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Zentrum für BioKomplexität & NaturTeleologie

The Waiting Time Problem

and a New Argument against Neo-Darwinism

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1999-2016 Curator for Amber and Fossil Insects at the *State Museum of Natural History* in Stuttgart
Senior Fellow with Discovery Institute's *Center for Science & Culture* in Seattle, USA
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Chairman of the German-speaking *Center for BioComplexity & Teleology in Nature*

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Explosions of Biological Novelty

Abrupt origins are the rule in all periods of Earth History, in all geographical regions, and all groups of organisms from protists, to plants, invertebrates and vertebrate animals.

Origin of Life

Origin of Photosynthesis

Avalon Explosion (Ediacara)

Cambrian Explosion

Great Ordovician Biodiversification Event

Silurio-Devonian Terrestrial Revolution

Carboniferous Insect Explosion

Triassic Radiations (Tetrapods, Dinos, Marine Reptiles)

Abominable Mystery (Flowering Plants)

Big Bang of Birds

Placental Mammal Explosion


New Scientist

FEATURE 11 June 2008

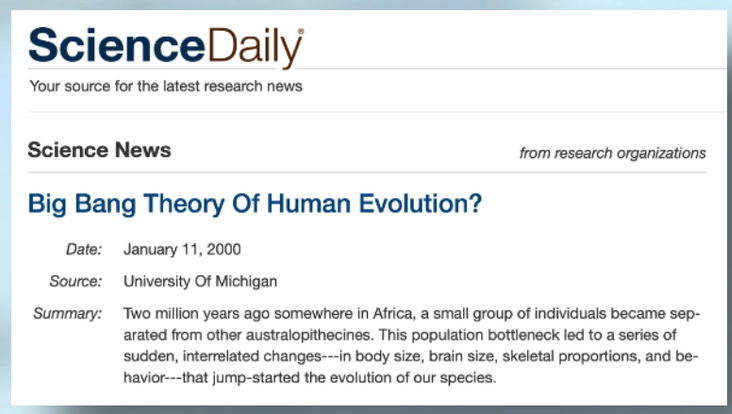
The Ordovician: Life's second big bang

By James O'Donoghue

Devonian Nekton Revolution

Odontode Explosion

Big Bang of Genus *Homo*


ScienceDaily

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Science News — *from research organizations*

Big Bang Theory Of Human Evolution?

Date: January 11, 2000

Source: University Of Michigan

Summary: Two million years ago somewhere in Africa, a small group of individuals became separated from other australopithecines. This population bottleneck led to a series of sudden, interrelated changes---in body size, brain size, skeletal proportions, and behavior---that jump-started the evolution of our species.

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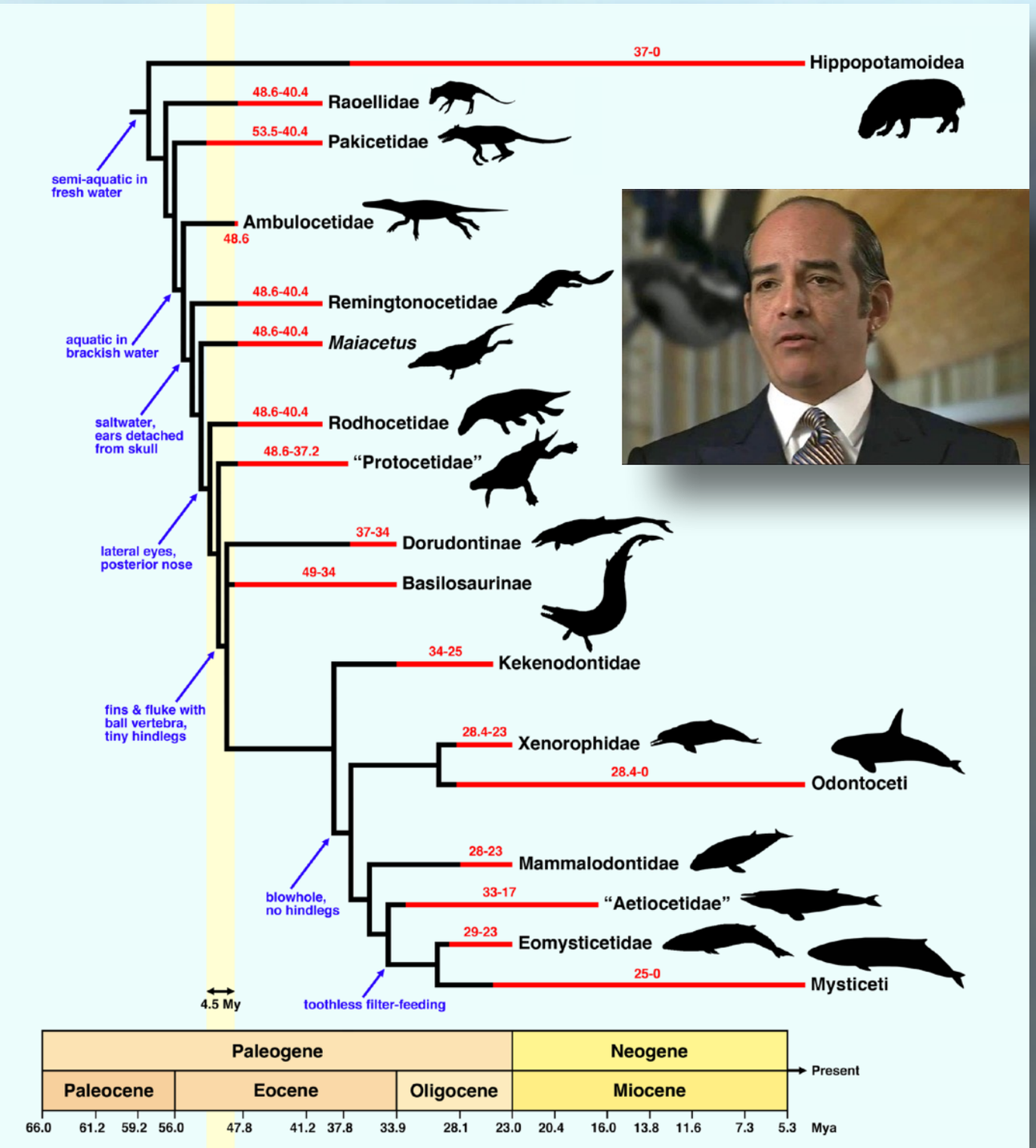
The Waiting Time Problem



The fossil record and population genetics combined do refute the mathematical feasibility of the Neo-Darwinian mechanism.

Geological available windows of time are much too short to accommodate the required genetic changes to arise and spread in the ancestral populations.

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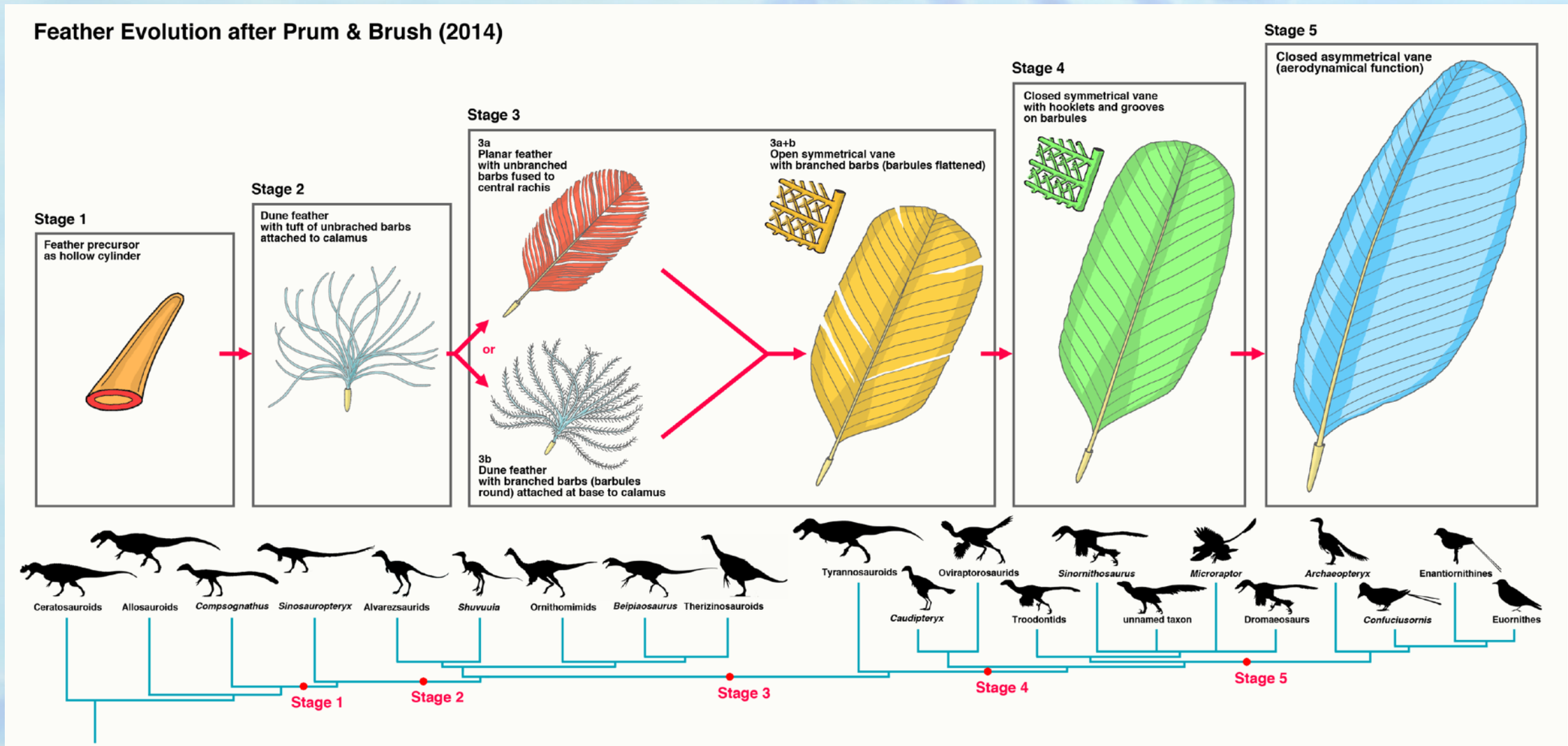
Paleontological Windows of Time

The fossil record provides very precise time frames for the appearance of certain groups of organisms and organs



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Coordinated Mutations

Coordinated Mutations **= two or more coincident genetic changes that only together produce an adaptive phenotypic effect that allows for selection to operate**

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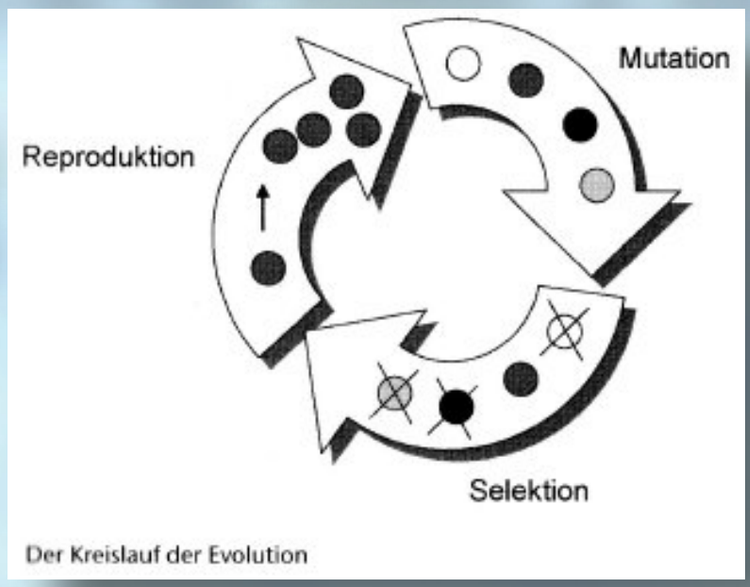
The Waiting Time Problem …

- Evolution is supposed to proceed by random mutation and natural/sexual selection
- Selection can only work on mutations with a positive or negative adaptive value
- At least some adaptive advantages require two or more coordinated mutations
- All mutations have two time constraints that depend on population size and generation time: the waiting time for a mutation to occur and the waiting time for the fixation of this mutation
- Does the history of life provide sufficient resources for evolution to accommodate these waiting times?



… is a Waiting Time Dilemma

- With large population the waiting time for a mutation to occur decreases, but fixation time increases (the same is true for neutral evolution)

- With small population sizes the waiting time for a mutation to occur increases, but fixation time decreases

Thus, there is no easy way for evolution to work around the waiting time problem!

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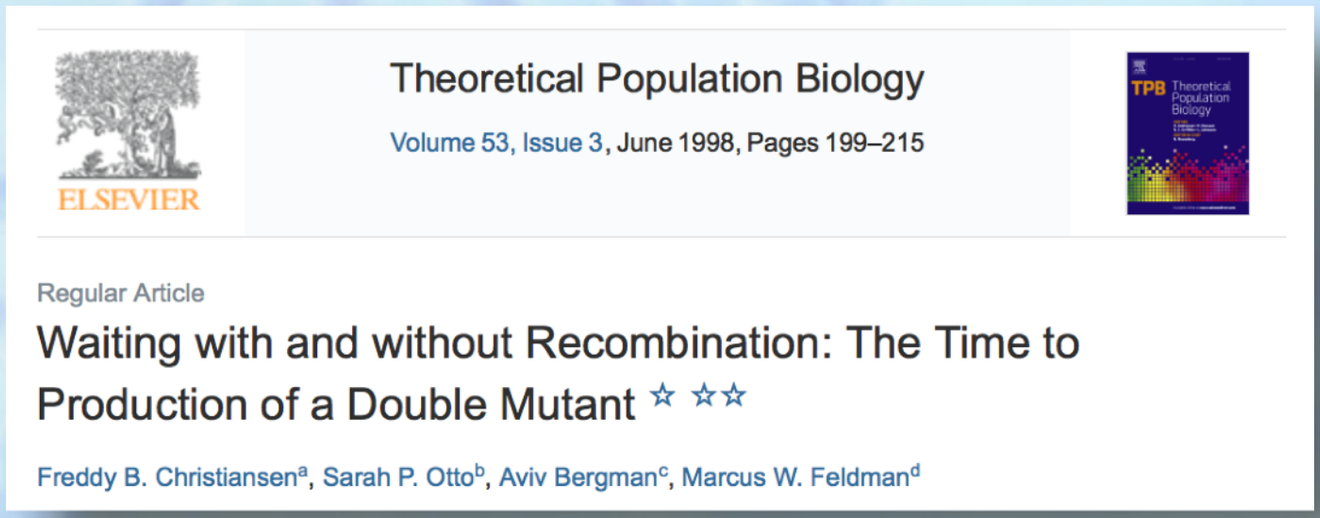
Recombination does not Help

A potential counter argument might be that recombination allows for neutral mutations (about 75% of all mutations) to occur separately in a population and to combine later by sexual recombination.



ELSEVIER

Theoretical Population Biology

Volume 53, Issue 3, June 1998, Pages 199–215

Regular Article

Waiting with and without Recombination: The Time to Production of a Double Mutant ☆ ☆☆

Freddy B. Christiansen[a], Sarah P. Otto[b], Aviv Bergman[c], Marcus W. Feldman[d]

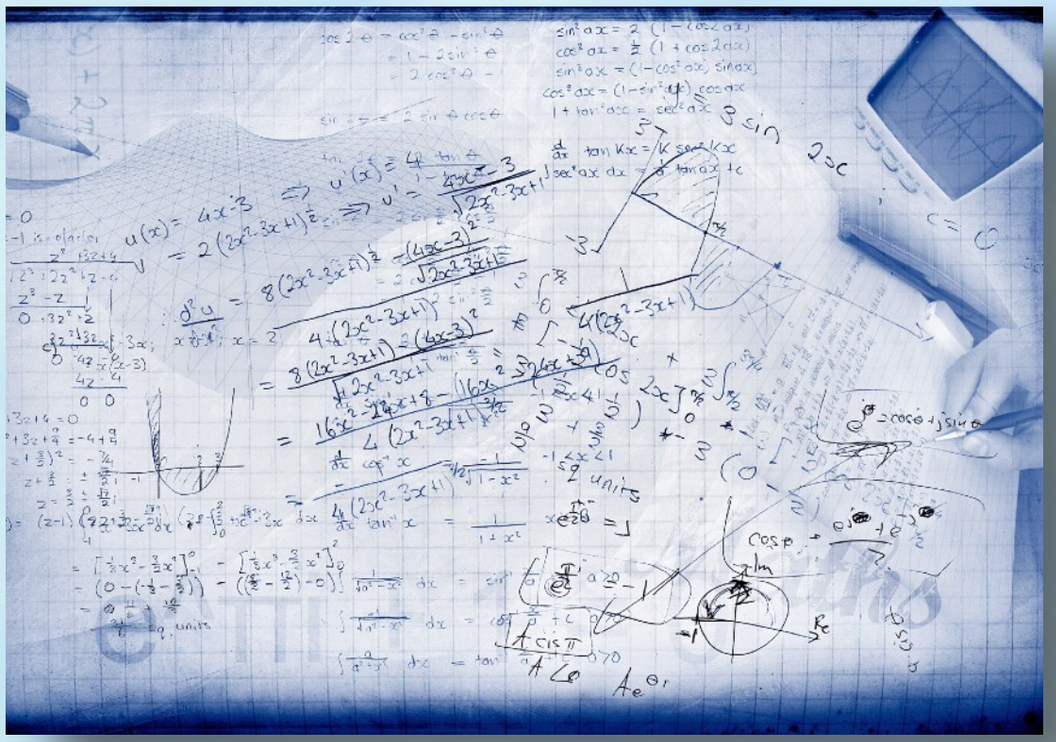
However, Christiansen et al. (1998) have shown that "*Recombination lowers the waiting time until a new genotypic combination first appears, but the effect is small compared to that of the mutation rate and population size*".

Doing the Math

While the fossil record provides the data for the available time frame, the standard formula of population genetics allows to do the math.

All you need are reasonable estimates of the following three parameters that can be established by comparison with recent organisms:

- **Mutation rate**
- **Effective population size per generation**
- **Generation turnover time**



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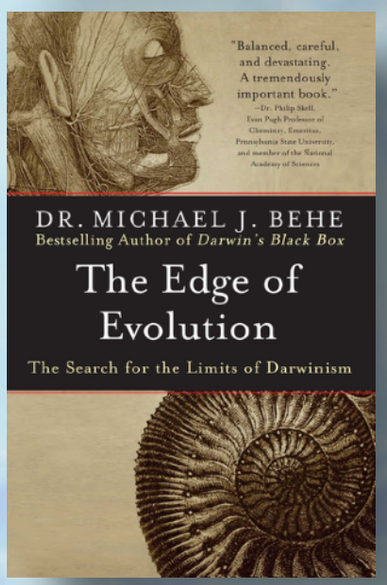
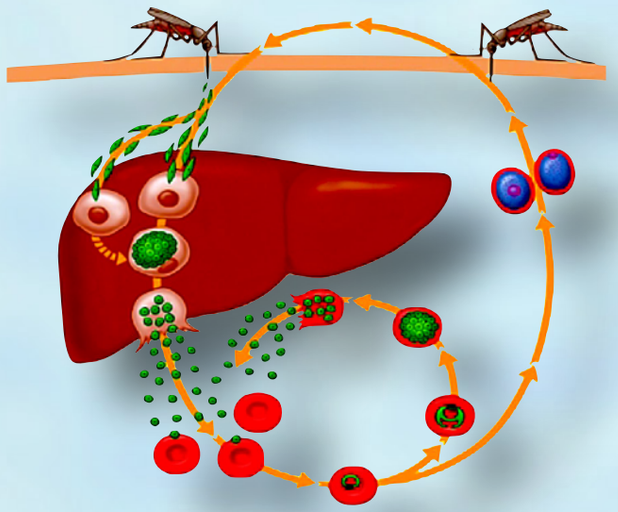
Discovery of the Problem

Behe & Snoke (2004) and Michael Behe in his book *The Edge of Evolution* (2007) made the argument that the waiting time for two coordinated mutations is prohibitive for the Neo-Darwinian mechanism of evolution to work.

Behe used the example of malaria resistance against the chloroquine drug, which required two mutually dependent mutations. Applying these data on human evolution predicted a waiting time of 10^{15} years!





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Example of Human Evolution

The mainstream Neo-Darwinian scientists Durrett & Schmidt (2008) criticized Behe's argument and claimed that his calculated waiting time of 10^{15} years is unrealistic.

However, their own calculations also resulted in a prohibitive waiting time of 216 million years, since only about 6 million years are available since the split of the human lineage from the chimp lineage.

100 YEARS marking the past. mapping the future. | GENETICS

Current Issue For Authors Editorial Board Submit a Manuscript

Genetics. 2008 Nov; 180(3): 1501–1509. PMCID: PMC2581952
doi: 10.1534/genetics.107.082610

Waiting for Two Mutations: With Applications to Regulatory Sequence Evolution and the Limits of Darwinian Evolution

Rick Durrett*,1 and Deena Schmidt†

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Example of Human Evolution

Sanford et al. (2015) used a computer simulation to calculate the following waiting times based on reasonable estimates for an ancestral hominin population of 10,000 individuals and a generation turnover time of 20 years:

- **fixation of a specific point mutation: 1.5-15.9 million years**
- **fixation of a single codependent mutation: 85 million years**

This is prohibitive considering 5% difference in the human vs chimp genome within 6 million years since the separation of their lineages.

Sanford *et al. Theoretical Biology and Medical Modelling* (2015) 12:18
DOI 10.1186/s12976-015-0016-z

THEORETICAL BIOLOGY AND MEDICAL MODELLING

RESEARCH Open Access

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The waiting time problem in a model hominin population

John Sanford[1*], Wesley Brewer[2], Franzine Smith[3] and John Baumgardner[4]

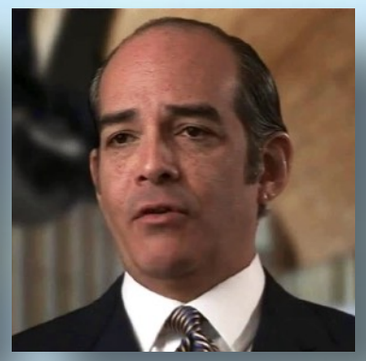
Discovery Institute - Research Project

… shall show that these are not exceptions but the rule, so that the waiting time problems represents a refutation of Darwinian evolution. It is a collaboration of Drs *Douglas Axe* (molecular biologist), *Günter Bechly* (paleontologist), *Ann Gauger* (molecular biologist), *Ola Hössjer* (mathematician), *Paul Nelson* (philosopher of biology), and *Richard von Sternberg* (evolutionary biologist).

In this multi-annual project we intend to do the calculations for a number of examples from protists, plants, invertebrate and vertebrate animals, covering most periods of earth history, and covering important key events in evolution.





A New Mathematical Model

Based on the mathematical models of Durrett & Schmidt (2008) and Sanford et al. (2015) as well as Behrens & Vingron (2010), we developed a new model, which does not depend on two specific mutation combinations, but allows for multiple combinations to work, and also incorporates back-mutations.

Journal of Theoretical Biology 524 (2021) 110657

Contents lists available at ScienceDirect

Journal of Theoretical Biology

journal homepage: www.elsevier.com/locate/yjtbi

On the waiting time until coordinated mutations get fixed in regulatory sequences

Ola Hössjer [a,*], Günter Bechly [b], Ann Gauger [b]

Phase-type Distribution Approximations of the Waiting Time Until Coordinated Mutations Get Fixed in a Population

Ola Hössjer*
Günter Bechly Ann Gauger†

Abstract

In this paper we study the waiting time until a number of coordinated mutations occur in a population that reproduces according to a continuous time Markov process of Moran type. It is assumed that any individual can have one of $m+1$ different types, numbered as $0, 1, \ldots, m$, where initially all individuals have the same type 0. The waiting time is the time until all individuals in the population have acquired type m, under different scenarios for the rates at which forward mutations $i \to i+1$ and backward mutations $i \to i-1$ occur, and the selective fitness of the mutations. Although this waiting time is the time until the Markov process reaches its absorbing state, the state space of this process is huge for all but very small population sizes. The problem can be simplified though if all mutation rates are smaller than the inverse population size. The population then switches abruptly between different fixed states, where one type at a time dominates. Based on this, we show that phase-type distributions can be used to find closed form approximations for the waiting time law. Our results generalize work by Schweinsberg (2008) and Durrett et al. (2009), and they have numerous applications. This includes onset and growth of cancer for a cell population within a tissue, with type representing the severity of the cancer. Another application is temporal changes of gene expression among the individual in a species, with type representing different binding sites that appear in regulatory sequences of DNA.

*Department of Mathematics, Stockholm University, 106 91 Stockholm, Sweden
†Biologic Institute, 16310 NE 80th Street, Redmond, WA 98052, USA

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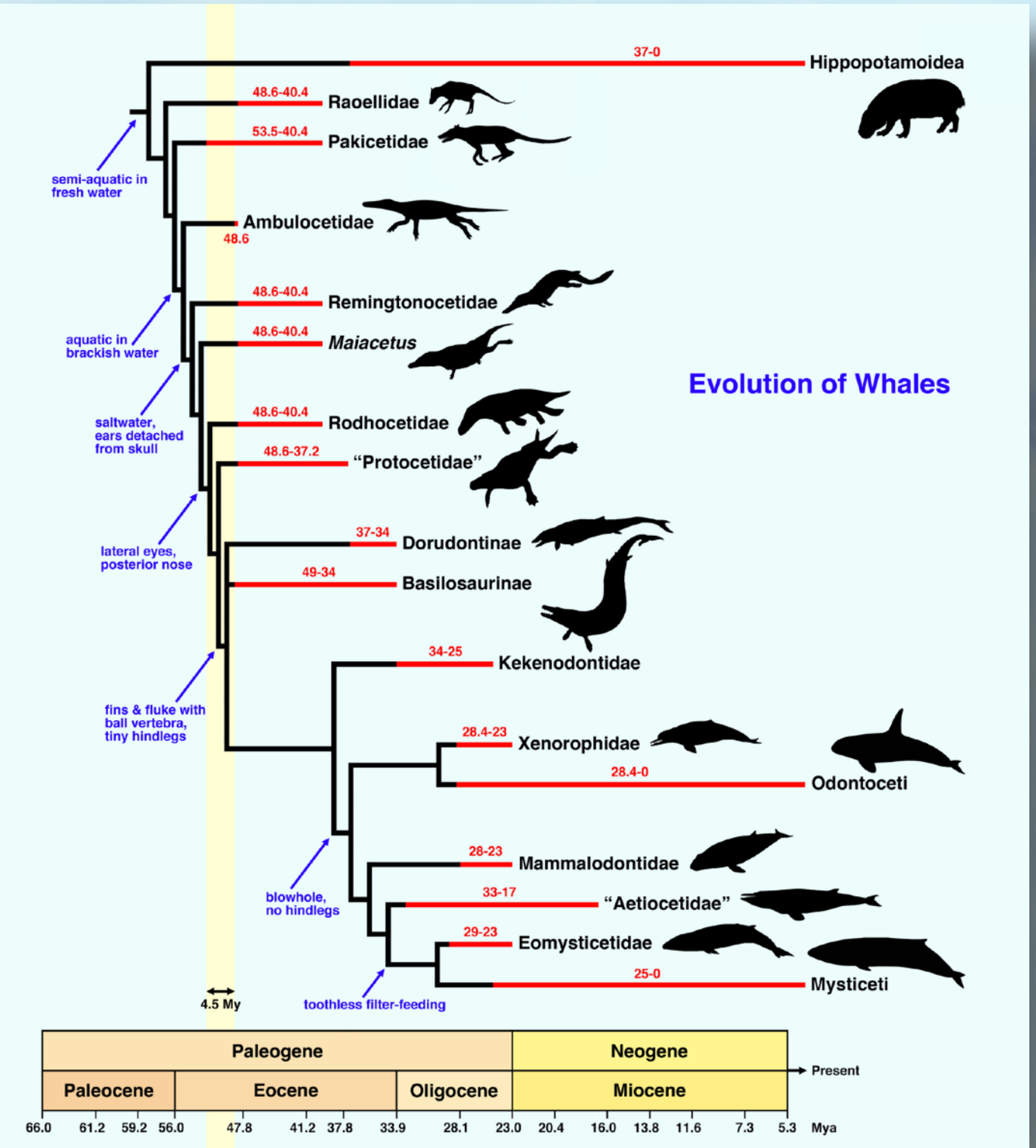
Example of Whale Evolution



ELSEVIER

Molecular Phylogenetics and Evolution

Volume 66, Issue 2, February 2013, Pages 479–506

Morris Goodman Memorial Symposium

A phylogenetic blueprint for a modern whale

John Gatesy[a], Jonathan H. Geisler[b], Joseph Chang[a], Carl Buell[c], Annalisa Berta[d], Robert W. Meredith[a, e], Mark S. Springer[a], Michael R. McGowen[f]

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Example of Whale Evolution

Richard von Sternberg did the math based on the formula in Durrett & Schmidt (2008), and very generous estimates for an effective population size of 100,000 individuals per generation and a generation turnover time of 5 years. The result was a waiting time of 43.4 million years for a single event of two coordinated mutations.

Dr. Richard v. Sternberg

The fossil record shows that only 4.5 million years are available between still walking ancestors (*Himalayacetus*, 53.5 mya) and the first truly aquatic whales (49 mya, Basilosauridae). This transition requires complex engineering like …

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Example of Whale Evolution

- forelimbs transformed into flippers, reduction of hind limbs and pelvis, tail transformed into fluke (incl. ball vertebra for up and down movement)
- re-orientation of the fetus for subaquatic birth (tail-first)
- modification of mammary glands for nursing under water
- reorganization of kidney tissue for intake of salt water
- special lung surfactant (lung has to re-expand rapidly upon coming up to the surface)
- intra-abdominal counter-current heat exchange system (testes are inside the body next to the muscles that generate heat during swimming)

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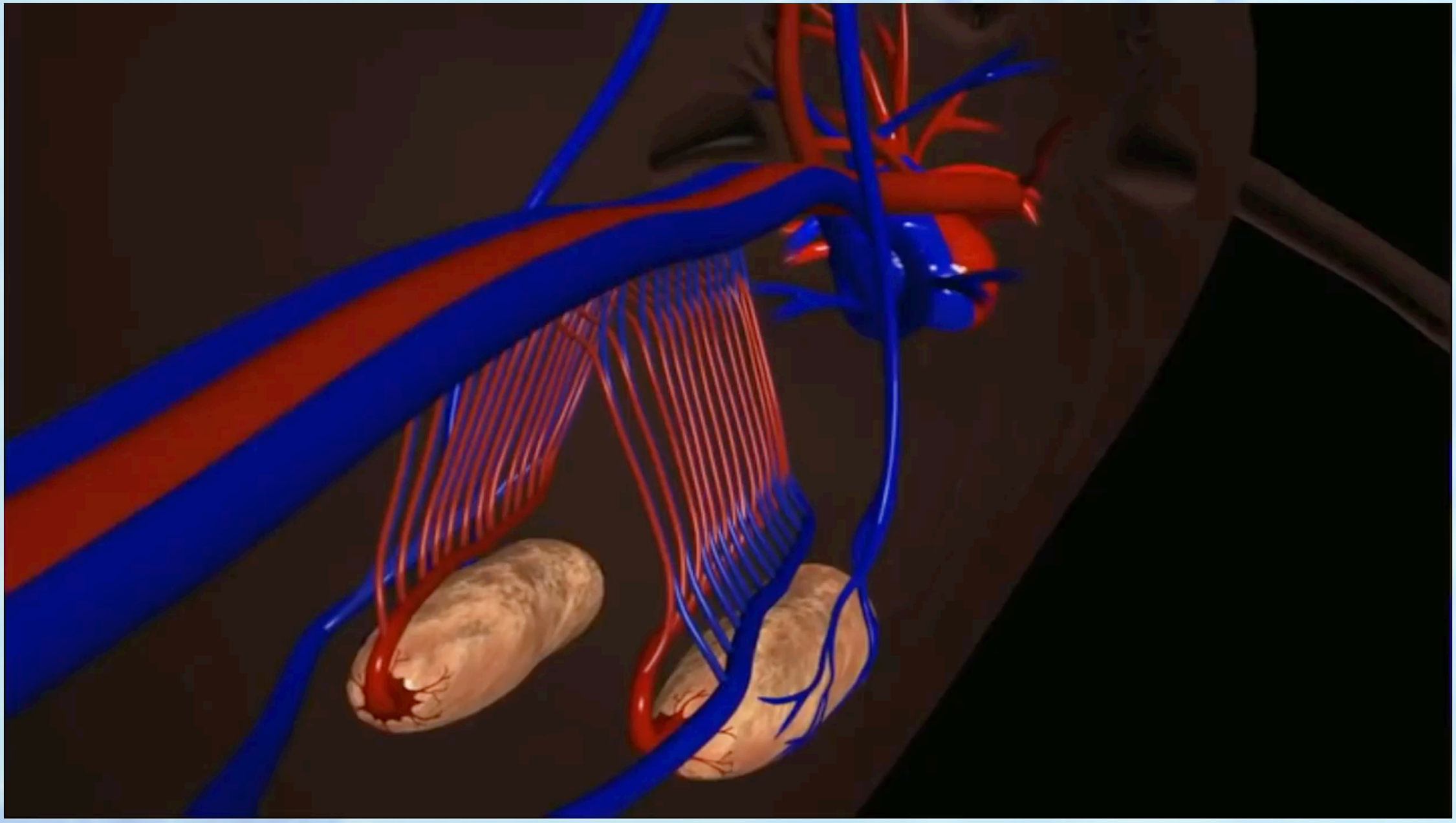
Example of Whale Evolution



from the DVD documentary *Living Waters* (2015) by Illustra Media

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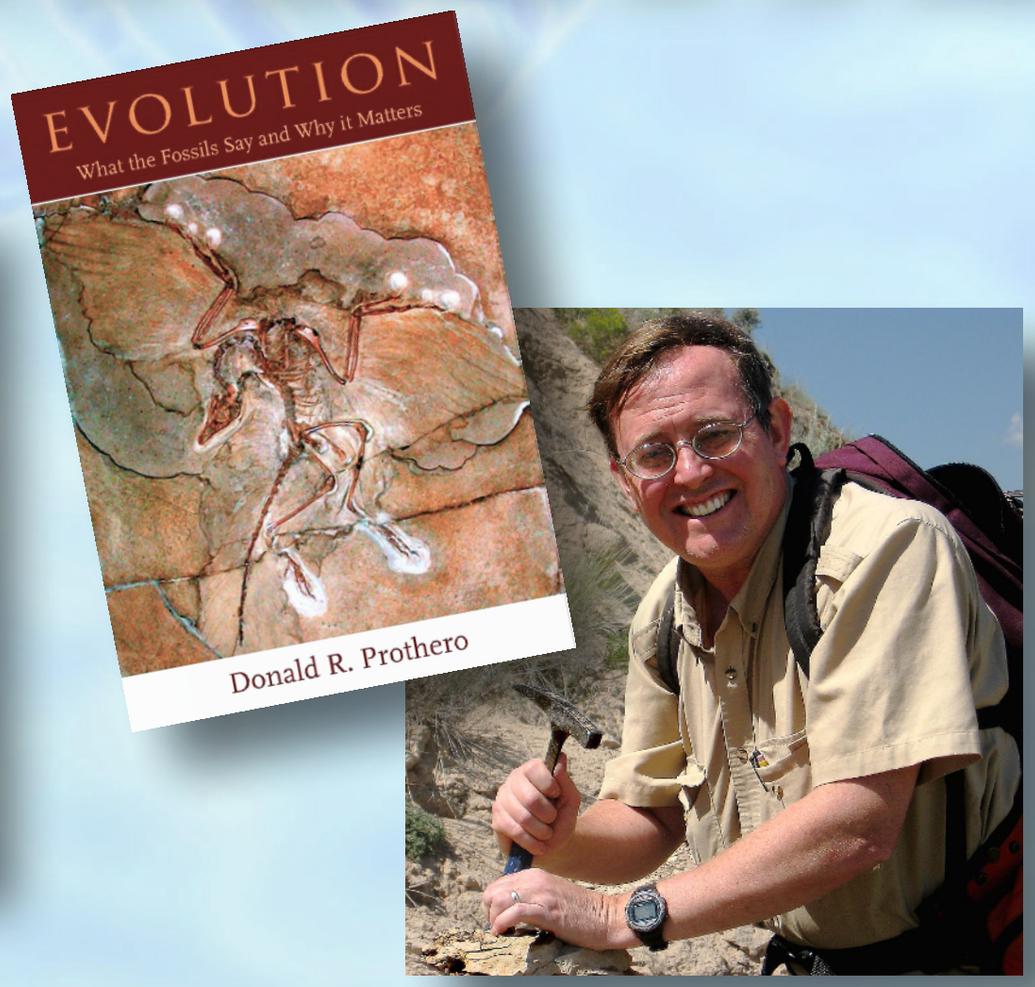
Example of Whale Evolution

In a public debate 2009 at Beverly Hills, famous paleontologist Dr. Donald Prothero, author of the book *Evolution - What the Fossil Say and Why it Matters*, was absolutely clueless how to respond to Dr. Richard Sternberg's argument, and apparently did not even understand it.



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Species Longevity implies Saltationism

The waiting time problem is amplified by Prothero's own result that the longevity (lifespan) of a larger artiodactyl mammal species, which would include whales and their ancestors, is more than 4 million years!

Basilosaurus

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The Species Pair Challenge

Why should anybody seriously believe that *Indohyus* / *Pakicetus* and *Basilosaurus* / *Dorudon* could diverge within 4-5 million years, including all the re-engineering from a terrestrial to a marine mammal?

Dorudon

Indohyus

Pakicetus

Basilosaurus

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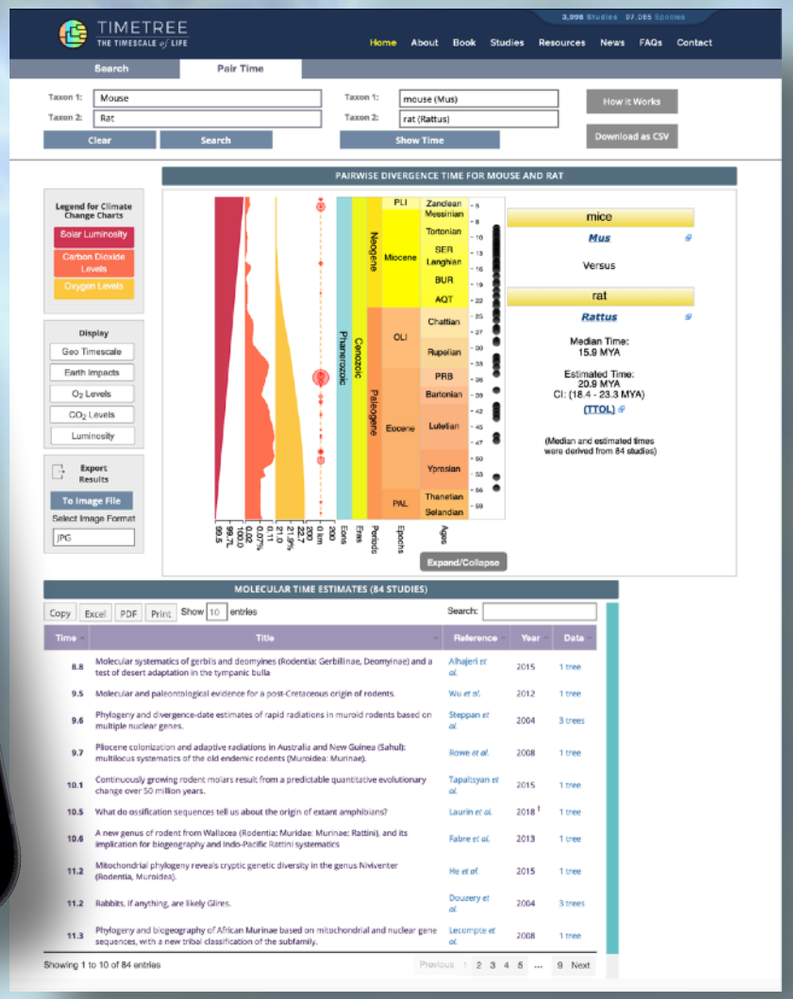
The Species Pair Challenge

A challenge to Darwinists: Find in the data base of *TimeTree.org* among 97k living species a single pair of species, that according to molecular clock estimates have diverged about 5 million years ago, and exhibit a remotely similar morphological divergence to *Pakicetus* and *Basilosaurus*.

TIMETREE
THE TIMESCALE of LIFE



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The Species Pair Challenge

Firs and cedars are conifers that diverged 141 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

***Abies* spec.**

***Cedrus* spec.**

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The Species Pair Challenge

The common house fly and small house fly diverged 48 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

Musca domestica

Fannia scalaris

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The Species Pair Challenge

The northern damselfly and the azure damselfly diverged 11.8 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

Coenagrion hastulatum

Coenagrion puella

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The Species Pair Challenge

The European common frog and the moor frog diverged 21.4 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

Rana temporaria

Rana arvalis

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The Species Pair Challenge

The Galapagos land iguanas and marine iguanas diverged 18.2 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

Conolophus ***Amblyrhynchus***

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The Species Pair Challenge

The two warbler species *Phylloscopus nitidus* and *P. bonelli* diverged 15.2 million years ago (at least 4-7 mya).

May still hybridize?

TIMETREE
THE TIMESCALE *of* LIFE

JOURNAL OF AVIAN BIOLOGY 26: 139–153. Copenhagen 1995

Genetic differentiation and phylogenetic relationships of Bonelli's Warbler *Phylloscopus bonelli* and Green Warbler *P. nitidus*

Andreas J. Helbig, Ingrid Seibold, Jochen Martens and Michael Wink

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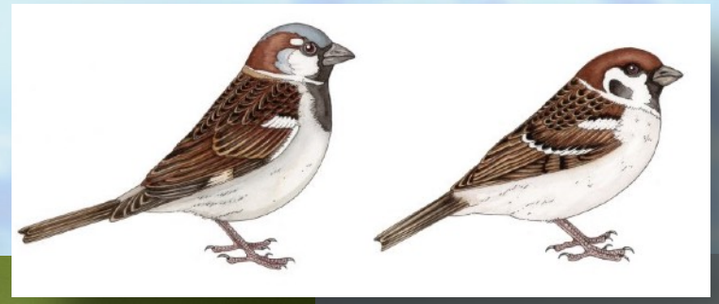
The Species Pair Challenge

The house sparrow and tree sparrow diverged 10.2 million years ago.

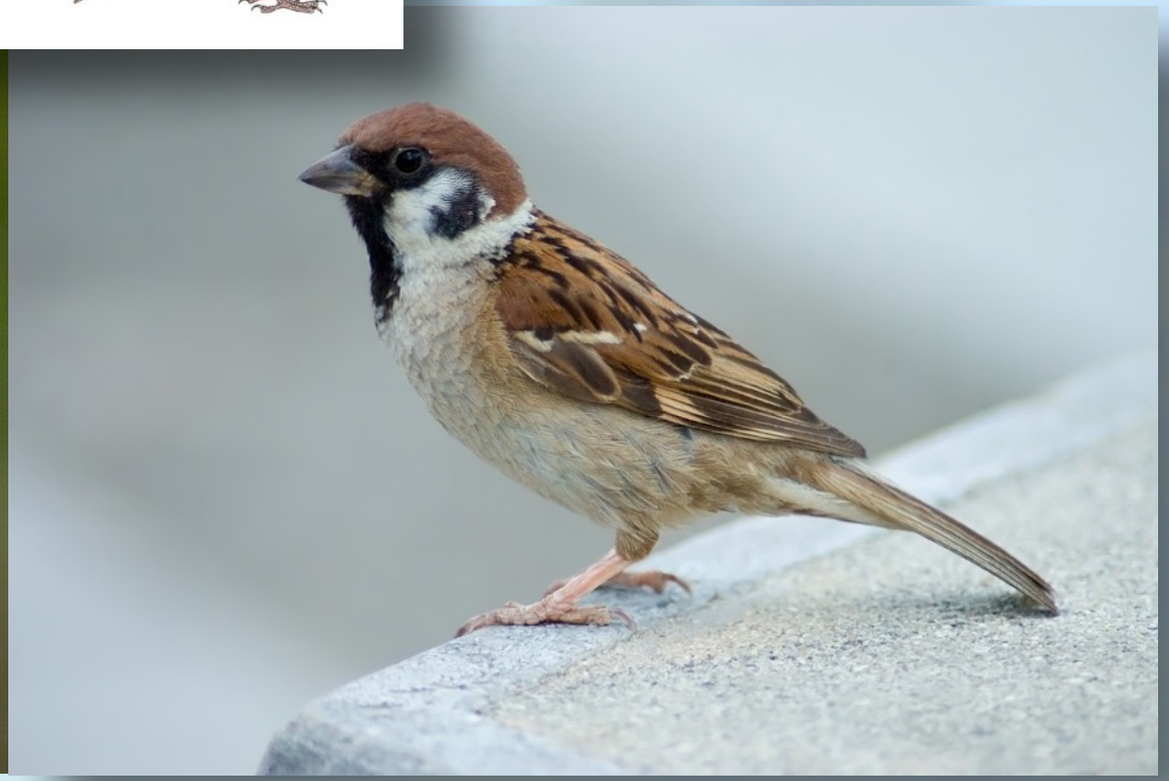
TIMETREE
THE TIMESCALE *of* LIFE

Still can hybridize!



Passer domesticus

Passer montanus



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The Species Pair Challenge

House mouse and rats diverged 20.9 million years ago (at least 12 mya).

TIMETREE
THE TIMESCALE *of* LIFE

Mus

SCIENTIFIC REPORTS

OPEN

Corrected placement of *Mus-Rattus* fossil calibration forces precision in the molecular tree of rodents

Received: 04 June 2014
Accepted: 14 August 2015
Published: 28 September 2015

Yuri Kimura[1,4], Melissa T. R. Hawkins[2,3], Molly M. McDonough[2,3], Louis L. Jacobs[4] & Lawrence J. Flynn[5]

Rattus

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The Species Pair Challenge

Cattle and European bison diverged 4.88 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

Can still hybridize as beefalo!

Bison bonasus

Bos taurus

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The Species Pair Challenge

Horse and ass diverged 7.7 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

Can still hybridize as mule!

Equus caballus

Equus asinus

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The Species Pair Challenge

Asian and African elephants diverged 25.9 million years ago (at least 7.6 mya).

African savannah and forest elephants diverged 7.6 million years ago (at least 4 mya).

TIMETREE
THE TIMESCALE *of* LIFE

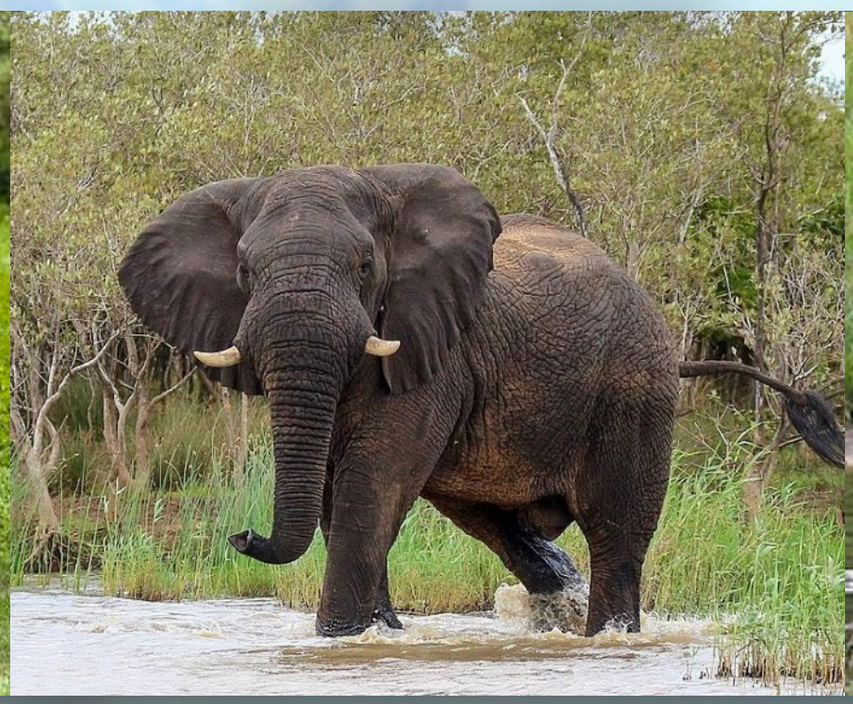
OPEN ACCESS Freely available online PLoS BIOLOGY

Proboscidean Mitogenomics: Chronology and Mode of Elephant Evolution Using Mastodon as Outgroup

Nadin Rohland[1☯], Anna-Sapfo Malaspinas[2,3☯], Joshua L. Pollack[2], Montgomery Slatkin[2], Paul Matheus[4], Michael Hofreiter[1*]

Elephas maximus

Loxodonta africana



Loxodonta cyclotis

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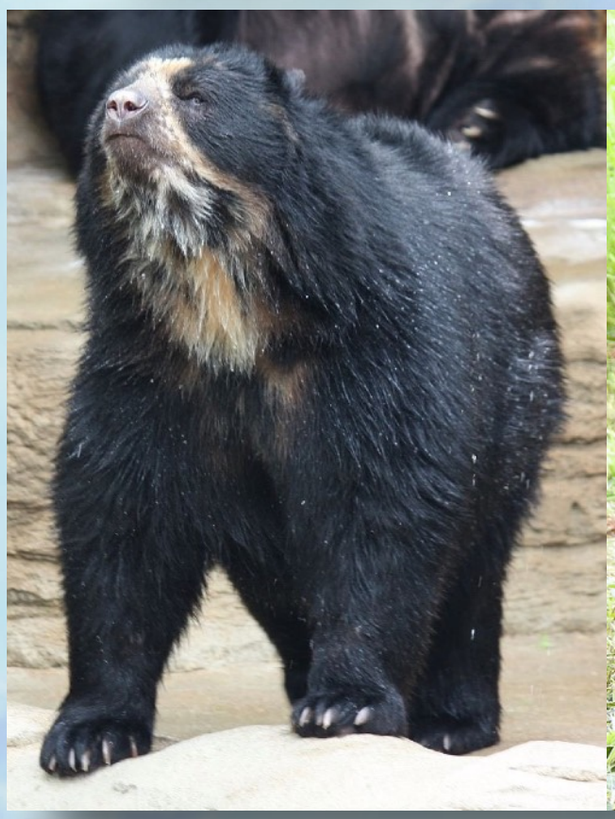
The Species Pair Challenge

Spectacled bear and Asian black bear diverged 16.5 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

Can still hybridize in captivity!

Tremarctos ornatus ***Ursus (Selenarctos) thibetanus***



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The Species Pair Challenge

River otter and brown fur seal diverged 40 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

Lutra lutra

Arctocephalus pusillus

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The Species Pair Challenge

Hippo and pygmy hippo diverged 9.6 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

Hippopotamus amphibius

Choeropsis liberiensis

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The Species Pair Challenge

The common dolphin and the bottlenose dolphin diverged 3.99 million years ago.

TIMETREE
THE TIMESCALE *of* LIFE

Delphinus delphis

Tursiops truncatus

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The Species Pair Challenge

Chimp and gorilla diverged 9.06 million years ago (humans 6.7 mya).

TIMETREE
THE TIMESCALE *of* LIFE

Pan troglodytes

Gorilla gorilla

Homo sapiens

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The Species Pair Challenge

Two following two facts need an explanation:

1.) There are many examples of fossil species pairs with very different body plans that diverged within 5 (± 5) million years. Even though only about 1% of all extinct species are preserved in the fossil record of about 350k described species.

2.) There are no living species pairs with even remotely similar differences in body plan that are dated to have diverged in a similar time frame. Even though there are an estimated 8.7 million living species, of which 2 million have been described.

What is the Bayesian likelihood that not a single living species exhibits the same phenomenon that is so common in the fossil record? Basically zero!

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Questions & Answers