Supplementary Material: **Why Naked Mole-Rats Have High Oxidative Damage But Live a Long Life: A Simple Explanation Based on the Oxidative Stress Theory of Aging**

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1 Variable description

Table A1: Variables and parameters used in the model.

Variables	Definition	Unit
B_{rest}	Resting metabolic rate, $B_{rest} = B_{rep} + B_{syn}$	energy/time
B_0	Normalization coefficient, a constant within a taxa. $B_{rest} = B_0 m^{3/4}$	energy/time/(biomass)$^{3/4}$
B_{rep}	Rate of metabolic energy allocated to repairing (somatic maintenance)	energy/time
B_{syn}	Rate of metabolic energy to synthesize new biomass, including growth and reproduction, $B_{syn} = E_m \times G$	energy/time
B_{act}	Rate of metabolic energy allocated to activities, $B_{act} \propto B_{rest}$	energy/time
B_{tot}	Total metabolic rate, $B_{total} = B_{act} + B_{rest} = f B_{rest}$, where f is a constant for given taxon. $f \approx 2 \sim 3$.	energy/time
B_{ms}	Mass-specific resting metabolic rate, $B_{ms} = B_{rest}/m(t)$	energy/time/mass
C	Threshold of the damage level	unitless
$D(t)$	Mass-specific accumulated damage	unitless
$D_{total}(t)$	Total accumulated damage	biomass
E_m	Energy required to synthesize one unit of biomass	energy/time
G	Growth rate, $G = dm/dt$	biomass/time
LS	Lifespan	time
$m(t)$	body mass at age t	biomass
m_0	body mass at birth	biomass
M	adult body mass	biomass

H	Rate of damage production, $H = \delta \times B_{rest}$	biomass/time
R	Rate of repair, $R = \eta \times B_{rep} = \eta(B_{rest} - E_m G)$	biomass/time
t	Age	time
δ	Damage coefficient, a constant within a species	damaged mass/energy
η	Repair coefficient, a constant within a species	damaged mass/energy

2 Derivation of Eq.1 in main text

Here we give a detailed derivation of Eq.1 in the main text based on Hou [25].

First we assume that the rate of raw damage production is proportional to the total metabolic rate (equivalent to oxygen consumption rate), i.e., $H = a \times B_{tot}$, where a is a constant within a species, indicating the production of damage that is associated with one unit of energy consumption. Numerous data have shown that, at least in birds and mammals, B_{tot} is proportional to B_{rest} [27-29], $B_{tot} = f \times B_{rest}$, where f is a constant indicating the level of activity. In general, f averages around $2 \sim 3$ within a taxon [27-30]. Using this relationship the raw damage production H can be expressed in terms of resting metabolic rate B_{rest}, $H = a \times B_{tot} = a \times f \times B_{rest} = \delta \times B_{rest}$, where $\delta = a \times f$. Thus, although H is expressed in terms of resting metabolic rate, it actually estimates the rate of the total raw damage production that is associated with the rate of total oxygen consumption, including the oxygen consumption at rest and that during activity. The activity contributes to damage through f, which is usually a constant. Below we will use the relationship $H = \delta \times B_{rest}$ to derive Eq. 1 in the main text.

We further assume that the amount of damage that can be repaired is proportional to one unit of metabolic energy allocated to repair as $R = \eta B_{rep}$, where η is a constant within a species, and B_{rep} is the energy allocated to repair. As explained in the main text, the resting metabolic energy is partitioned between the energy allocated to maintain existing biomass, B_{rep}, and the energy allocated to synthesize new biomass, B_syn, i.e., $B_{rest} = B_{rep} + B_{syn}$. The energy allocated to synthesize new biomass is $B_{syn} = E_m G$, where E_m is the energy required to synthesize one unit of biomass, and G is growth rate (biomass gain per unit time). Putting these relationships together we have $R = \eta B_{rep} = \eta(B_{rest} - B_{syn} = \eta(B_{rest} - E_m G)$.

Having the raw damage production rate H and the repair rate R, the rate of net damage production,

$$\begin{aligned} H - R &= \delta B_{rest} - \eta(B_{rest} - E_m G) \\ &= (\delta - \eta) B_{rest} + \eta E_m G. \end{aligned}$$

Damage accumulates over time. Thus, the total net damage, D_{total}, at a certain age, t, can be estimated as the integral of the rate over time

$$\begin{aligned} D_{total}(t) &= \int_0^t (H - R) dt \\ &= \int_0^t [(\delta - \eta) B_{rest} + \eta E_m G] dt \\ &= \int_0^t (\delta - \eta) B_{rest} dt + \int_0^t \eta E_m G dt \end{aligned}$$

Because δ, η, and E_m are independent of time, t,

$$D_{total}(t) = (\delta - \eta) \int_0^t B_{rest} dt + \eta E_m \int_0^t G dt. \tag{A1}$$

Here, we use the general observed scaling relation, $B_{rest} = B_0 m(t)^{3/4}$, and then the integral becomes $\int_0^t B_{rest} dt = B_0 \int_0^t m(t)^{3/4} dt$. This integral requires the analytic expression of growth curve, $m(t)$. The ontogenetic growth model (Eq. 1 in West et al. [32]) gives a growth curve,

$$m(t) = M(1 - [1 - (\frac{m_0}{M})^{1/4}] e^{\frac{-B_0 t}{4 E_m M^{1/4}}})^4.$$

Below we show that the integral of $m(t)^{3/4}$ over age t can be approximately expressed at $M^{3/4} \times t$, where M is the adult mass.

$$\begin{aligned}\int_0^t m(t)^{3/4}dt =& \int_0^t M^{3/4}\{1-[1-(\frac{m_0}{M})^{1/4}]e^{\frac{-B_0t}{4E_mM^{1/4}}}\}^3dt\\ =& \int_0^t M^{3/4}dt\\ &+\int_0^t M^{3/4}\{-3[1-(\frac{m_0}{M})^{1/4}]e^{\frac{-B_0t}{4E_mM^{1/4}}}\\ &+3[1-(\frac{m_0}{M})^{1/4}]^2e^{\frac{-B_0t}{2E_mM^{1/4}}}]\\ &-[1-(\frac{m_0}{M})^{1/4}]^3e^{\frac{-3B_0t}{4E_mM^{1/4}}}\}dt\end{aligned}$$

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Adult size M is independent of t, which gives

$$\begin{aligned}\int_0^t m(t)^{3/4}dt =& M^{3/4}t\\ &+M^{3/4}\int_0^t\{-3[1-(\frac{m_0}{M})^{1/4}]e^{\frac{-B_0t}{4E_mM^{1/4}}}\\ &+3[1-(\frac{m_0}{M})^{1/4}]^2e^{\frac{-B_0t}{2E_mM^{1/4}}}]\\ &-[1-(\frac{m_0}{M})^{1/4}]^3e^{\frac{-3B_0t}{4E_mM^{1/4}}}\}dt\\ =& M^{3/4}t\\ &+\frac{E_mM}{B_0}\{e^{\frac{-B_0t}{4E_mM^{1/4}}}[-12+12(\frac{m_0}{M})^{1/4}]+[12-12(\frac{m_0}{M})^{1/4}]\\ &+e^{\frac{-B_0t}{2E_mM^{1/4}}}[6-12(\frac{m_0}{M})^{1/4}+6(\frac{m_0}{M})^{1/2}]\\ &-[6-12(\frac{m_0}{M})^{1/4}+6(\frac{m_0}{M})^{1/2}]\\ &-e^{\frac{-3B_0t}{4E_mM^{1/4}}}[4/3-4(\frac{m_0}{M})^{1/4}+4(\frac{m_0}{M})^{1/2}-4/3(\frac{m_0}{M})^{3/4}]\\ &+[4/3-4(\frac{m_0}{M})^{1/4}+4(\frac{m_0}{M})^{1/2}-4/3(\frac{m_0}{M})^{3/4}]\}.\end{aligned}$$

Put all the time dependent terms together as Z_1 and time independent terms together as Z_2.

$$\int_0^t m(t)^{3/4}dt = Z_1 + Z_2,$$

where

$$
\begin{aligned}
Z_1 =&M^{3/4}t \\
&+ \frac{E_m M}{B_0}\{e^{\frac{-B_0 t}{4E_m M^{1/4}}}[-12 + 12(\frac{m_0}{M})^{1/4}] \\
&+ e^{\frac{-B_0 t}{2E_m M^{1/4}}}[6 - 12(\frac{m_0}{M})^{1/4} + 6(\frac{m_0}{M})^{1/2}] \\
&- e^{\frac{-3B_0 t}{4E_m M^{1/4}}}[4/3 - 4(\frac{m_0}{M})^{1/4} + 4(\frac{m_0}{M})^{1/2} - 4/3(\frac{m_0}{M})^{3/4}]\} \\
. =&M^{3/4}t + Z_3
\end{aligned}
$$

and

$$
\begin{aligned}
Z_2 =&[12 - 12(\frac{m_0}{M})^{1/4}] \\
&- [6 - 12(\frac{m_0}{M})^{1/4} + 6(\frac{m_0}{M})^{1/2}] \\
&+ [4/3 - 4(\frac{m_0}{M})^{1/4} + 4(\frac{m_0}{M})^{1/2} - 4/3(\frac{m_0}{M})^{3/4}]\} \\
=&\frac{22}{3} - 4(\frac{m_0}{M})^{1/4} - 2(\frac{m_0}{M})^{1/2} - \frac{4}{3}(\frac{m_0}{M})^{3/4}
\end{aligned}
$$

Let

$$
\begin{aligned}
Z_3 =&\frac{E_m M}{B_0}\{e^{\frac{-B_0 t}{4E_m M^{1/4}}}[-12 + 12(\frac{m_0}{M})^{1/4}] \\
&+ e^{\frac{-B_0 t}{2E_m M^{1/4}}}[6 - 12(\frac{m_0}{M})^{1/4} + 6(\frac{m_0}{M})^{1/2}] \\
&- e^{\frac{-3B_0 t}{4E_m M^{1/4}}}[4/3 - 4(\frac{m_0}{M})^{1/4} + 4(\frac{m_0}{M})^{1/2} - 4/3(\frac{m_0}{M})^{3/4}]\}
\end{aligned}
$$

then $Z_1 = M^{3/4}t + Z_3$. When age, t, is large, Z_3 becomes negligible, because it decrease exponentially with time, $\lim_{t\to\infty} Z_1 = M^{3/4}t$. Z_2 is a constant over time. It is small compared to $M^{3/4}t$ in the integral for a large t. For example, if $M = 500$gram (for a rat), for 1000 days, $Z_2 \approx 5\% M^{3/4}t$; if $M = 50$gram (for a mouse), for 1000 days, $Z_2 \approx 2\% M^{3/4}t$. Therefore, here we simplify

$\int_0^t m(t)^{3/4}dt \approx M^{3/4}t$. Substituting this approximation to Eq.A1 gives

$$\begin{aligned}
D_{total}(t) &= (\delta - \eta)\int_0^t B_{rest}dt + \eta E_m \int_0^t G dt \\
&= (\delta - \eta)B_0 \int_0^t m(t)^{3/4}dt + \eta E_m \int_0^t G dt \\
&= (\delta - \eta)B_0 M^{3/4}dt + \eta E_m \int_0^t G dt \\
&= (\delta - \eta)B_{adult,rest}t + \eta E_m \int_0^t G dt
\end{aligned}$$

Since $G = dm/dt$, $\int_0^t G dt = \int_0^t dm = (m(t) - m_0)$, which gives

$$D_{total}(t) = (\delta - \eta)B_{adult,rest}t + \eta E_m(m(t) - m_0). \tag{A2}$$

Therefor, the mass-specific damage, D, as a function of age t,

$$D(t) = (f\delta - \eta)B_{ms}t + \eta E_m(1 - \frac{m_0}{m(t)}) \tag{A3}$$

where B_{ms} is the mass-specific metabolic rate, $B_{ms} = B_{rest}/m(t)$, and the term $(1 - \frac{m_0}{m(t)})$ comes from $\frac{m(t)-m_0}{m(t)}$.

3 Estimate of E_m using data on growth curve and metabolic rate

The energy for biosynthesis comes from the resting metabolic energy. As different energetic growth models suggested [32,33,37], the rate of resting metabolic energy can be partitioned between the rates of energy allocated to maintenance and that allocated to biosynthesis, i.e., $B_{rest} = B_{rep} + B_{syn}$, where $B_{syn} = E_m \times G$, and G is the growth rate, $G = dm/dt$. The value of E_m can be obtained by fitting the empirical growth curve with this energy partition equation using the resting metabolic rate, B_{rest}. In other words, no matter what the energy for activity is, as long as the resting metabolic rate is given, one can use this energy partition equation to fit the data and obtain E_m. In this study, we use the resting metabolic rates of mice and NMR and employed this equation to estimate the values of E_m. Thus, even if the activity level of NMR is extremely high (which does seem to be possible for a species with low body temperature and living underground, but lets assume it is the case), as long as the value of the resting metabolic rate (B_{rest}) that we used to fit the equation is correct, the value of E_m is reliable.

Below we explain how the value of E_m can be obtained from the growth curve. Rearranging the growth curve

$$m(t) = M \times [1 - (1 - (m_0/M)^{0.25})e^{-(B_0 \times t)/(4E_m M^{0.25})}]^4$$

gives

$$E_m = \frac{B_0 \times t}{4M^{0.25}} \times ln\frac{1 - (m_o/M)^{0.25}}{1 - (m(t)/M)^{0.25}}. \tag{A4}$$

Since birth mass m_0 is 5 grams for both species, adult M is 32 grams for both species, and the values of B_0 are given in the text. E_m is the only free parameter, and is can be obtained by fitting a simple linear regression via Eq.A4.