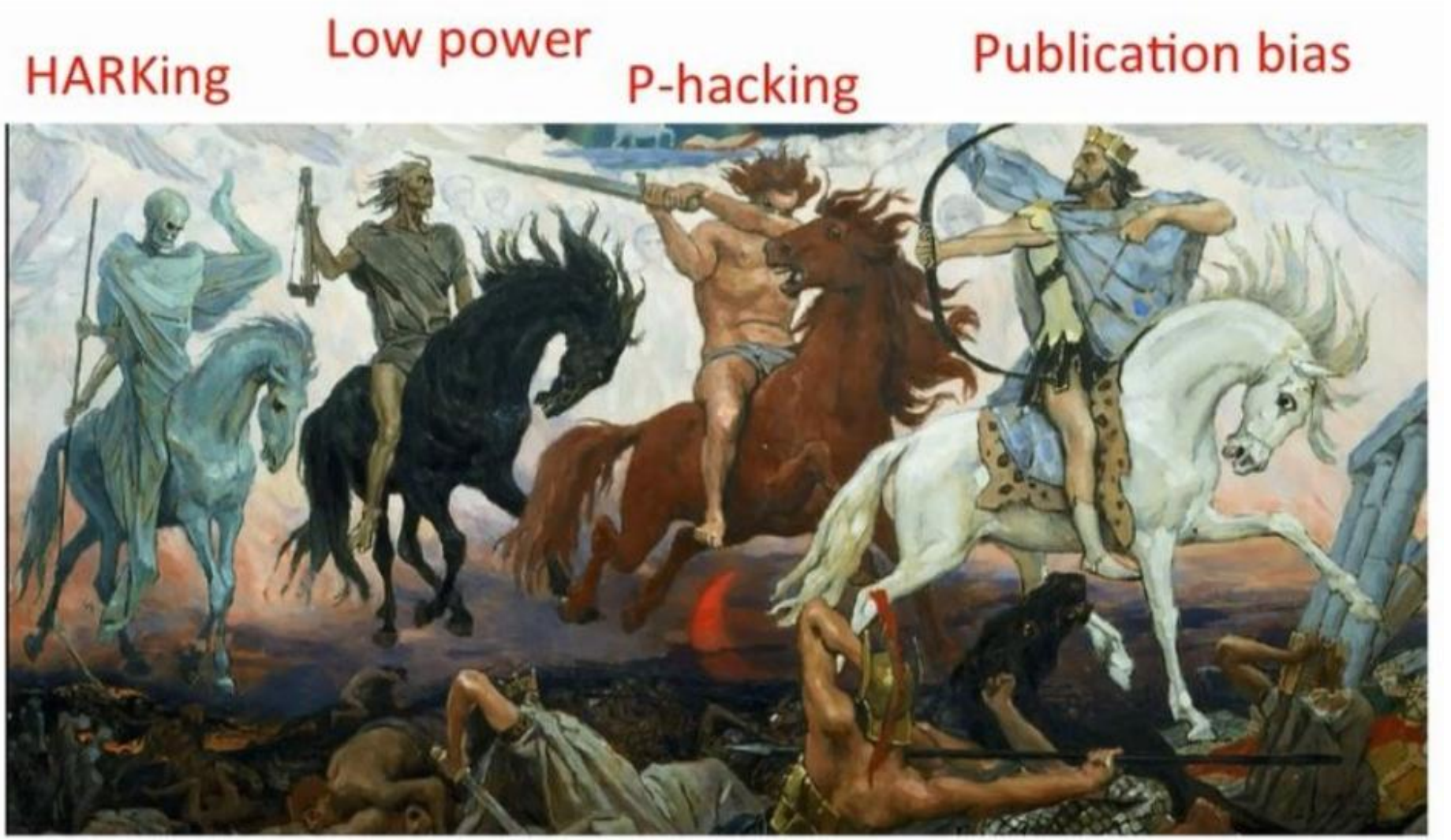
factors that influence this problem and some corollaries thereof.

Modeling the Framework for False Positive Findings

Several methodologists have pointed out [9–11] that the high rate of nonreplication (lack of confirmation) of research discoveries is a consequence of the convenient, yet ill-founded strategy of claiming

is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be postulated. Let us also consider, for computational simplicity, circumscribed fields where either there is only one true relationship (among many that can be hypothesized) or

Ioannidis JPA (2005) Why most published research findings are false. PLoS Med 2(8): e124.



Dorothy Bishop,

Professor of Developmental Neuropsychology, Department of Experimental Psychology, University of Oxford

http://neuroanatody.com/2017/11/oxford-reproducibility-lectures-dorothy-bishop/

- **HARKing (Hypothesizing After Results are Known)** – изобретение гипотез post hoc, объясняющих совокупность достоверных результатов в исследовании;

- **Low power** – низкая статистическая мощность (например, из-за маленьких выборок, не представляющих генеральную совокупность);

- **P-hacking** – перебор статистических анализов с целью получить нужное значение $p<0,05$

- **Publication bias** – предвзятая оценка полученных результатов с точки зрения уже опубликованных данных

Hanno Würbel

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Bestätigte E-Mail-Adresse bei vetsuisse.unibe.ch - Startseite

Ethology Animal Behaviour Animal Welfare Laboratory Animal Science

TITEL Z

A reaction norm perspective on reproducibility
B Voelkl, H Würbel
Theory in Biosciences, 1-8

'Puppy dog eyes' are associated with eye movements, not communication
A Bremhorst, DS Mills, L Stolzlechner, H Würbel, S Riemer
Frontiers in psychology 12, 163

Breakdown of the ideal free distribution under conditions of severe and low competition
J Sirovnik, B Voelkl, LJ Keeling, H Würbel, MJ Toscano
Behavioral ecology and sociobiology 75 (2), 1-11

A systematic review and meta-analysis of the relationship between social dominance status and common behavioral phenotypes in male laboratory mice
JA Varholick, JD Bailoo, A Jenkins, B Voelkl, H Wuerbel
Frontiers in Behavioral Neuroscience 14

The standardization fallacy

OB1S2

How standardization causes poor reproducibility in animal research

Wuerbel Hanno and Voelkl B.
Division of Animal Welfare, University of Bern, Bern, Switzerland

" systematic variation (heterogenization) rather than more rigorous standardization is needed to improve reproducibility…"

Гетерогенность и пластичность (различные ответы на экспериментальны воздействия) – фундаментальные свойства живых организмов.

Уменьшая гетерогенность выборки мы искусственно ограничиваем ее, делаем «перекошенной». Такие выборки не отражают генеральной совокупности, так как полученные результаты могут быть отнесены исключительно к какой-то линии, возрастной группе или полу животного.

Environmental standardization: cure or cause of poor reproducibility in animal experiments?

S Helene Richter[1,2], Joseph P Garner[3] & Hanno Würbel[1]

Nature Methods volume 6, pages257–261 (2009)

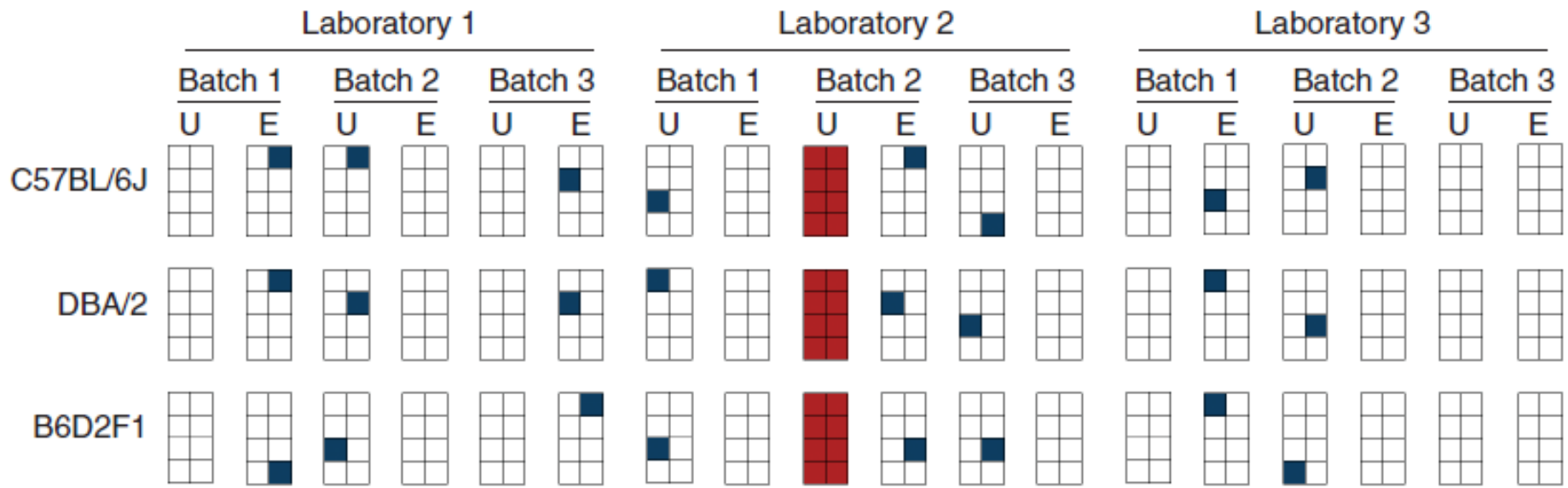
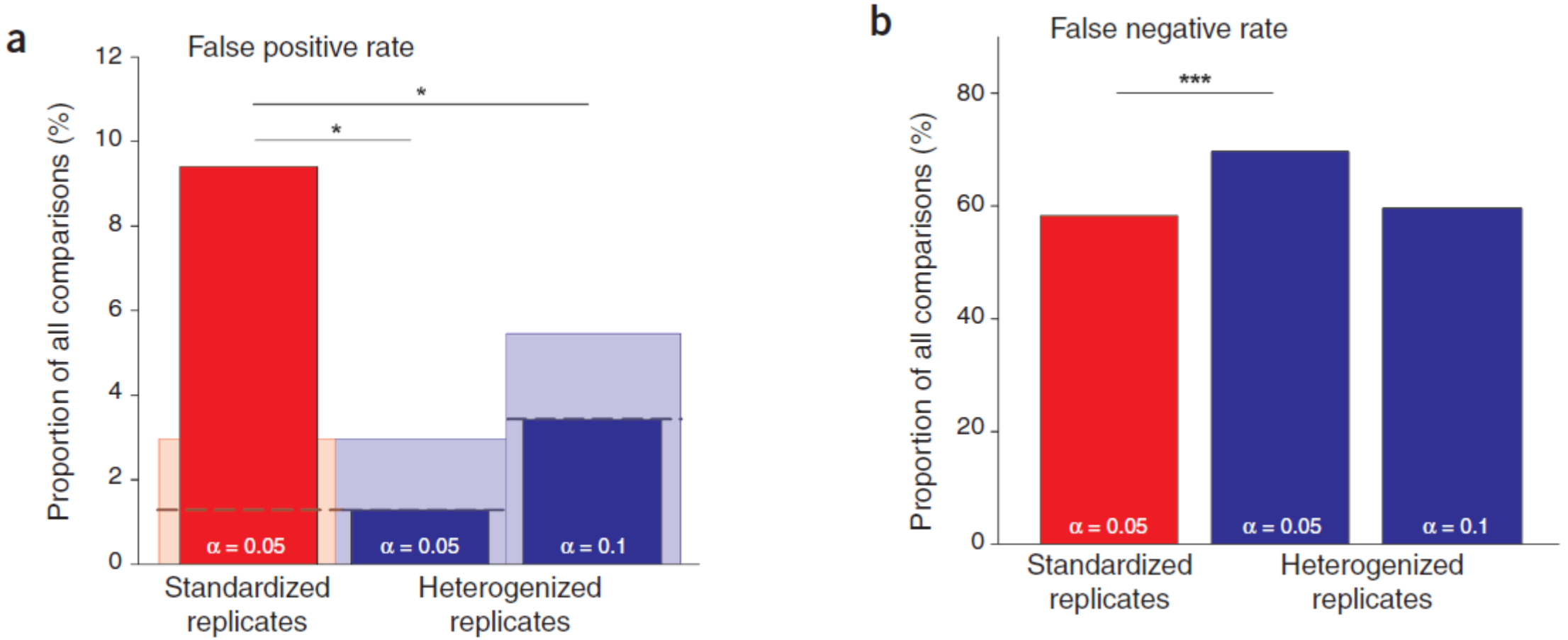


Figure 1 | Study design. In this study, 432 female mice (represented by squares) of three strains (C57BL/6J, DBA/2, B6D2F1), distributed across three laboratories, three batches per laboratory and two housing conditions (U, unenriched cages and E, enriched cages), were allocated to 18 standardized and 18 heterogenized replicate cohorts. Examples of one standardized (red squares) and one heterogenized replicate (blue squares) are displayed. Note that the heterogenized cohorts were selected such that each mouse was matched with two mice of the other two strains from the same environment.



В гетерогенных выборках вероятность ложноположительного результата была значительно ниже, а вероятность ложноотрицательного – незначительно выше.

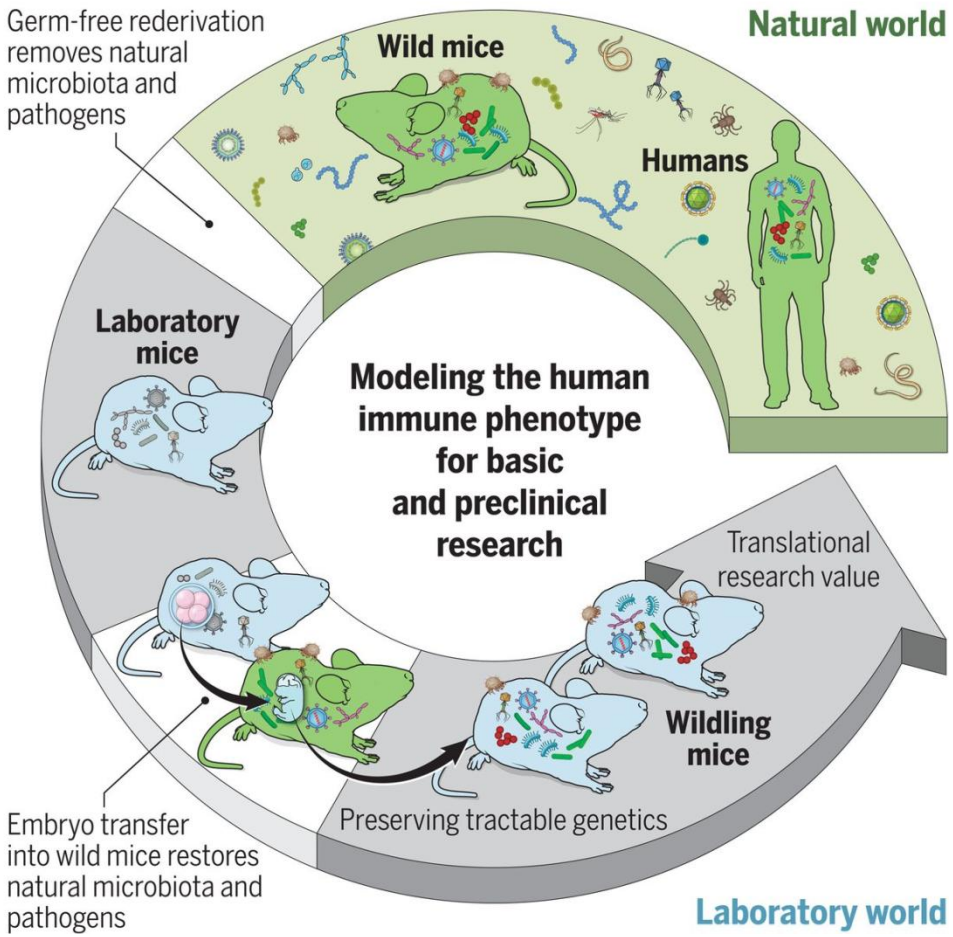
SHARE

RESEARCH ARTICLE

Laboratory mice born to wild mice have natural microbiota and model human immune responses

Stephan P. Rosshart[1,*,†], Jasmin Herz[2,‡], Brian G. Vassallo[1,‡,§], Ashli Hunter[1], Morgan K. Wall[2], Jonathan H. Badge...
+ See all authors and affiliations

Science 02 Aug 2019:
Vol. 365, Issue 6452, eaaw4361
DOI: 10.1126/science.aaw4361



В этой работе была произведена «обратная редеривация» - эмбрионы от стандартных SPF мышей C57Bl/6 были пересажены мышам, пойманным в дикой природе.

В результате животные, родившиеся из пересаженных эмбрионов, унаследовали естественную микробиоту диких мышей.

При использовании таких мышей в двух доклинических исследованиях были получены результаты, хорошо предсказывающие клинические данные

Camilla Hartmann Friis Hansen

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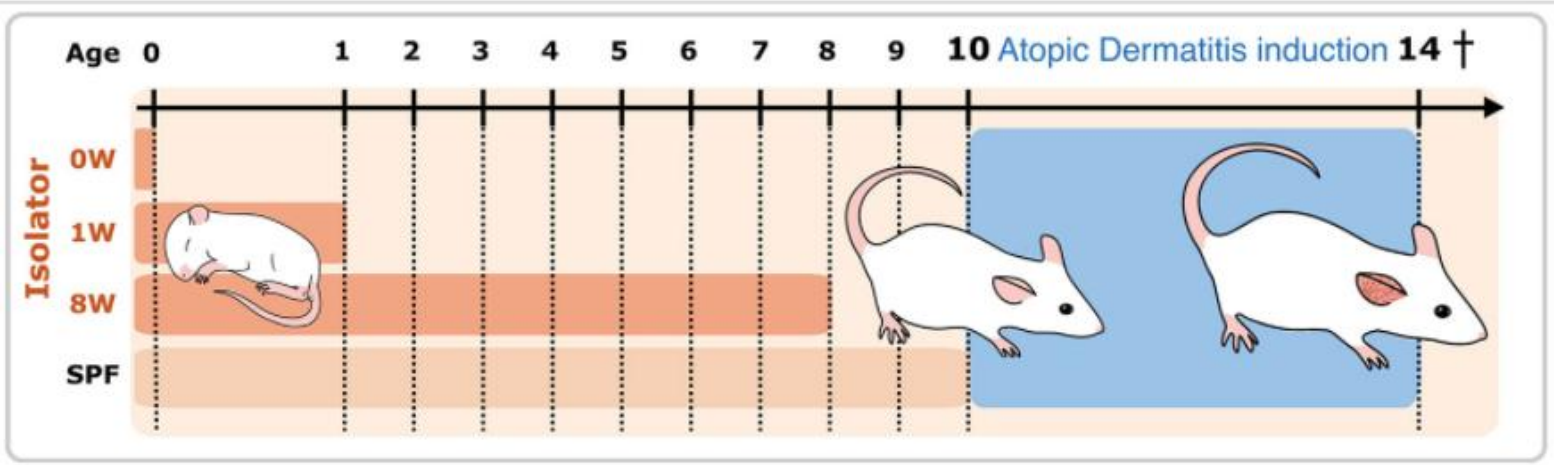
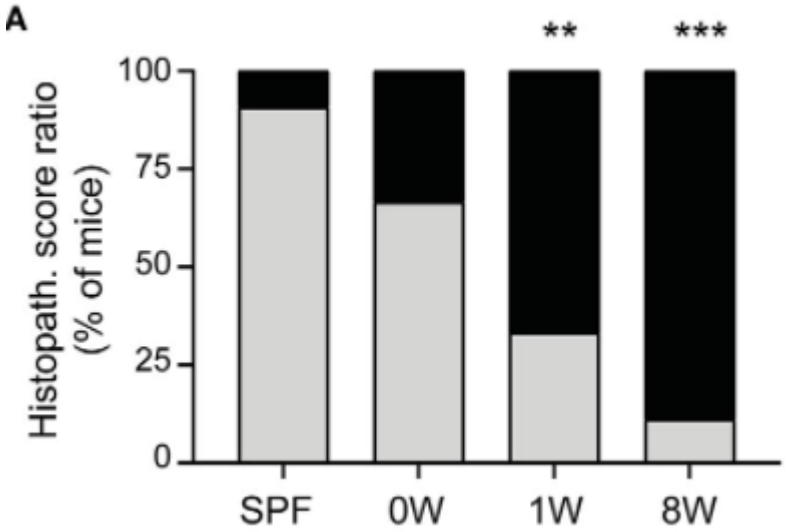
Подтвержден адрес электронной почты в домене sund.ku.dk

Diabetes Gut microbiota Immunology





https://www.frontiersin.org/articles/10.3389/fimmu.2021.650621/full

Theory in Biosciences (2021) 140:169–176
https://doi.org/10.1007/s12064-021-00340-y

ORIGINAL ARTICLE

A reaction norm perspective on reproducibility

Bernhard Voelkl[1] · Hanno Würbel[1]

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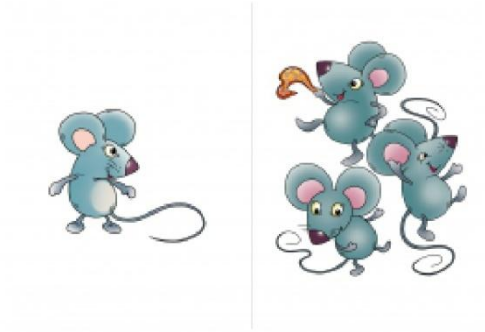
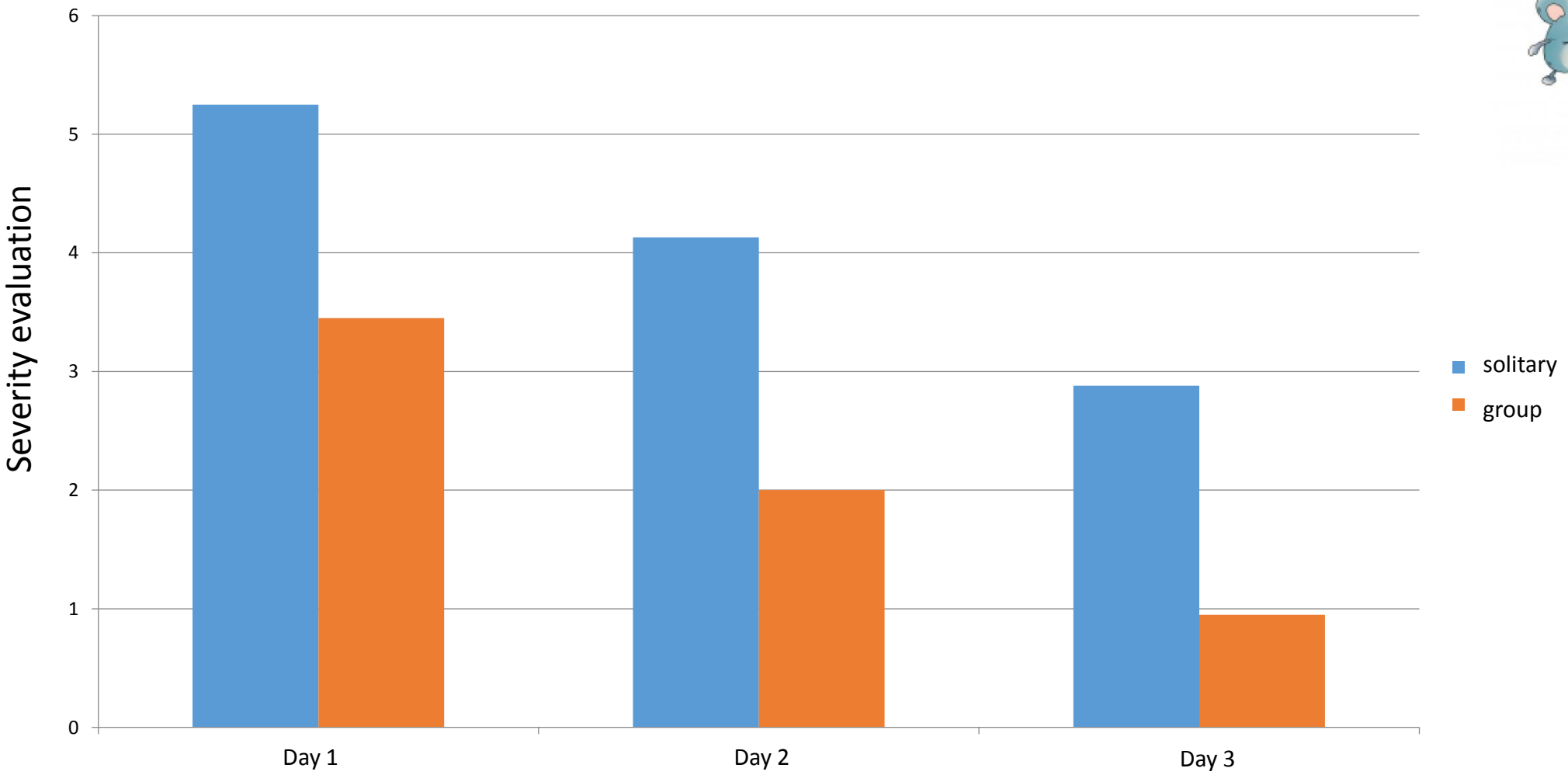
Abstract
Reproducibility in biomedical research, and more specifically in preclinical animal research, has been seriously questioned. Several cases of spectacular failures to replicate findings published in the primary scientific literature have led to a perceived reproducibility crisis. Diverse threats to reproducibility have been proposed, including lack of scientific rigour, low statistical power, publication bias, analytical flexibility and fraud. An important aspect that is generally overlooked is the lack of external validity caused by rigorous standardization of both the animals and the environment. Here, we argue that a reaction

When studying living organisms, we are faced with inherent biological variation which is distinct from random noise or measurement error and which is fundamental to the correct interpretation of experimental results.

Theory in Biosciences (2021) 140:169–176 https://doi.org/10.1007/s12064-021-00340-y

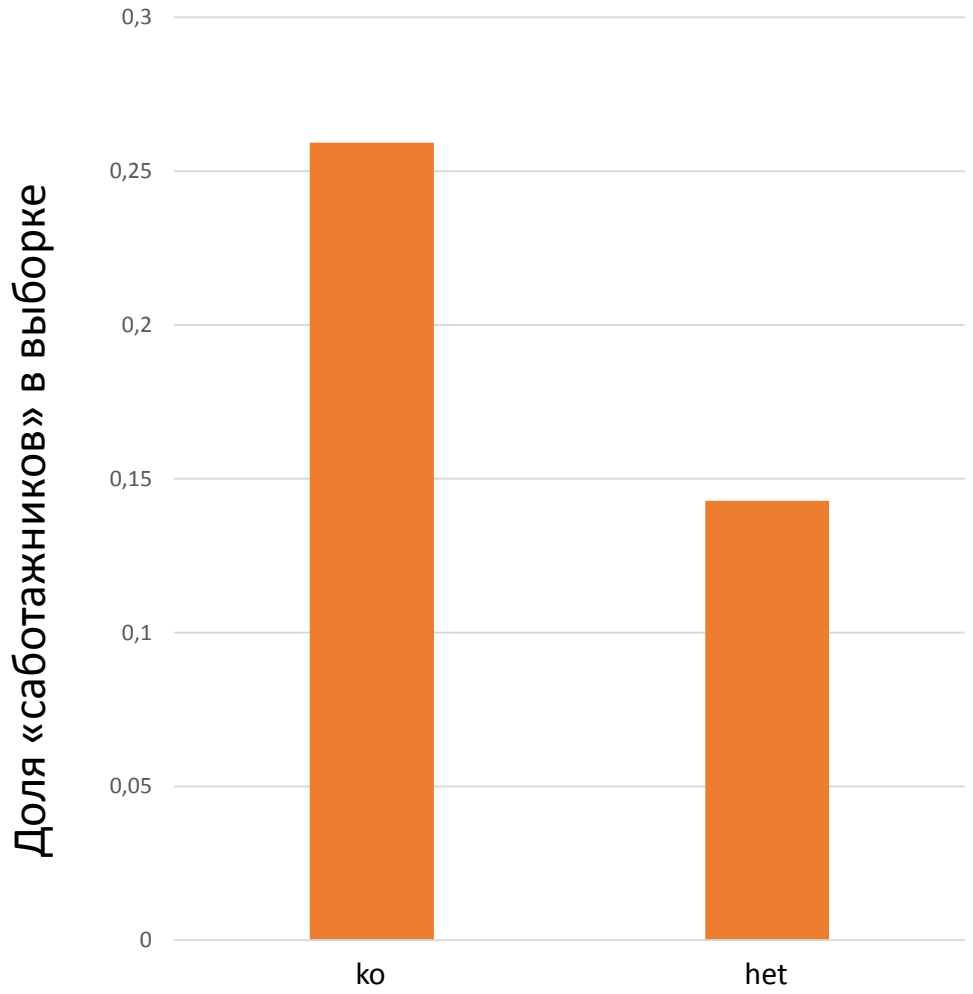
What animals tell us? Example #1 familiar vs solitary housing





Тем, кто сидит по одному, достоверно хуже, чем тем, кто сидит в домашних группах и на всех сроках наблюдения. Эффект не зависит от размера группы.

What animals tell us? Example #2 High responders vs low responders



Достоверных различий в пройденной дистанции не было, но доля отказавшихся бежать среди нокаутов в два раза больше