From Mouse to Whale
A Universal Scaling Relation for the PR Interval of the Electrocardiogram of Mammals

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Background—On the ECG, the PR interval measures the time taken by an electrical impulse generated in the sinoatrial node to propagate from atria to ventricles. From mouse to whale, the PR interval increases $\approx 10^4$, whereas body mass (BM) augments $\approx 10^6$. Scaling of many biological processes (eg, metabolic rate, life span, aortic diameter) is described by the allometric equation $Y = Y_0 \cdot BM^b$, where $Y$ is the biological process and $b$ is the scaling exponent that is an integer multiple of 1/4. Hierarchical branching networks have been proposed to be the underlying mechanism for the 1/4 power allometric law.

Methods and Results—We first derived analytically the allometric equation for the PR interval. We assumed that the heart behaves as a set of “fractal-like” networks that tend to minimize propagation time across the conducting system while ensuring a hemodynamically optimal atrioventricular activation sequence. Our derivation yielded the relationship $PR = BM^{0.24}$. We subsequently obtained previously published values of PR interval, heart rate, and BM of 541 mammals representing 33 species. Double-logarithmic analysis demonstrates that PR interval increases as heart rate decreases, and both variables relate to BM following the 1/4 power law. Most important, the best fit for PR versus BM is described by the equation $PR = 53 \cdot BM^{0.24}$. Hence, the empirically determined exponent (0.24) is close to 1/4, as predicted.

Conclusions—We have demonstrated that the PR interval of mammals scales as the 1/4 power of the BM, following the universal law for allometric scaling to ensure an optimal atrioventricular activation sequence. (Circulation. 2004;110:2802-2808.)

Key Words: atrioventricular node ■ conduction ■ electrocardiography
PR interval, which measures the time taken by an electrical impulse generated in the sinoatrial node to propagate from atria to ventricles, changes by no more than a single order of magnitude when the BM changes by \( \approx 6 \). Meijler et al.\(^7\)\(^,\)\(^10\) have addressed this question by proposing that the PR interval scales linearly with heart length. The fact that such a relationship is not applicable to large-size animals like the humpback whale has been attributed to possible anatomic and/or functional differences in the AV conducting systems of small and large animals.\(^8\) Günther et al.\(^11\) proposed in a preliminary study that the scaling of ECG intervals (RR, PR, QRS, QT) could be described according to concepts derived from fractal geometry. In this article, we use an analytical model in combination with double-logarithmic plots of ECG data to demonstrate for the first time that the universal law for allometric scaling in biology also governs the PR interval of mammals across 33 species and 6 orders of magnitude in BM.

**Methods**

**Theory**

The theoretical prediction of the relation between PR interval and BM was adapted from the derivation of a universal geometric scaling by West et al.\(^3\) These authors have developed a general model frame that is based on the assumption that biological rates and times are restricted by the rates at which limited energy and materials can be supplied to cells through a hierarchical branching network. Their model further assumes that the distribution system has 3 characteristics: (1) it is space-filling (ie, it reaches all parts of the organism); (2) it minimizes the energy required for the distribution; and (3) it has size-invariant terminal units (eg, capillaries or terminal bronchioles). Following such arguments, we have treated the conduction system of the heart as a “fractal-like” network consisting of cardiac myocytes with multiple hierarchies in the atrium, the AV node, and the His-Purkinje system.\(^12\)

**Data Collection and Analysis**

PR interval (ms), HR (bpm), and BM (kg) of 541 animals representing 33 mammalian species ranging from the mouse to the whale were collected from the literature.\(^3\)\(^–\)\(^10\)\(^,\)\(^13\)\(^–\)\(^10\) The collected data fall into 4 different categories based on the mode in which they were reported in the literature for each of the 3 parameters (ie, PR, HR, and BM): (1) measurements from single animals, (2) multiple animal measurements reported as mean values without SD, (3) multiple animal measurements reported as means with SDs, and (4) values reported as mean values without SD, (3) multiple animal measurements reported as means with SDs, and (4) values reported as mean values without SD, (3) multiple animal measurements reported as means with SDs, and (4) values reported as mean values without SD. For convenience, the allometric equation \( Y = Y_0 \cdot BM^p \) can be transformed into a logarithmic form, \( \ln Y = \ln Y_0 + p \ln BM \), which describes a straight line of the form \( y = \text{intercept} + bx \). Double-logarithmic graphs were plotted: HR versus BM, PR versus HR, and PR versus BM for 33 species spanning 6 orders of magnitude in BM. In addition, double-logarithmic plots were constructed for PA, AH, and HV “subintervals,” defining separate propagation times in the atria, AV node, and His-Purkinje system, respectively.\(^16\) Such plots were constructed by use of published data obtained from 5 different species (rat, rabbit, dog, human, and horse) spanning 4 orders of magnitude in BM. Best fit, 95% confidence limit, and 95% prediction limit lines were determined with Origin 7.0 software (OriginLab Corp).

**Results**

**Model Prediction**

Branching networks have been proposed to be the underlying mechanism for the scaling of biological processes as the quarter power of BM.\(^2\)\(^,\)\(^3\) We applied a similar model to the conduction system of the heart and used it as the basis for scaling of the PR interval of the ECG as a measure of AV conduction time in all animals surveyed. Our model is based on the following set of assumptions.

1. The conduction path has 3 major components, including the atrium, the AV node, and the His-Purkinje system, with respective lengths being \( l_a, l_v, \) and \( l_{hp} \).
2. The basic unit of the conducting path is the individual myocyte, whose length, \( l_c \), is almost fixed across species.\(^3\)\(^,\)\(^11\)
3. The conduction velocity, \( v_l \), at each component of the path is preserved across species.\(^10\)\(^,\)\(^21\) in such a way that conduction velocity, \( v_l \), in the mouse atrium, for example, is close to that in the human atrium.
4. Because the heart mass is linearly proportional to BM,\(^8\) we further assume that the mass of the conduction system \( m \) is linearly proportional to that of BM.\(^6\) Furthermore, the myocardial tissue density is uniform across the spectrum of species studied.\(^3\)\(^2\)

Given the above assumptions, we can establish the following relations between the mass of the conduction system \( m \), and its length \( l \), and between the PR time interval \( t \) and the conduction system’s length \( l \):

\[
\begin{align*}
  m &= l^p(t_a, l_v, l_{hp}) \\
  t &= f(l, v_c, l_v, v_{av}, l_{av}, v_{hp}, l_{hp}) = t(l_a, l_v, l_{hp})
\end{align*}
\]

For convenience, these will be expressed in units of the atrial parameters as \( m = l_c^p f(l, v_c, l_v, v_{av}, l_{av}, v_{hp}, l_{hp}) \) and \( t = f(l, v_c, l_v, v_{av}, l_{av}, v_{hp}, l_{hp}) \), where \( f \) and \( w \) are dimensionless functions of the dimensionless ratios. When the body size changes by a factor of \( \eta \), the heart size also changes while conserving its shape, and thus the lengths \( l_a, l_v, \) and \( l_{hp} \) are transformed as \( \eta l_a, \eta l_v, \) and \( \eta l_{hp} \). However, \( l_c, v_c, v_{av}, \) and \( v_{hp} \) remain almost constant. In this case, the scaled mass is

\[
  m' = \eta l_c^3 f(l_c, l_v, l_{av}, v_{av}, l_{hp}, v_{hp})
\]

where \( f(l_c/v_c, l_v, l_{av}, v_{av}, l_{hp}, v_{hp}) \) can be expressed as

\[
  \eta^3 f(l_c, l_v, l_{av}, v_{av}, l_{hp}, v_{hp})
\]

Similarly, the changed PR time interval \( t' \) is scaled as

\[
  t' = \eta l_v^3 w(l_v, v_{av}, l_{av}, v_{av}, l_{hp})
\]

where \( w(l_v, v_{av}, l_{av}, v_{av}, l_{hp}) \) can also be expressed as

\[
  \eta l_v^3 w(l_v, v_{av}, l_{av}, v_{av}, l_{hp})
\]

Combining Equations 1 and 2 for the scaled mass yields

\[
  m' = \eta^{3+\epsilon} l_c^3 f(l_v, l_{av}, l_{hp}) = \eta^{3+\epsilon} m(l_c, l_v, l_{av}, l_{hp})
\]

and similarly, combining Equations 3 and 4 for the scaled time yields

\[
  t' = \eta^{1+\epsilon} l_v^3 w(l_v, l_{av}, l_{hp}) = \eta^{1+\epsilon} t(l_v, l_{av}, l_{hp})
\]

where \( \epsilon_a \) and \( \epsilon_p \) are the fractal dimensions of the mass and the time, respectively.

Mandelbrot\(^3\)\(^3\) established that the fractal dimension of a surface \( A \) is \( 2+\epsilon_a \), where \( 0 \leq \epsilon_a \leq 1 \), and the fractal dimension of a length \( L \) is \( 1+\epsilon_p \), where \( 0 \leq \epsilon_p \leq 1 \). With 0 being the euclidian limit and 1 being the maximal fractal limit. As such,
the fractal dimension of a volume and, consequently, of a linearly proportional mass will be $3 + \varepsilon_a + \varepsilon_t$. Equation 5 therefore becomes
\begin{equation}
m' = \eta_{1}^{(3 + \varepsilon_a + \varepsilon_t)}m(l_a, a, A_{\text{av}}, b_0).
\end{equation}

and since we are considering $t = \sqrt[3]{l}$, we can take $\varepsilon_t$ as $\varepsilon_t$ and rewrite Equation 6 as
\begin{equation}
t' = \eta_{1}^{(3 + \varepsilon_a)}t(l_a, a, A_{\text{av}}, b_0).
\end{equation}

From Equations 7 and 8, it follows that the scaled time and mass maintain
\begin{equation}
t \propto m^{1/4},
\end{equation}

Because the mass of the conduction pathway is proportional to the BM, and because the PR interval reflects the time taken by an impulse to propagate across that pathway, then it is established that
\begin{equation}
PR \propto BM^{1/4}.
\end{equation}

West et al.\textsuperscript{2,3} argue that maximization of exchange surface areas and minimization of transport distances and times have been key to the evolution of living organisms. As a result, the mass of the heart increases linearly proportional to BM, and because the PR interval reflects the time taken by an impulse to propagate across that pathway, then it is established that
\begin{equation}
PR \propto BM^{1/4}.
\end{equation}

**Investigational**

**Scaling of PR Interval and HR**

The data collected encompass 33 species, ranging from the mouse to the humpback whale (Table 1). In Figure 1, we present actual photographs of the hearts of 3 different species (horse, cat, and mouse) to provide a visualization of the magnitude of the changes in euclidian dimensions, including BM. Because heart mass scales as 0.6% of BM,\textsuperscript{8} it follows that the heart of a 600-kg horse weighs 3600 g, whereas the heart of a 4-kg cat weighs 24 g and that of a 32-g mouse weighs 0.192 g, which represents a change of 4 orders of magnitude in heart weight. If one also includes the humpback whale, whose body weight is $\approx 30,000$ kg and heart weight is $\approx 180,000$ g, the change occurs over 6 orders of magnitude. Yet, from mouse to whale, PR interval changes only from 40 to 400 ms.\textsuperscript{8} Similarly, HR changes from 600 bpm in the conscious mouse\textsuperscript{25} to $\approx 30$ bpm in the humpback whale,\textsuperscript{21} and West et al.\textsuperscript{2} have already found that $HR \propto BM^{-1/4}$.

In Figure 2, we have plotted $\ln(PR)$ versus $\ln(BM)$, whose best linear fit is $y=3.98+0.24x$. The slope of the line is the exponent $b$ in $Y = Y_0 \cdot BM^b$, and the PR interval dependence on BM is described by the equation:
\begin{equation}
PR = 53 \cdot BM^{0.24}.
\end{equation}

Figure 3 shows the best linear fit of average HR and BM data from Table 1 on a double-logarithmic plot. The equation describing this relationship is $y=5.46-0.2x$; ie, our data indicate that HR scales with BM as
\begin{equation}
HR = 235 \cdot BM^{-0.2}.
\end{equation}

which is close to the relation reported by West et al.\textsuperscript{2} From the above results, one may predict that $\ln(HR)$ and $\ln(PR)$ should be inversely correlated over the entire range of BMs of mammalian species. As demonstrated in Figure 4, plotting $\ln(HR)$ versus $\ln(PR)$ yields a relationship in which the slope of the best fit is $-1.08$, which is very close to $-1$, as expected, if $PR \propto BM^{-0.25}$ and $HR \propto BM^{-1/4}$.

**Scaling of PA, AH, and HV Subintervals**

As an additional strategy to test the validity of our results, we decided to look at the scaling of the subintervals (PA, AH, and HV) that define separate propagation times in the atria, AV node, and His-Purkinje system that compose the overall PR interval. To this aim, we used some limited data (see Table 2) available to us from 5 different species that range from rat to horse.\textsuperscript{16} Our rationale for this strategy was based on the fact that our model postulates that the PR interval represents the behavior of 3 separate “fractal-like” networks (the atrium, the AV node, and the His-Purkinje system) working in concert to bring the impulse from the sinus node to the ventricles. Therefore, unless there are any leaks in the overall system, every one of these subintervals should scale with BM to the 0.25 power, with the proportionality coefficient being different for each case. If the equation for scaling is $Y = Y_0 BM^b$, then $Y_0$ is the proportionality coefficient.

Figure 5 shows the 3 double-logarithmic plots of PA versus BM, AH versus BM, and HV versus BM with the corresponding fits. The slopes of all regression lines are likely to be equal or very close to 0.25 when the standard error is considered. As such, we feel that it is safe to conclude that all the components at play behave according to theory.

If the best fits of $\ln(PA)$ versus $\ln(BM)$, $\ln(AH)$ versus $\ln(BM)$, and $\ln(HV)$ versus $\ln(BM)$ are converted into power form, then the coefficient of proportionality will be as follows:
\begin{align}
PA &= 14 \cdot BM^{0.25} \\
AH &= 33.8 \cdot BM^{0.22} \\
HV &= 16.6 \cdot BM^{0.22}
\end{align}

If all the scaling exponents are 0.25, then the percentage of contribution of the different subintervals to the PR interval will be a fixed value that does not depend on the size of the animal. Thus
\begin{align}
\%PA &= PA/PR \times 100 = (14 \cdot BM^{0.25})/(53.5 \cdot BM^{0.24}) \times 100 \\
&= (14/53.5) \times 100 = 26\%;
\end{align}

similarly,
\begin{align}
\%AH &= 63\% \\
\%HV &= 31\%.
\end{align}

As demonstrated,\textsuperscript{16} if the relative subinterval contributions are plotted against the size of the heart, which is directly proportional to that of the body, the outcome is that PA contributes 20% to 30%, AH contributes 50% to 60%, and for HV, the contribution is 20% to 30%, which agrees with the calculations we made from the best fits.

**Discussion**

The most important result of this study is that AV conduction time, measured by the PR interval in 541 published ECGs from 33
mammalian species, scales as the 1/4 power of BM, following a law for allometric scaling. Moreover, because HR has also been found to be proportional to BM to the negative quarter power,\(^2\) the demonstration that the ln PR interval and the ln HR scale linearly with a slope that is close to negative unity independently supports the finding that the PR follows the universal law of allometric scaling and scales as a \(1/4\) power of the BM.

From the simplest unicellular organism to the largest and most complex mammal, nature attempts to maximize efficiency by minimizing energy expenditure on transport and time and by maximizing active surface areas across which exchange of nutrients and waste happens with the environment.\(^3\) During each heartbeat, the efficiency of the heart’s output is maximized by the optimization of the time taken by an electrical impulse to travel from the SA node to the ventricles. Our theoretical prediction is that

\[
PR \approx \frac{BM^{1/4}}{L^{3/4}}. 
\]

The theory of maximization of active surfaces and minimization of transport distances and times implies that \(\epsilon_A \rightarrow 1\) and

<table>
<thead>
<tr>
<th>Species</th>
<th>N</th>
<th>PR, ms</th>
<th>Body Mass, kg</th>
<th>Heart Rate, bpm</th>
</tr>
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<tbody>
<tr>
<td>Beluga whale</td>
<td>1</td>
<td>310</td>
<td>487</td>
<td></td>
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<tr>
<td>Camel</td>
<td>72</td>
<td>220</td>
<td>545</td>
<td>49</td>
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<tr>
<td>Cat</td>
<td>48</td>
<td>70±10</td>
<td>4</td>
<td>97±27</td>
</tr>
<tr>
<td>Chimpanzee</td>
<td>23</td>
<td>44±14</td>
<td>50.6±10</td>
<td>15±20</td>
</tr>
<tr>
<td>Cynomolgus monkey</td>
<td>16</td>
<td>80±10</td>
<td>5</td>
<td>179±26</td>
</tr>
<tr>
<td>Dog</td>
<td>81</td>
<td>94±15</td>
<td>25±14</td>
<td>133</td>
</tr>
<tr>
<td>Elephant</td>
<td>13</td>
<td>398±48</td>
<td>3437±114</td>
<td>35</td>
</tr>
<tr>
<td>Elephant seal</td>
<td>18</td>
<td>120±20</td>
<td>91.6±17.9</td>
<td>136.6±11</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>180±60</td>
<td>171–373</td>
<td>106±39</td>
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<tr>
<td></td>
<td>2</td>
<td>170±40</td>
<td>171–373</td>
<td>107</td>
</tr>
<tr>
<td>Guinea pig</td>
<td>10</td>
<td>65±5</td>
<td>0.593±0.166</td>
<td>260±30</td>
</tr>
<tr>
<td>Hamster</td>
<td>10</td>
<td>43±3</td>
<td>0.09±0.013</td>
<td>400±25</td>
</tr>
<tr>
<td>Horse</td>
<td>35</td>
<td>308±64</td>
<td>494±152</td>
<td>40</td>
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<tr>
<td>Human</td>
<td>36</td>
<td>164±16</td>
<td>66±3</td>
<td>80</td>
</tr>
<tr>
<td>Humpback whale</td>
<td>1</td>
<td>400</td>
<td>30 000</td>
<td>30</td>
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<tr>
<td>Japanese monkey</td>
<td>16</td>
<td>88.5±10.8</td>
<td>6.6±0.9</td>
<td>147±18</td>
</tr>
<tr>
<td>Killer whale</td>
<td>1</td>
<td>350</td>
<td>3208</td>
<td></td>
</tr>
<tr>
<td>Mouse</td>
<td>24</td>
<td>33.1±1.6</td>
<td>0.027±0.003</td>
<td>723±34.8</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>35±1.5</td>
<td>723±9.6</td>
<td></td>
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<td>100</td>
<td>110</td>
</tr>
<tr>
<td>Orca</td>
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<td>250</td>
<td>1775</td>
<td></td>
</tr>
<tr>
<td>Peromyscus</td>
<td>10</td>
<td>32±6</td>
<td>0.022±0.004</td>
<td>420±98</td>
</tr>
<tr>
<td>Polar bear</td>
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<td>160</td>
<td>375</td>
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<td>6</td>
<td>56±2</td>
<td>2.5–3.5</td>
<td>273±8</td>
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<tr>
<td>Rat</td>
<td>7</td>
<td>56</td>
<td>0.26</td>
<td>250</td>
</tr>
<tr>
<td>Roe deer</td>
<td>16</td>
<td>120±20</td>
<td>20.7±2.9</td>
<td>104±44.1</td>
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<tr>
<td></td>
<td>12</td>
<td>110±20</td>
<td>20±4.5</td>
<td></td>
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<tr>
<td>Sheep</td>
<td>8</td>
<td>149±16</td>
<td>51±3</td>
<td>103±7</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>140±20</td>
<td>32–40</td>
<td>107±20</td>
</tr>
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<td>1</td>
<td>110</td>
<td>220</td>
<td>82</td>
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<td>Meerkat</td>
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<td>80</td>
<td>5</td>
<td>190</td>
</tr>
<tr>
<td>Spermophiles</td>
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<td>48±10</td>
<td>0.189±0.038</td>
<td>290±27</td>
</tr>
<tr>
<td>Syrian bear</td>
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<td>180</td>
<td>250</td>
<td>70</td>
</tr>
<tr>
<td>Talapoin</td>
<td>5</td>
<td>49±15</td>
<td>1.04±0.68</td>
<td>233±41</td>
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<tr>
<td>White mouse</td>
<td>10</td>
<td>43±4</td>
<td>0.029±0.004</td>
<td>376±49</td>
</tr>
<tr>
<td>White rat</td>
<td>10</td>
<td>42±5</td>
<td>0.237±0.025</td>
<td>347±31</td>
</tr>
<tr>
<td>Wild mouse</td>
<td>10</td>
<td>32±5</td>
<td>0.022±0.007</td>
<td>480±46</td>
</tr>
<tr>
<td>Total</td>
<td>541</td>
<td></td>
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</table>
$e_\varepsilon \to 0$, so the exponent becomes $1/4$. The $1/4$ scaling power is an essential component in biological scaling.\(^2\)\(^3\) It has been demonstrated repeatedly that numerous biological variables, such as circulation time (1/4), HR ($-1/4$), and cardiac output (3/4), follow the quarter-power law of scaling.\(^2\) In our study, the theoretical derivation of the scaling behavior of the PR interval agrees very well with the empirically obtained data (Figure 2) in that the best fit has a slope of 0.24, which is close to $b=1/4$. Should the scaling of the propagation of the electrical impulse from the atria to the ventricles have obeyed the euclidian geometry, the exponent would have simply been 1/3, which is much higher than the best-fit slope of 0.24 demonstrated by our data. Such data demonstrate that the PR interval is more sensitive to the heart mass than to its length.

It may be argued that scaling the PR interval to the BM is limited by the fact that extrapolation of the data to the intercept would result in a PR interval of sizable value for a hypothetical heart of mass 0, which would be meaningless.\(^7\) Clearly, this argument may be legitimate from the point of view of the limitations imposed by the intrinsic properties of a properly working heart, where the mammalian PR interval may never be briefer than a certain limit value because of genetically determined structural, anatomic, and electrophysiological constraints. In fact, on the basis of hemodynamic considerations, West et al\(^4\) calculated that the lowest possible limit of BM for a mammalian species is 1 g. It is therefore worth noticing that allometry describes the relation between

![Figure 1. Photographs of mammalian hearts illustrate change in 4 orders of magnitude in weight from mouse to horse.](image)

![Figure 2. Double-logarithmic plot of PR interval vs BM. Number of data points is 183. Best-fit line is $y = 3.98 \pm 0.03 + 0.24x \pm 0.008$. $R = 0.92$. Outer broken lines, 95% prediction limit; inner dotted lines, 95% confidence limit; solid line, best-fit regression.](image)

![Figure 3. Double-logarithmic plot of HR vs BM. Number of data points is 33. Best linear fit is $y = 5.46 \pm 0.05 - 0.2x \pm 0.012$. $R = 0.96$. Outer broken lines, 95% prediction limit; inner dotted lines, 95% confidence limit; solid line, best-fit regression.](image)

![Figure 4. Double-logarithmic plot of PR interval vs HR. Number of data points is 184. Solid line is regression fit, outer dashed lines are 95% prediction limits, and inner dotted lines are 95% confidence limits. Slope of line is $-1.08 \pm 0.05$, $R = 0.96$.](image)
the 2 sets of values (eg, BM and HR) only within an observed range.\(^1\) In other words, extrapolation beyond the observed mammal size provides no useful information in allometric scaling.

The PR interval of the humpback whale (400 ms) has been given much attention because it is very close to the PR interval of a much smaller 3000-kg elephant (398 ms). Possibly, this might be because the AV node is somehow different in such a way that AV conduction delay is reduced in larger animals such as the humpback whale.\(^8\) However, the results presented in Figures 2 and 3 show that the data from the whale fit well within the limits of prediction for the allometric relation between the HR, the PR interval, and BM. Furthermore, when plotted on a double-logarithmic scale (Figure 4), the slope of the relation between HR and PR interval is equal to \(-1.08\). The significance of the \(-1\) slope is that because the HR was already shown to scale as BM to the \(-1/4\) power, the PR interval should scale as \(BM^{1/4}\). Importantly, the single PR-interval value from the humpback whale agrees with the fit to the overall data, suggesting that in fact, the structural and electrophysiological properties of the whale AV node need not differ substantially from those of other mammals. In fact, as demonstrated by James et al\(^{14}\) in the sperm whale, cell size, histological organization, and innervation of the whale’s sinus node, AV node, and His bundle are similar to those of most other mammalian hearts.

![Figure 5](image)

**Figure 5.** Double-logarithmic plots showing scaling of subintervals PA, AH, and HV. See text for details.

TABLE 2. Scaling of the Subintervals PA, AH, and HV in the ECGs of 5 Different Species

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
<th>Rabbit</th>
<th>Dog</th>
<th>Human</th>
<th>Horse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight, kg</td>
<td>0.26</td>
<td>3</td>
<td>25</td>
<td>80</td>
<td>600</td>
</tr>
<tr>
<td>PA, ms</td>
<td>11.4</td>
<td>(\ldots)</td>
<td>22.8</td>
<td>42.8</td>
<td>80</td>
</tr>
<tr>
<td>AH, ms</td>
<td>31.1</td>
<td>35</td>
<td>60</td>
<td>85</td>
<td>165</td>
</tr>
<tr>
<td>HV, ms</td>
<td>13.9</td>
<td>(\ldots)</td>
<td>26.1</td>
<td>40</td>
<td>84</td>
</tr>
</tbody>
</table>

Normally, the atrial contraction occurs in diastole after rapid ventricular filling by relaxation, allowing for increased stretch of the myocardial fibers in the ventricles and resulting in enhanced contractile force.\(^{35,36}\) Thus, atrial contraction contributes to \(>20\%\) of the ventricular filling.\(^{37}\) and its timing requires optimal AV propagation for the electrical impulse to trigger the ventricular contraction. On the ECG, the PR interval is an indicator of AV conduction time. The atrial systole is an important determinant of ventricular performance.\(^{38}\) It has been demonstrated in humans and dogs\(^{35,39,40}\) that there is a wide range of timings that allows atria and ventricles to work sequentially. However, there is also an optimal PR interval that is associated with the best ventricular hemodynamic efficiency.\(^{39}\) If the PR interval is excessively long, the atria would contract when the AV valves are closed, and thus, the atrial kick would not contribute to the ventricular filling.\(^{35,39}\) Conversely, if the PR interval is too short,\(^{39}\) the atrial contraction would be followed immediately by ventricular systole, and there would be less time to complete the ventricular diastolic filling. In both cases, the stroke volume will be reduced because of an inefficient atrial kick, which normally contributes to end-diastolic ventricular volume and helps the ventricles to operate optimally.

In humans, Benchimol et al\(^{39}\) showed that with a PR interval shorter than 300 ms, the hemodynamic parameters (systemic pressure and maximum dP/dt of arterial brachial pressure) increased by 14% and 33%, respectively, compared with a condition of no atrial contribution (P inscribed on the T wave). In 10 patients with intact AV conduction who underwent cardiac surgery, Hartzler et al\(^{39}\) demonstrated that shortening the PR interval by sequential artificial pacing could significantly improve the cardiac output up to 18%. For each subject, they described a bell-shaped curve of the relationship between AV interval and cardiac output. The optimal PR intervals ranged between 150 and 250 ms, depending on the age and the specific cardiac disease. This illustrates that in humans, the normal PR interval of \(\approx 200\) ms is optimal and contributes to an efficient hemodynamic function of the heart. Because our allometric model uses optimal heart function as its basis, the fact that all species obey a relation between their respective BM and PR interval similar to that of humans (Figure 2) further suggests the optimal value of PR intervals for all mammals. We conclude that a 0.25 scaling exponent offers a favorable placement of the atrial kick in the cardiac cycle.

**Limitations**

The PR interval is only an approximation of the actual time that the impulse needs to cross the conduction pathway. The collection of data used is a partial representation of mammals. ECG recordings from some species are more easily available than others, and so the number of animals in our sample varies significantly from one species to another; for example, only 1 value is used for the humpback whale, whereas 81 are used for dogs. Also, acquisition conditions were not similar across animals: some ECGs were obtained from anesthetized animals; it was impossible to account for the different body temperatures, autonomic tone, and environmental circumstances of the animals.
studied. These factors may have contributed to some alterations in the PR.

Acknowledgments
This study was supported in part by grants from the National Heart, Lung, and Blood Institute, National Institutes of Health (R01-HL39707, R01-HL70074, and R01-HL60843 to Dr Jalife); by an American Heart Association Scientist Development Grant (0230311N to Dr Berenfeld); and by an Educational Grant from Medtronic Bakken Research Center, Maastricht, Netherlands (Dr Meijler).

References
From Mouse to Whale: A Universal Scaling Relation for the PR Interval of the Electrocardiogram of Mammals

Sami F. Noujaim, Elena Lucca, Viviana Muñoz, Dharmendra Persaud, Omer Berenfeld, Frits L. Meijler and José Jalife

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An erratum has been published regarding this article. Please see the attached page for:
/content/111/3/379.1.full.pdf
In the article by Huynh et al., “Aspirin, Warfarin, or the Combination for Secondary Prevention of Coronary Events in Patients With Acute Coronary Syndromes and Prior Coronary Artery Bypass Surgery,” which published in the June 26, 2001, issue (Circulation. 2001;103:3069–3074), the authors now realize errors appeared in Tables 3 and 4. The percentages of events and complications were presented on the basis of the number of patients’ visits rather than on the total number of patients.

Overall, the corrected results did not change the implication of the study. There was no benefit of warfarin alone or combined with aspirin in the secondary prevention of ischemic events in this study of patients with previous coronary artery bypass surgery and an acute coronary syndrome; there was a significant excess in minor bleeding compared with the aspirin-alone group.

Corrected versions of Tables 3 and 4 appear below.

**TABLE 3. End-Point Events According to Treatment**

<table>
<thead>
<tr>
<th>Events</th>
<th>Warfarin + Placebo (n=45)</th>
<th>Aspirin + Placebo (n=46)</th>
<th>Warfarin + Aspirin (n=44)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary end point, n (%)</td>
<td>18 (40.0)</td>
<td>13 (28.3)</td>
<td>11 (25.0)</td>
<td>0.27</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>1 (2.2)</td>
<td>0 (0.0)</td>
<td>2 (4.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>MI, n (%)</td>
<td>4 (8.9)</td>
<td>1 (2.2)</td>
<td>2 (4.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>UA, n (%)</td>
<td>16 (35.6)</td>
<td>13 (28.3)</td>
<td>10 (22.7)</td>
<td>0.41</td>
</tr>
<tr>
<td>PCI, n (%)</td>
<td>6 (13.3)</td>
<td>1 (2.2)</td>
<td>3 (6.8)</td>
<td>0.12</td>
</tr>
<tr>
<td>Repeat CABG, n (%)</td>
<td>2 (4.4)</td>
<td>2 (4.3)</td>
<td>2 (4.5)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

UA indicates unstable angina requiring rehospitalization; PCI, percutaneous coronary intervention; and MI, myocardial infarction. Primary end point is any-cause mortality, MI, or UA requiring hospitalization.

**TABLE 4. Complications and Adherence to Protocol by Patients**

<table>
<thead>
<tr>
<th>Complications</th>
<th>Warfarin + Placebo (n=45)</th>
<th>Aspirin + Placebo (n=46)</th>
<th>Warfarin + Aspirin (n=44)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor bleeding, n (%)</td>
<td>10 (22.2)</td>
<td>2 (4.3)</td>
<td>9 (20.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Major bleeding, n (%)</td>
<td>1 (2.2)</td>
<td>0 (0.0)</td>
<td>2 (4.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>Blood transfusions, n (%)</td>
<td>2 (4.4)</td>
<td>0 (0.0)</td>
<td>2 (4.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>Compliance, %*</td>
<td>90.1</td>
<td>86.7</td>
<td>86.1</td>
<td>0.66</td>
</tr>
<tr>
<td>Protocol completion, %*</td>
<td>77.6</td>
<td>78.5</td>
<td>69.9</td>
<td>0.22</td>
</tr>
</tbody>
</table>

*Compliance and protocol completion were calculated per visit.

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In the article by Haïssaguerre et al, “Mapping and Ablation of Ventricular Fibrillation Associated With Long-QT and Brugada Syndromes,” which appeared in the August 26, 2003, issue (Circulation. 2003;108:925–928), the authors would like to note the following errors:

1. In the byline, Jerónimo Farré’s name incorrectly appeared as “Gerónimo Farre.”
2. José Angel Cabrera and Jerónimo Farré work at Fundación Jiménez Díaz in Madrid, Spain.
3. The work of Drs Cabrera and Farré was supported by Redes Temáticas de Cooperación, Red Cardiovascular C01/03.

In the article by McRae and Ginsberg, “Initial Treatment of Venous Thromboembolism,” which appeared in the August 31, 2004, supplement sponsored by the Society for Vascular Medicine and Biology (Circulation. 2004;110[suppl I]:I-3–I-9), an error appeared in Table 2. The footnote of the table erroneously states that “For enoxaparin, 100 anti-Xa U/kg corresponds to a dose of 100 mg/kg.” The legend should have read, “For enoxaparin, 100 anti-Xa U/kg corresponds to a dose of 1 mg/kg.”

In the article by Bauer et al, “Acute Improvement in Global and Regional Left Ventricular Systolic Function After Percutaneous Heart Valve Implantation in Patients With Symptomatic Aortic Stenosis,” which appeared in the September 14, 2004, issue (Circulation. 2004;110:1473–1476), two errors of note appeared in the table on page 1474. Under “Endocardiographic data,” the rows for “LV end-systolic volume, mm Hg” and “LV end-diastolic volume, mm Hg” should have appeared as the following:

<table>
<thead>
<tr>
<th>LV end-diastolic volume, mL</th>
<th>102±36 (baseline)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV end-systolic volume, mL</td>
<td>49±25 (baseline)</td>
</tr>
</tbody>
</table>

Because of a typesetting error, several mathematical symbols appeared incorrectly in the article by Solomon et al, “Effect of Candesartan on Cause-Specific Mortality in Heart Failure Patients: The Candesartan in Heart failure Assessment of Reduction in Mortality and morbidity (CHARM) Program,” which appeared in the October 12, 2004, issue (Circulation. 2004;110:2180–2183). On page 2180, in the abstract and in the text of the article, there were several instances in which “LVEF=40%” should have appeared as “LVEF≤40%.” In addition, in the last sentence of the first paragraph of the article, please note that “9% borderline risk” should read “9% borderline significant risk.” The corrected version is available online at http://circ.ahajournals.org/cgi/content/full/110/15/2180. (The previous version can be accessed by selecting the “Previous Version of This Article” link.) We regret these errors.

In the AHA Scientific Statement by Drew et al, “Practice Standards for Electrocardiographic Monitoring in Hospital Settings: An American Heart Association Scientific Statement From the Councils on Cardiovascular Nursing, Clinical Cardiology, and Cardiovascular Disease in the Young,” which appeared in the October 26, 2004, issue (Circulation. 2004;110:2721–2746), Figure 4 contained an error. The text in the figure refers to the “Angle of Lewis.” The correct name is “Angle of Louis.” The Association regrets this error.
In the article by Noujaim et al, “From Mouse to Whale: A Universal Scaling Relation for the PR Interval of the Electrocardiogram of Mammals,” which appeared in the November 2, 2004, issue (Circulation. 2004;110:2802–2808), the name of Ary L. Goldberger, MD, was misspelled as “Goldberg” in reference 12. The authors regret this error.

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In the article by Spargias et al, “Ascorbic Acid Prevents Contrast-Mediated Nephropathy in Patients With Renal Dysfunction Undergoing Coronary Angiography or Intervention,” which appeared in the November 2, 2004, issue (Circulation. 2004;110:2837–2842), the name of author Panagiotis Iokovis was spelled incorrectly as “Panagiotis Iocovis.” The authors regret this error.

DOI: 10.1161/01.CIR.0000155487.34492.0D


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