

THE BIOLOGICAL PHYSICIST

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March Meeting Update!!

Call for Symposium Proposals

From the DBP March 2003 Program Chair

We are in the midst of planning the DBP program for next year's March meeting, held 3-7 March, 2003, in Austin, Texas. Our previous call for Focus Session topics in May has led to the DBP sponsoring or co-sponsoring a total of 11 Focus Sessions on a broad range of topics. These can be found at the APS website: www.aps.org/meet/MAR03/abs.html.

Now we need to fill out our allotment of Symposia, and are reissuing our previous call for suggestions from the DBP membership. By cooperating with the other Divisions participating in the March meeting we can leverage our visibility at the meeting far beyond the base number of Symposia we are allotted, so we want to hear any and all suggestions right away (the deadline is 30 August). Please email them to the program chair, Ray Goldstein (gold@physics.arizona.edu) with a cc to our Division Head, Bob Austin (austin@princeton.edu). Alternatively, you can submit your symposium proposal to us online at <http://www.aps.org/DBP/meetings.html>.

-- Raymond Goldstein, MAR03 Program Chair

DBP Elections: Solicitation for Nominations

An Open Letter from the Chair of the Nominating Committee

The Division of Biological Physics is seeking a few good men and women to serve on the Division's Executive Committee. We are happy to announce that this year, for the first time ever, the Division is soliciting nominations from the general membership.

This year we will be electing a Vice Chair (who will serve one year as Vice Chair, followed by a year as Chair-Elect, a year as Division Chair, and a year as Past Chair) as well as two Members-at-Large. In addition to these usual offices to fill, we lost our recently-elected Vice-Chair, meaning that a Chair-Elect also needs to be chosen.

The duties of the Vice-Chair are to shape the DBP tutorials at the March Meeting, while the Chair-Elect constructs the March Meeting symposia and focus sessions and is responsible for the overall scheduling of sessions. Members-at-Large are assigned duties, as needed, by the Chair. All of these offices participate in general policy making and in shaping the futures both of the Division and of the field.

For more details on these and other offices, see our bylaws on the Division web site <http://www.aps.org/DBP/govern.html#responsibilities>.

If you have any suggestions for nominees for these offices, please send them to me at mark.spano@mailaps.org. Prospective nominees, who must have been DBP members for at least two years, are asked to send the Nominating Committee a 1-paragraph bio and a short statement of why they are interested in serving the Division. These will be distributed with the ballot.

Note that the Nominating Committee reserves the right to make the final selection of nominees, after screening for compliance with the APS and Division bylaws.

Sincerely,

Mark Spano
*Past Chair, Division of Biological Physics
and
Chair, 2003 Nominating Committee*

Biological Physics at the NEC Research Institute, Princeton

Ned S. Wingreen and Chao Tang

For a little over 13 years, the NEC Research Institute (NECI) in Princeton, New Jersey has been home to a group of physicists pursuing research at the interface of physics and biology. The diversity of the whole Institute, which spans Computer and Physical Sciences, is reflected by diversity within the biology group. Research in molecular biology, from protein structure to *in*



Fig. 1 The NEC Research Institute in Princeton NJ.

vitro evolution and DNA computing, has coexisted with theoretical and experimental neuroscience. In what follows, we give a flavor of the research in biology, present, past, and future, at NEC's Princeton Lab.

Our own group which generally includes three or four postdocs and visitors, plus one or two summer interns, has a primary focus on protein design. In nature, there are thought to be around 1000 qualitatively different folds for proteins. While it took billions of years to find these folds, nature was stuck using trial and error. Our approach is to identify the qualities that make a good structure, and then see which structures nature has missed. From work on simple lattice models, we found that some structures are inherently more "designable"

than others -- namely they are ground states of many more than their share of sequences. Along with designability goes fast folding and thermodynamic stability. For example, the structure in the top panel of Fig.2 was the most designable or popular in an early study [1]. We've come a long way toward the real world since then, and our current structures are configurations a real protein chain can adopt [2,3]. In fact, we're working with Michael Hecht, a protein chemist in Princeton's Chemistry Department, to synthesize the structure shown in the bottom panel of Fig. 2.

Other projects in the group include protein-DNA interactions, protein and metabolic networks, RNA folding, and lattice models for protein dimers. The members of the group are all theorists; we have to work hard to stay abreast of new developments in biology. Thanks to good planning by the founders of our Lab, we're just a few minutes from Princeton University and 30 minutes from Rutgers University and their world-class programs in biology and biophysics. We also keep up to date with an active seminar series.

Research in biology at NECI is not limited to theory. Experimental molecular biology is done in the laboratory of Albert Libchaber, a prominent experimentalist in dynamical systems and turbulence, who a decade ago started a new research direction in biology. Sharing his time, first at Princeton University and then at Rockefeller in New York, Libchaber and his students and postdocs have studied the biophysics of actin and microtubule polymerization, DNA-protein interaction, and recently *in vitro* and *in vivo* evolution. In addition to elucidating the physical basis of biological behavior,

Libchaber and his group have developed new probes of biological systems, including imaging techniques, fluorescence reporters of DNA sequences, and fluorescent labeling of cell lines. These techniques are having an impact on how biology is done.

Biophysics at NECI began in late 1990 with the arrival of William Bialek (now at Princeton University) from Berkeley. A theoretical physicist with interests in neural coding and computation, he helped to recruit

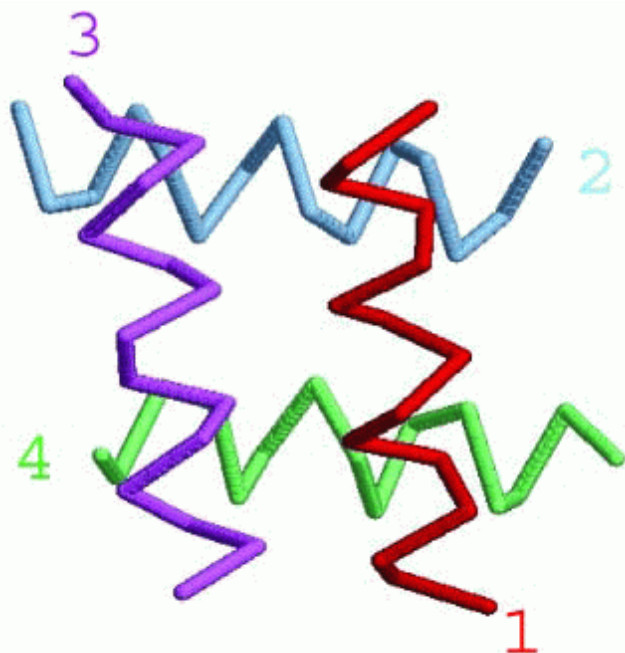
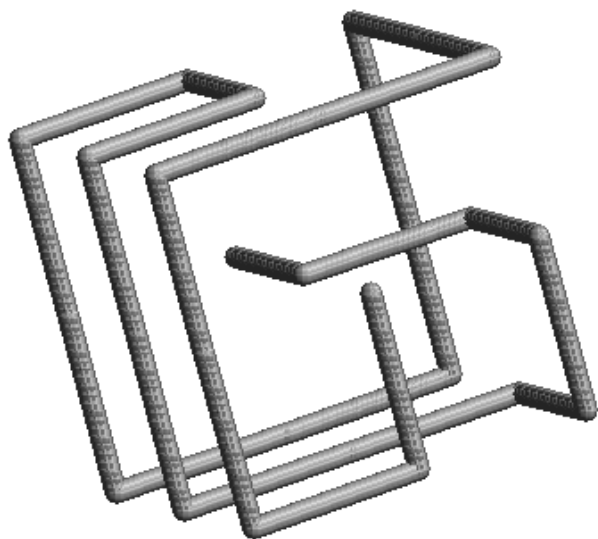


Fig. 2 Work on protein structure has evolved from (top) simple lattice models to (bottom) realistic backbones for the design of novel protein folds.

experimental colleagues Rob de Ruyter van Steveninck (now also at Princeton) and Hanan Davidowitz (now at PharmaSeq, Inc.). Perhaps the best known results from the NEC group were the collaborative efforts of Bialek, de Ruyter, and colleagues on the visual brain of the fly, where they showed that computation works with such precision that it is limited by photon shot noise and diffraction, that information transmission across synapses between neurons operates near the limits imposed by the 'quantization' of signals into discrete packets of chemical transmitter, that deep inside the brain signals are represented by sequences of action potentials or 'spikes' with nearly optimal efficiency, and that this optimization results from a continuous adaptation of the brain's coding and computational strategies to the statistical structure of the visual world. The concepts and methods of analysis which they introduced in this work are now being used widely for studies on other systems, and their example of theory/experiment collaboration is viewed as a model for quantitative approaches to neuroscience.

Bialek also organized the NEC Lectures on Biophysics, which was first held in 1991. In recent years, the two of us have taken over running these summer schools, which are aimed at young physicists considering a move into biology. Recent topics have included Proteins, Genomics, and, this past June, Biological Networks. We tentatively plan to hold the next NEC Lectures on Biophysics in June 2004.

What does the future hold for biological research at NEC's Princeton Lab? One promising development is that some of the NECI computer scientists, including Eric Baum, a physics Ph.D. from Princeton '82, have begun to work on biological problems. A synergy between Computer Science and Physical Science was one of the original goals of the Lab. It may come to fruition in a shared interest in bringing theoretical tools to biology.

For our part, we plan to continue the program of protein design, with the long-term goal of making new structures in assembly-line fashion. We think the next big wave in

biophysics is going to be molecular recognition, and by working on protein-DNA interaction we hope to be part of it.

References

1. H. Li, R. Helling, C. Tang, and N. S. Wingreen, *Science* **273**:666 (1996).
2. J. Miller, C. Zeng, N. S. Wingreen, and C. Tang, *Proteins* **47**:506 (2002).

3. E. G. Emberly, N. S. Wingreen, and C. Tang, *Proc. Nat. Acad. Sci.*, **99**:11163 (2002).

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FEATURE

Vortex-Swarming of the Zooplankton *Daphnia*

Anke Ordemann

Herding or swarming can often be observed in certain mammals, fish, insects, and birds for various benefits such as enhanced feeding and mating as well as more successful predator avoidance.¹ Many species that are at high risk of becoming prey of visually hunting predators are commonly known to form swarms as a predator-confusing mechanism. “Confusing” because it is far more difficult for a predator to identify and track one prey animal out of the whirl of a



Fig. 1: Lateral view of the zooplankton Daphnia (typical body length: 2-4mm) with a juvenile in the brood pocket, the head and the swimming antennae are visible on the right. Picture by D.F. Russell.

swarm than to focus on and catch a single individual. This is true all the way up to human predators. It is well known to duck and quail hunters that shooting blindly into a flock rarely succeeds while focusing on one bird (often an outlier) affords a much better probability of success. The swarms are self-organized systems, i.e. no leader exists and the global patterns are emerging properties of the local interactions. In rare events in the field, some swarming animals have been observed to perform a fascinating vortex-like motion. Unfortunately, not much is known about the biological and physical aspects of these vortex-swarms, because it is difficult to perform experiments on this phenomenon under well defined lab conditions, mainly because of the size of the animals or the difficulty of understanding the local interactions. For example bacterial and slime mold colonies move quite slowly under the influence of poorly understood chemotactic, thermal and viscous gradients, while flocks of birds and schools of fish are too large for well controlled lab experiments. The zooplankton *Daphnia*, intermediate in size and biological complexity between bacteria

and birds, obviates many of these difficulties as we show below.

Theoretical Models

Lately, swarming of so called self-propelled agents has become of significant interest to theoretical physicists,² leading to variants of the two-dimensional models of Active Brownian particles^{3,4} and Self-Propelled Interacting Particles⁵ that predict circular motions of the agents. In the following, a short overview of the two models that successfully lead to circular motions of the agents without an external rotational force or special boundary conditions is given, focusing on the minimum necessary ingredients for circling to occur.

In the two-dimensional single-particle model of Active Brownian Particles with an internal energy depot from Schweitzer *et al.*³ the agent, characterized by mass m , position \vec{x} , and velocity \vec{v} , experiences a self-propelling force which is connected to an energy storage depot $e(t)$, a friction force with friction coefficient γ_0 , an external force given by a parabolic potential $U(\vec{x})$, and noise $F(t)$:

$$m\partial_t\vec{v} = d_2e(t)\vec{v} = \gamma_0\vec{v} - \vec{\nabla}U(\vec{x}) + F(t),$$

$$\partial_t\vec{x} = \vec{v}$$

The energy depot equation consists of the terms for energy take-up ('feeding') $q(\vec{x})$, internal dissipation ('metabolism'), and conversion of internal energy to kinetic energy ('moving'):

$$\partial_t e(t) = q(\vec{x}) - c e(t) - d_2 v^2 e(t).$$

Schweitzer *et al.* consider both a homogenous energy supply, i.e. $q(\vec{x}) \equiv q_0$, and patchy energy sources. Carrying out a depot analysis for $q(\vec{x}) \equiv q_0$ leads to a Hopf bifurcation with control parameter

$$\mu = \frac{q_0}{\gamma_0} - \frac{c}{d_2}. \text{ For } \mu \leq 0 \text{ the model shows}$$

(passive) Brownian motion while for $\mu > 0$, or supercritical supply of energy

$q_0 > q_0^{\text{crit}} = \gamma_0 c / d_2$, the agent moves to a stochastic limit cycle where the radius of the circular motion depends on the ratio of energy take-up to used energy.

In addition, many-particle models with various interactions among the Active Brownian Particles were investigated.⁴ On the one hand, it was found that incorporating an attraction to the center of mass of the swarm leads to clusters of agents with approximately equal numbers circling in both directions and changing their circling

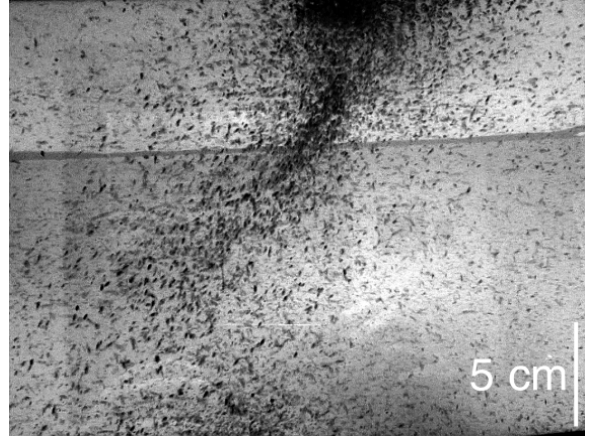


Fig. 2: Side view of vortex-swarming *Daphnia* in a rectangular aquarium. Picture by D.F. Russell.

direction due to the noise. In contrast, a global coupling to the mean angular momentum of the agents ('aligning') breaks the symmetry of the system under certain conditions leading to circling of all agents *in the same direction* and thus forming a vortex state.

In the discrete two-dimensional many-particle model of Levine *et al.*⁵ each particle experiences a self-propelling force \vec{f}_i , a friction force with coefficient β as well as an attractive and a repulsive force between the particles given by an exponentially decaying interaction potential U :

$$m_i\partial_t\vec{v}_i = \alpha\vec{f}_i - \beta\vec{v}_i - \vec{\nabla}U,$$

$$\partial_t\vec{x}_i = \vec{v}_i$$

The model has been investigated using two different rules for the determination of the

self-propelling force \vec{f}_i : either (i) without any averaging, $\vec{f}_i = \vec{v}_i$, or (ii) aligning it with the average velocity direction of the neighboring particles within a certain interaction length, processes that mimic the two aforementioned motions. For certain parameter values Levine *et al.* find stable states with circular motion of the agents, independent of the explicit form of the interaction potential and for various initial conditions, such as randomly distributed agents having velocities of constant magnitude but random directions. Depending on the implementation of the self-propelling force the agents either (i) circle both clockwise and counterclockwise randomly or (ii) circle all in the same direction after a certain transition time, which leads to a vortex state. The circular motions are observed to be stable under reasonable noise and the agent density always drops off sharply at the boundary of the agent swarm consistent with observations of the boundaries of real biological swarms.

Experimental Observations

All the above mentioned authors complain about the lack of experimental data to compare their models with. Experimental observations of circling behavior in biological systems under well defined conditions have up to now only been reported for disc-shaped aggregates of the bacteria *Paenibacillus vortex* and aggregated cells of the mold amoeba *Dictyostelium*. These systems are on a low evolutionary level compared with birds and fish. Moreover, the physical and behavioral aspects of the observed motions are difficult to compare with the ones for swarms of fish or birds. However, several chance observations of different freshwater zooplankton performing a horizontal circular motion under lab conditions as well as one vortex-swarming incidence of the oceanic zooplankton *Anchylomera blossevilli* have been reported.⁶

Although the specific circumstances for these behaviors to occur in zooplankton are difficult to define, it is striking that in all observed circling events special light conditions were recorded. These can be roughly summarized as the existence of a vertical shaft of light in the water to which the animals are attracted. In the view of the aforementioned difficulties, we were led to consider zooplankton as a promising genus of animals for lab experiments in order to better understand vortex-swarming behavior. In addition, zooplankton, which are old from an evolutionary point of view, have been well studied for a variety of reasons.

Reproducibly inducing swarms of the common fresh-water zooplankton *Daphnia* (see Fig. 1) to carry out a vortex motion (see Fig. 2) in our lab surprisingly reveals that the water within the *Daphnia* swarm also circles in the same direction as the animals. The final actual turning direction of the vortex appears to be random. Important environmental conditions for vortex-swarms to occur in our set-up are the presence of predator kairomones, high enough *Daphnia* and food (i.e. algae) densities, as well as light from above together with a reflective bottom and sides of the aquarium. Although the exact light conditions necessary for vortex-swarming are not well defined for our initial observations, they are consistent with the conditions reported for the vortex-swarm of *Anchylomera blossevilli* as well as with earlier swarming experiments which showed that the presence of predator kairomones enhances the tendency to swarm. The major cost of swarming to plankton is limited food availability, since the food density significantly decreases inside a swarm.

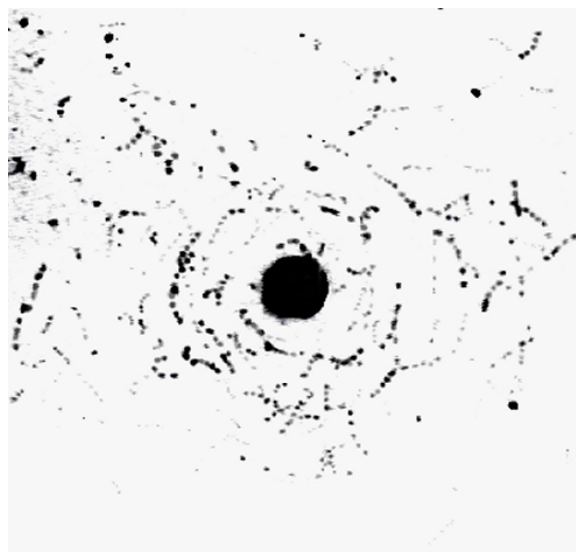
To characterize the circling behavior of *Daphnia* in a more well defined set-up, we studied the motion of single *Daphnia*, as well as of swarms with respect to a vertical shaft of light in cylindrical symmetry. The light acts as an optical marker to which they are individually attracted. *Daphnia* are known to

heavily depend on phototaxis, chemotaxis and mechanoreceptors to sense their surroundings.⁷ Most likely *Daphnia* cannot form an image with their eyes, but they can determine wavelength, intensity, and direction of light. In contrast to fish and birds, close range alignment between neighboring animals has not been observed. No means of direct communication between pairs of *Daphnia* are known.⁸ Their swimming behavior is instead dominated by the low Reynolds number hydrodynamic environment in which they live. This motion consists of ‘hopping’ at a rate of on average three moves per second, with an overall speed of 4-16 mm/s and a sinking rate 3 mm/s.

In our experiment we observe the development of circular motions around the light shaft in both directions with frequent changes of the rotational direction for swarming *Daphnia* (see Fig. 3) and, surprisingly, also for individual *Daphnia*. The fact that single *Daphnia* also circle indicates that circling is not a collective motion emerging in a swarm of animals, e.g. due to alignment of neighboring animals as observed for fish and birds, but instead is an individual reaction to a certain light pattern. The vortex motion evolving at a natural light marker can then be explained as a self-organization phenomenon, with the water drag being the positive feedback and the indirect alignment interaction between *Daphnia*.⁹

Comparison of Theories and Observations

Since *Daphnia* do not directly interact with each other, the group of models on Self-Propelled Interacting Particles⁵ are only partially applicable to these animals. The single-particle model on Active Brownian particles³ more closely simulates the observed circular motion in single *Daphnia*, although in the theory the agents rely on a



*Fig. 3: Bottom view of the aquarium showing five successive positions of many *Daphnia* in respect to the centered vertical light shaft (radius of light shaft 0.6 cm). Snapshots taken in intervals of 0.3 s. The lighter dots mark the positions earlier in time. Most of the *Daphnia* close to the center can be observed to circle in both directions. In the outer regions several *Daphnia* can be seen to move towards the light.*

continuously replenished and depleted energy depot that is on the wrong time scale for *Daphnia*. Moreover, the agents in the model speed up when encountering an energy supply while *Daphnia* slow down inside a food patch for feeding. A general question arising when considering the self-propelled agent models that lead to circular motion is, which ingredients are essential for circular motion to occur and which are not necessary? To answer this question we developed a simple two-dimensional, stochastic model for discretely moving self-propelled agents based on a random walk with short-range, temporal correlations. Instead of choosing the direction of the next step randomly from a uniform distribution as in the simple random walk model, our walker chooses its direction according to a distribution of turning angles (DTA) between two successive steps which were previously measured for *Daphnia* moving in darkness (see Fig. 4). Note that the sum of the left and the right turning angles is

approximately equal. This bimodal symmetric distribution with maxima around $\pm 35^\circ$, similar to those observed for the zooplankton copepod¹⁰, introduces a short-time memory into the model. Adding an attraction to light proportional to the distance between agent and light source leads to circular motion. Individual agents circle in both directions and frequently change direction. Without including the short-range correlation no circular motion develops. Characterizing the movement of the agents with the same measures we used for the *Daphnia* movements shows very good agreement between experiment and simulation. Comparing our random walk model with the Active Brownian Particle models for single agents and for agent swarms due to Ebeling and Schweitzer, as well as with the variant of the Self-Propelled Interacting Particle model introduced by

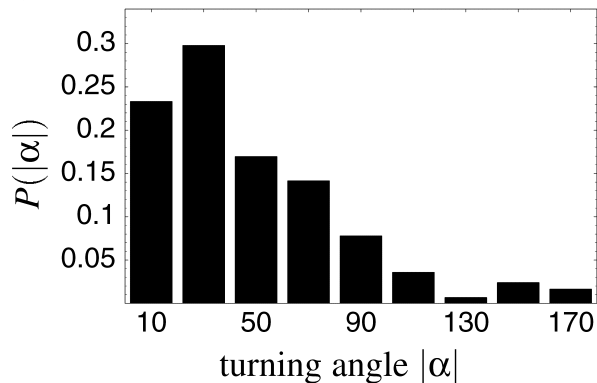


Fig. 4: Probability distribution $P(|\alpha|)$ of the absolute turning angle $|\alpha|$ of *Daphnia* between successive moves, determined from data of 1600 moves obtained from the tracks of eight different *Daphnia* observed in darkness

Levine *et al.* reveals the essential ingredients for circling to occur: (i) self-propelled agents with a preference to move forward within a certain velocity range, (ii) a point attraction, either directly in form of an external parabolic potential as in the Active Brownian Particle models and the random walk model or indirectly in form of an effective mean field potential resulting from the particle-particle interaction in a certain parameter range. The additional condition necessary for

the vortex motion is a symmetry breaking tendency to align.

In conclusion, experiments on vortex-swarming *Daphnia* in the lab can shed more light on the general physical, chemical and biological aspects of vortex-swarming in prey animals, although the interaction that leads to vortex-swarming in *Daphnia* is not a direct one, as it is the case of birds and fish, but an indirect one via the water drag. Further experiments with *Daphnia* have to include systematical investigations of the factors observed to enhance vortex-swarming such as kairomone intensity, *Daphnia* density and food density. In particular the detailed light conditions, as well as the light perception of the *Daphnia* and the physical aspects of the fluid dynamic vortex to occur need more attention.

Acknowledgements

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References

- ¹*Diffusion and Ecological Problems*, A. Okubo and S. A. Levin, Springer-Verlag, New York, 2002.
- ²*Fluctuations and Scaling in Biology*, T. Vicsek, Oxford University Press, Oxford, 2001.

³F. Schweitzer *et al.*: Complex Motion of Brownian Particles with Energy Depots. *Phys. Rev. Lett.* **80**, 5044 (1998).

⁴F. Schweitzer *et al.*: Statistical mechanics of canonical-dissipative systems and applications to swarm dynamics. *Phys. Rev. E* **64**, 021110-(1-12) (2001).

W. Ebeling and F. Schweitzer: Swarm of Particle Agents with Harmonic Interactions. *Theory Biosci.* **120**, 207-224 (2001).

⁵H. Levine *et al.*: Self-organization in systems of self-propelled particles. *Phys. Rev. E* **63**, 017101 (2001).

⁶P.S. Lobel, and J.E. Randall: Swarming behavior of the hyperiid amphipod *Anchylomera blossevilli*. *J. Plankton Res.* **8**, 253-262 (1986).

⁷Zooplankton: Sensory Ecology and Physiology, edited by P.H.Lenz *et al.*, Gordon and Breach Publishers, Amsterdam, 1996.

⁸P. Larson and S. Dodson: Invited Review: Chemical communication in planktonic animals. *Arch. Hydrobiol.* **129**, 129 (1993).

⁹*Self-Organization in Biological Systems*, S. Camazine *et al.*, Princeton University Press, Princeton and Oxford, 2001.

¹⁰F.G. Schmitt and L. Seuront: Multifractal random walk in copepod behavior. *Phys. A* **301**, 375 (2001).

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ESSAY

KLIEBER'S LAW: A QUESTION OF UNIVERSALITY?

FRANK J. BROOKS

The headline of an article by Vaclav Smil (*Nature* **403**, 597; 2000) reads: "Every living thing obeys the rules of scaling discovered by Max Kleiber." The word "every" implies universality. That is, the notion that Kleiber's $\frac{3}{4}$ law is always applicable to all species. The author justifies this notion by citing the work of West, Brown and Enquist (*Science* **276**, 122–126; 1997) where the $\frac{3}{4}$ law is developed based on a theoretical, space-filling fractal network of branching tubes that transport "essential materials" in the living organism. Although the proposed fractal network may, indeed, be a crucial step toward the discovery of a biological "theory of

everything," hypotheses based upon it should not be used to generalize beyond experimentally verifiable data.

Kleiber's $\frac{3}{4}$ law (*Hilgardia* **6**, 315-353; 1932) is a power scaling law of the form $BMR = k \cdot M^b$ that specifically relates body mass (M) to basal metabolic rate (BMR). Using straightforward Euclidean scaling applied to body surface area and heat flux through said surfaces as starting premises, Max Kleiber's great contribution was to observe that there is a power law relation between mammalian mass and BMR. Additionally, he recognized that his empirically derived mass exponent ($b = 0.74$), which he later refined to exactly $\frac{3}{4}$, was

different from that predicted by the original premises alone ($b = \frac{2}{3}$).

There is no disputing the validity of Kleiber's law (or other quarter-power scaling laws) as applied to many, perhaps even most, interesting biological scaling relations. However, accepting the notion that Kleiber's law applies to "every living thing" dismisses a large body of work that explicitly indicates other scaling scenarios. One notable example is offered by Bennett and Harvey (*J. Zool.* **213**, 327-363; 1987) who experimentally verify a mass exponent of $\frac{2}{3}$ for the allometric scaling of BMR to mass across several species of birds.

It also should be noted that accepting Kleiber's law as the dominant means of calculating energy requirements for an entire organism does not necessarily imply that other mass-dependent biological variables scale similarly. For instance, it has been experimentally shown by Hu and Layton (*AAPS PharmSci*, **3** (4) article 29; 2001) that the mammalian capacity for the clearance of xenobiotics eliminated mainly via renal excretion scales as mass to the $\frac{2}{3}$ power. This result holds true over a 10^4 span of masses. At the very least, this serves as evidence that the transport of some "essential materials" (in this case, waste material) scales as a power other than $\frac{3}{4}$.

Why is all of this important? Qualification of the scope of Kleiber's law is, pun intended, huge. As argued by Azbel' (*PNAS* **96**, 15368–15373; 1999), universality, as applied to biological scaling phenomena, likely implies an underlying statistical mechanism that governs biological systems analogous to the once hidden, probabilistic world of the quantum particle. While attempting to distinguish between one power and another less than nine-one hundredths its junior may be only an exercise in error propagation to some, to others it could literally signify an entirely new field of life science.

Toward verification of universality, it is crucial that one discern between data representing underlying processes that *contribute to* a general rule and data representing those that are *approximated by* a general rule. Consider, for example, the well-known relation that governs air resistance (β) as a function of

instantaneous velocity (v). For a sphere falling at low speed, $\beta \propto v$. Of course, at higher speeds $\beta \propto v^2$. While it may be possible to approximate the overall behavior of this piecewise function by a single quadratic, it is equally possible for the piecewise function, and thus the underlying physics, to be missed if first given (empirically) the "best-fit" quadratic. In fact, Heusner (*J. Nutr.* **121 Suppl 11**, S8 17; 1991) showed that the log-log relationship between mammalian mass and BMR is not accurately described by a single regression line (slope = mass exponent). Acceptance of universality necessarily requires that observed deviations, in any portion of the range that is to adhere to the proposed law, be carefully scrutinized and explained.

Unfortunately, in a *New York Times* (sec F, 1 col. 2; January 12, 1999) interview, a principal researcher in the field is said to be "not too bothered by these seeming exceptions." The reporter then dismisses "recalcitrant data" as something physics models eventually always have driven into submission. Of course, such data only bolster the robustness and acceptance of a given model via tweaking the model or illustrating that the data were not actually applicable to the given situation. In both scenarios, satisfactory explanation of apparent exceptions to the model serve to further general understanding.

If search results for key phrases such as "Max Kleiber" or "biological scaling" in Google™ and Lexus-Nexis™ are representative of the generally accepted opinion of Kleiber's law, then it has gained an as yet undeserved omnipresence. Within the discovered online

reprints and personal websites of scientific researchers and students, precious few papers are cited and alternative viewpoints are not well represented. If a researcher's first method of triage is to search online for information, that researcher could be lead into thinking that Kleiber's law is universally true. Worse yet, subsequent research (e. g., *PNAS* **99 Suppl 1**, 2473-2478; 2002) that *presumes* Kleiber's law to be universal, may not be taken as it should, that is, *cum grano salis*.

Currently, for the proposed *universal* allometric scaling law relating basal metabolic rate to body mass, there is no conclusive evidence for choosing $\frac{3}{4}$ over $\frac{2}{3}$ or, for that matter, $\frac{17}{24}$. Furthermore, it has been experimentally shown that, in more than one specific case, $\frac{3}{4}$ scaling is just plain wrong. What is likely to be correct, is that while quarter-power scaling dominates certain aspects in certain species, other powers better apply to other situations. Perhaps, as in the case of recent developments in earthquake research (*PNAS* **99 Suppl 1**, 2509-2513; 2002), a unified scaling law will be developed such that a particular case in question is merely a limiting case of the greater rule. However, for the nonce, we simply must accept that the matter is unresolved.

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