Living history: G. Edgar Folk, Jr.

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In 2005, the American Physiological Society (APS) initiated the Living History Project to recognize senior members who have made significant contributions during their career to the advancement of the discipline and profession of physiology. During 2007, the APS Section of Environmental and Exercise Physiology selected Prof. G. Edgar Folk, Jr., of the University of Iowa to be profiled in Advances in Physiology Education.

American Physiological Society history; Living History program

G. EDGAR FOLK, JR., was born on November 12, 1914, in Natick, MA (Fig. 1). He was the only son of May Davis Folk and Reverend G. E. Folk. The Reverend, a Methodist minister of the British naturalist curate type, encouraged his children to be curious about plants and animals in the woods while conducting hybridization experiments with flowers in his garden (to produce blue gladiolus, etc.). After years of dinner table conversations on the progress of his “experiments,” it was not surprising that the Reverend’s only son chose experimental biology as a career.

After graduating from Philip Andover Academy in 1933, G. Edgar Folk enrolled in Harvard University, where he received an A.B. Degree in Biology in 1937, an M.A. Degree in the Biological Sciences in 1940, and a Ph.D. Degree in the Biological Sciences during 1947, with Prof. John H. Welsh serving as his advisor.

Dr. Folk’s interest in hibernating research began with a school-boy friendship with Donald R. Griffin, who achieved national recognition as an animal behaviorist. While an undergraduate, Griffin was able to recruit students, including Folk, to band all the hibernating bats in New England during the winter months. As a result, Folk became intrigued with the biology of hibernation and had published two studies on the subject by 1940. The first study was conducted with hibernating bats in the Indian Oven Cave in Ancram, NY, from October to March. Folk found there was a shift in the total population studied and a change in their periods of activity during the winter, which suggested that the bats had moved from cave to cave during the hibernating period and that more animals were awake at night (29). His second study concerned the longevity of sperm, involving keeping isolated female bats in a hibernating state for 16 wk before euthanization, and resulted in two embryos being discovered (35).

Although Folk was interested in selecting a hibernation topic for his dissertation, Prof. Welsh encouraged him to investigate biological clocks, which were capable of inducing hibernation. A great admirer of Welsh, Folk followed his advice and conducted a dissertation entitled “The influence of light and restricted time of feeding upon running activity of the white rat.”

Between 1943 and 1947, Folk was a Research Associate in the renowned Harvard Fatigue Laboratory directed by Dr. David Bruce Dill (39). In addition to being one of the oldest American Physiological Society (APS) members who is still active and productive in a physiological laboratory, Dr. Folk is the last surviving member of that famous laboratory, which closed in 1947. During his tenure within the laboratory, he participated in an important research project for the Quartermaster Corps with Drs. H. S. Belding, H. D. Russell, and R. C. Darling concerning the effectiveness of Army-issued arctic uniforms for operational purposes (sitting, standing, and exercising) in extreme cold conditions (0–40°F), with the majority of the tests being conducted at 0°F (4, 5).

The study necessitated the use of heat balance equations and measurements that recorded convection, radiation, sweating, vaporization, insulation, condensation, thermal barriers, skin temperatures, body temperature, and work performed. As exercise in the cold was of prime importance, they reported that the insulation provided was a curvilinear function of the movement speed of the individual and the convection currents between the layers of permeable clothing and the air under the windbreaker layer. Moreover, they found that much of the sweat that originally evaporated at the skin was recondensed into the clothing, giving back a portion of the heat of condensation to the skin. The recontributed heat was proportional to a ratio obtained by dividing the amount of insulation lying outside the point of condensation by the total insulation. During a treadmill walk (3.5 mph) at 0°F, the net sweating efficiency was greatest at low rates of sweat production and least when sweating was profuse. The practical result emerging from the study was to recommend soldiers working in the cold of the Arctic to modify their activity levels to the point of feeling cold but comfortable. Consequently, sweating and the accumulation of moisture would be minimal (4).

Prof. Folk and Bowdoin College

From 1947 to 1953, Dr. Folk was an Assistant Professor of Biology at Bowdoin College in Brunswick, ME, and from 1951 to 1953 was Director of the Bowdoin Scientific Station on Kent Island, located in New Brunswick, Canada. The station was established as a research facility and sanctuary for nesting seabirds. Of the 200 bird species that have been identified on the island, 55 species have nested there. The Leach Petrel is a small seabird found on Kent Island that lays one egg per year in an underground burrow. As they are associated with a long lifespan and an extended incubation period, Prof. Folk studied (n = 12) their body and nesting temperatures during the incubation period (40 days) and found very low body temperatures, which indicated a semitorpid physiological condition (14). However, it was unclear whether this state was intrinsic to the petrel or the result of fasting during the incubation period.

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While at Bowdoin College, Dr. Folk received a contract with the United States Army (arranged by Prof. H. S. Belding) to do human experiments on faculty members and students on the topic of the influence of impermeable gloves and boots on human skin in the cold. As a result of the Folk and Peary research (9), the United States Army Quartermaster Corps ordered several thousand foam-rubber boots to be worn in the cold. During the subsequent Korean War, they became invaluable during the winter months.

Prof. Folk’s Career at the University of Iowa

In 1953, Prof. Folk became an Associate Professor in the Department of Physiology within the College of Medicine at the State University of Iowa, which subsequently became known as the University of Iowa. Later (1965), he became a Professor of Physiology and, in 1985, was designated as an Emeritus Professor of Physiology while continuing his research and grantsmanship.

Prof. Folk’s educational responsibilities pertained to the teaching of medical physiology to medical and graduate students while supervising and teaching their laboratory activities. Because of his experiences at the Harvard Fatigue Laboratory, he proposed that the Department of Physiology offer a new course to graduate and advanced undergraduate students entitled “Environmental Physiology.” They agreed and established the first course in environmental physiology for graduate students. It became an interesting and popular course that earned Prof. Folk the distinction of being selected as Teacher of the Year for the College of Medicine and was responsible for the University of Iowa bestowing upon him the prestigious Excellence in Teaching Award. Once the course had been established, Prof. Folk authored, in 1966, the first text devoted to environmental physiology for advanced students: Introduction to Environmental Physiology (21). It became widely accepted by Departments of Physiology and Biophysics, Kinesiology, and Exercise Sciences. Eight years later, with extensive revisions and additions, he introduced the Textbook of Environmental Physiology (31), which was equally well received by similar academic units. More recently, in 1998, Folk and colleagues at the University of New Mexico and University of Iowa prepared an advanced text known as Principles of Integrative Environmental Physiology, which was most appropriate for an era in which the integration of subject matter had become a major objective of physiological instruction (26).

Prof. Folk’s courses and textbooks on environmental physiology served as a magnet in attracting talented students, fellows, and faculty to the University of Iowa throughout his career. Summarized in Table 1 is a partial list of individuals who came to Iowa City to be in his laboratory. However, it was his research on biological clocks and rhythms, hibernation, and, to some degree, temperature influences that established his national and international reputation as an investigator. As space does not permit discussion of his extensive investigations, only select studies will be mentioned in subsequent sections.

Biological Clocks and Rhythms

The overwhelming majority of Prof. Folk’s research has been conducted with animals. Of the human investigations, one of his early studies was conducted with the late Steven Horvath concerning day-night differences in body temperature and heart rates after exercise. While the results were not statistically significant, they did exhibit a biological trend suggesting that the day-night differences in heart rate and body temperature were governed by intrinsic factors (45). Later, he collaborated with others to examine the relationship between age and day-night circadian rhythms. They found with age an increased disassociation between the circadian rhythms concerned with core temperature, heart rate, urine flow, and potassium concentration (6).

In the assessment of physiological rhythms, Prof. Folk has been very innovative in perfecting equipment (43) and techniques for implanted radiotransmitters to record changes in physical activity, body temperature, heart rates, and electrical activity (ECG) of the heart (7, 30). Before Aschoff’s rule (3) was established, which can be explained as follows: “In continuous light with increasing intensity of illumination, light-active animals increase their spontaneous frequency, while dark-active animals decrease it” (21), he was conducting studies on the influences of a light cycle on activity rhythms (22).

After determining the 24-h. rhythm of the running activity of white rats, Folk initiated studies in which 1) rats were raised...
without exposure to cycles of light and darkness and without the influences of a maternal 24-h rhythm of activity, 2) rats were raised in a standard light cycle (12 h daily of either light or darkness) before being tested in continuous light, 3) rats were exposed to a reversal of a 24-h solar light cycle, and 4) rats were exposed to a 16-h light cycle. The photoperiodic concepts emerging from these investigations were as follows: 1) rats raised without maternal influences or periodic daylight stimuli exhibited an activity rhythm of \(12\ h\) of activity and \(12\ h\) of inactivity, 2) rats exposed to continuous light exhibited an activity rhythm that remained \(8-12\ h\) in duration but with a delayed starting time of \(45\ min/day\) and an activity block that “travels around the clock,” 3) rats exposed to reversal conditions exhibited a gradual delay when exposed to light that became \(3\ h/day\) until the activity block fell into darkness, and 4) rats experiencing \(8\ h\) illumination or darkness demonstrated a dynamic response that exhibited a delay in starting time of \(1\ h/day\) (22). A graphic example of the recording activity records while changes in rectal temperature were measured is shown in Fig. 2.

As these conditions were vastly different from those found during the summer months in Arctic and Antarctic regions where 82 days of continuous light will occur, Prof. Folk traveled to polar regions to secure data on this subject. This process was facilitated by federal and local research grants and by an affiliation with the Arctic Research Laboratory in Point Barrow, Alaska. (This laboratory was founded in 1947 by Prof. Laurence Irving, a long-time member of the APS.) Over a period of several summers, Prof. Folk, with the assistance of his late wife Mary and colleagues, studied the influence of continuous Arctic light on the rhythms of ground squirrels, foxes, wolverines, and wolves using implanted radiocapsules to transmit physiological data to recording units. After analyzing their extensive data, they concluded that continuous Arctic light had no significant influence on the Aschoff rule and postulated that Arctic animals were conscious of the position of the sun on the horizon and that their biological clocks had no reason to change (2, 10). Approximately four decades later, they repeated the experiment in Alaska with porcupines and ground squirrels and found that both species had specific times for activity and resting during a nearly 24-h scale while exhibiting no evidence for a delay in the appearance of their activity peaks (11, 31) (Fig. 2). In essence, their previous research was confirmed.

In mammals, the synthesis of the hormone melatonin by the pineal gland is stimulated by darkness and inhibited by light (26). Prof. Folk has had a long interest in its antigonadotropic action, especially as it pertains to the Arctic brown lemming, which experiences \(80\ days\) of continuous light and/or darkness (19). In fact, Folk and colleagues demonstrated that the surgical removal of the pineal glands of lemmings eliminated their reproductive responses to the photoperiod (26). In addi-
tion, of the Arctic animals studied, the brown lemming had the heaviest pineal gland/body weight of any mammal. Prof. Folk’s interests in biological rhythms have extended into studies involving isolated and cultured organs and cells. When using cultured adrenal glands from hamsters, Folk and colleagues found a conspicuous circadian pattern in oxygen consumption (60% above and below the mean) and in steroid secretion (increased corticosterone) (1). Using the Langendorff isolated rat heart preparation, they found a rhythm that exhibited its highest rate between 3 PM and 3 AM. On the other hand, with cultured rat heart cells, they recorded the highest heart rates between 8 PM and 12 AM (44). Collectively, these results were the first to indicate that isolated organs had intrinsic biological rhythms that were operational with intact physiological systems.

Temperature and Its Influences

For more than 50 years, it has been known that mammals suffer more from heat than from cold because there are more physiological mechanisms for combating cold than for heat (31). This difference, plus the paucity of heat research being conducted on laboratory mammals, stimulated Prof. Folk and colleague J. G. White to investigate heat acclimation in the beagle dog (13). After having the dogs run daily (3.2 km) for 14 days at below 0°C, dogs were trained to run on a treadmill in ambient temperatures for additional weeks before becoming exposed to 10 days of heat (38°C, black bulb = 43°C) while running 1 h/day. As with humans, postexercise mean rectal and skin temperatures and heart rates with heat exposure indicated that heat acclimation had occurred. Moreover, the inclusion of exercise in ambient conditions appeared to enhance the process, as it does in humans. Previously, Prof. Folk demonstrated heat tolerance in monkey would be influenced by restraint (37) and published articles pertaining to the long term physiological effects of warming on animals and on the evolution of sweat glands (33).

While Professor Folk has demonstrated an interest in heat research, it is evident that he has a passion for research in the cold and especially in the polar regions. As the responses to cold can be classified into maintaining a normal body temperature (normothermic) and hibernation, only the former will be mentioned here. To study the effects of hypothermia on the circadian rhythms associated with EEG activity and heart rates, a cat’s rectal temperature was lowered from 34 to 26°C, which reduced the heart rate rhythm by 62% and the electrical activity of the brain by 27%. This unexpected result led him to suggest that a temperature-independent clock could be present within the brain (23).

In addition to hibernation, cold acclimatization and its mechanisms have been a major interest of Prof. Folk. In an early study (38) with two species of bats, he suggested that the acclimatization process involved neural and hormonal mechanisms. He was the first to demonstrate that exposure to short photoperiods of light would enhance the process of cold acclimatization in rats and mice, to achieve a state of “cold acclimatization without cold” (28). His study in hedgehogs and woodchucks was important because it demonstrated that cold acclimatization was not a “necessary requirement for the dormancy of mammalian hibernation” (20). Equally significant was his acclimatization study (31) with brown lemmings because they conclusively showed that their physiological adjust-
Type | Examples | Blood Temperature
--- | --- | ---
A | Small hibernators, such as ground squirrels | 3–13°C
B | Small mammals that exhibit daily torpor | 15°C
C | Large mammals, such as bears | 31°C

One of the early studies was concerned with the influences of light on the periodic movement patterns of awakening hibernators (hamsters and ground squirrels) (12). They found that the presence of light had more of an awakening effect on squirrels than hamsters, but the collective effect activity profiles suggested the existence of a biological clock that was independent of temperature. As temperature regulation can be altered by increased concentrations of magnesium, Riedesel and Folk (42) measured the serum concentrations of six hibernating mammals and found marked elevations in five mammals, with the hedgehog having the highest (92% over controls) and the golden hamster having the lowest (25%), thus suggesting that magnesium could be a “contributing trigger” for the onset of hibernation.

Although it was known that small mammals did not hibernate for long periods of time, there were limited data concerning the number of bouts being experienced, the duration of such bouts, the time awake during bouts, or the animals’ feeding, urination, or defecation habits. Consequently, Prof. Folk and colleagues selected three species of small hibernators (the edible dormouse, garden dormouse, and Franklin ground squirrel) and found that the range of hibernation bouts varied from 4 to 17 depending on the species and the mean duration of a bout ranged from 3 to 9 days with a mean duration between bouts of 1.3 days with feeding, urination, and defecation behavior occurring essentially when active, thus resolving an uncertainty that prevailed for many decades (27).

Sleeping heart rate recordings from Arctic marmots and woodchucks before and during hibernation (−34 to 48°C) demonstrated a 10-fold reduction in mean heart rate to 8 beats/min (17). When the QT intervals of woodchucks (a small nondormant hibernator) were compared with intervals associated with bears and humans, the woodchuck had a shortened interval that was similar to the bear and dissimilar to the human (8). Prof. Folk’s expertise with radiocapsules and an affiliation with the Arctic Research Laboratory in Point Barrow, AL, enabled him to initiate the research on bears (Fig. 3), which proved they do hibernate and will not eat, drink, defecate, or urinate for periods from 4 to 7 mo (18).

Table 2. Urinary nitrogenous values from a hibernating grizzly bear and a control grizzly bear

<table>
<thead>
<tr>
<th>Time to fill bladder, days</th>
<th>Hibernating Bear</th>
<th>Control Bear</th>
</tr>
</thead>
<tbody>
<tr>
<td>135</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Urine volume, ml</td>
<td>181</td>
<td>2,080</td>
</tr>
<tr>
<td>Total nitrogen, g</td>
<td>1.43</td>
<td>34.00</td>
</tr>
<tr>
<td>Urea, g</td>
<td>0.98</td>
<td>55.05</td>
</tr>
<tr>
<td>Ammonia, mg</td>
<td>72.20</td>
<td>1,785.00</td>
</tr>
</tbody>
</table>

Modified from Ref. 24.
the University of Illinois proposed that the hibernation of bears would be a good research model to study the problem of human starvation (34). They also identified several behavior stages during the process. These stages were 1) hibernation, 2) walking hibernation, 3) intermediate muscular activity, and 4) hyperphagic behavior (34, 41). Of the four stages, stage 3, the intermediate stage, had the most relevance to humans. When winter activity measurements were made of two black and two grizzly bears in stage 2, the bears were in a state of lethargy most of time and unresponsive to a light stimulus. Although the frequency of activity changed little during this time, when changes were noted, the bears became very active around noon and very inactive at midnight (27).

Transmitted heart rate and ECG data from unrestrained bears (3 species) during various stages of hibernation revealed summer resting rates of ~42 beats/min that could increase with exercise to 156 beats/min. During the winter months and entering the dormancy phase, heart rates oscillated between 40 and 110 beats/min, with gradual reductions to oscillations between 8 and 20 beats/min (Figure 4) (26, 31). As with small mammals, the QT interval became reduced with hibernation (0.14–0.23 s), markedly lower than normal human values (0.39 s) (8).

Prof. Folk found that polar bears exist on an all-fat diet and will consume only the blubber and small amounts of skin from seals they kill (25). When their lipid levels were compared with levels of fasted brown bears, Folk and colleagues (28) were surprised that lipid concentrations (lethal to rabbits and dogs) were lower than those reported for fasted animals. This result indicated a “unique” feature of fat metabolism in Arctic bears (28).

Although hibernating bears will lose ~27% of their body mass, they conserve lean body mass (41). To gain insights on protein metabolism, Folk secured urine samples from hibernating and nonhibernating animals and confirmed that hibernation would significantly decrease urine volume while demonstrating, in unanesthetized bears, that nitrogen was conserved (24) (Table 2). As for the source of protein for polar bears, Prof. Folk believed that it came from the skin of seals.

**Conclusion**

Professor Folk is truly an environmental physiologist for all seasons and a most deserving APS member to be recognized and included in the Living History Program. His seminal contributions to the discipline and profession of physiology will be long remembered by those who follow him.

**REFERENCES**

32. Folk GE Jr, Folk MA, Brewer MC. The day-night (circadian) physiological rhythms of carnivorous in natural continuous light (summer) and continuous darkness (winter). Int J Biometeorol 11: 154, 1967.