were securely ligated proximal to the submaxillary gland. A longitudinal slit, placed in the trachea below the ligature, permitted the animal to breathe freely. The animals were then placed on their feet in an upright position—that is, normal stance with the head slightly raised—and held by means of a head-holder.

A solution of uniformly labeled ^{14}C-glucose (0.0173*M*, 0.2 ml containing 10 μc) was pipetted into the oropharynx of each of the ten rats of group 1. The solution was permitted to remain there 4 minutes; the mouth of the rat was subsequently thoroughly rinsed with distilled water over a 30-second period. Throughout this procedure the animal was held in its normal position, that is, with feet down. Immediately after the rinsing, a sample of blood was obtained from four of the animals by cardiac puncture. Each animal was then frozen by immersion in liquid nitrogen and kept at −9°C. In the two control animals, the ^{14}C-glucose was introduced directly into the first portion of the duodenum by means of a polyethylene tubing inserted by way of gastrostomy through the pylorus.

To ascertain whether the activity in the brain was restricted to the cerebral circulation or appeared in the parenchymal tissue, the brains of two animals in the experimental group were perfused. Four minutes after glucose was placed in the oropharynx, the animal's chest was opened and a sample of cardiac blood was obtained. A metal cannula was then introduced through the left ventricle and tied into the ascending aorta for perfusion. The right atrium was cut, a clamp was placed on the descending aorta, and perfusion of the head region with normal saline at 120 mm-Hg pressure was begun. The perfusion was continued for 2 minutes before the animal was frozen as described.

Autoradiograms of the whole body were prepared from the frozen animals by the tape-sectioning method of Ullberg (*2*), with modifications (*3*). All manipulations were carried out in a cold room at −9°C. At this temperature, smearing of tissue during sectioning did not occur. All sections were cut, beginning at the tail or at the head, with the long axis of the animal perpendicular to the knife. Kodak No-Screen x-ray film was used with exposure times of 7 to 15 weeks.

The massive radioactivity in the head region which was seen after placing labeled glucose into the mouth is shown in Fig. 1. The unstained tissue section from which the autoradiogram was made is shown above the autoradiogram. There is no activity beyond the ligature or any spread in the direction of sectioning. Activity is present throughout the face region and clearly evident in the intracranial cavity. Apparently the glucose or labeled fragments of it can pass directly from the mouth to the brain, bypassing the gut. The autoradiograms of head-perfused animals were indistinguishable from those prepared from animals which were not perfused (Fig. 1). This suggests that the radioactivity is within the tissue of the brain rather than its being a reflection of radioactivity in the blood in transit. In support of this contention, the radioactivity in the cardiac blood samples of the experimental animals of group 1 was not significantly above background.

An autoradiogram from a control rat (group 2) which had received the ^{14}C-glucose by duodenal administration is shown in Fig. 2. In contrast to Fig. 1, where radioactivity was limited to the head region, Fig. 2 illustrates the diffuse distribution of glucose or metabolites when carried by the circulation.

The whole body autoradiogram (Fig. 1) established that the radioactivity moved through all the tissue in the head region up into the intracranial cavity. Inspection of 12 to 60 serial sections from each animal failed to reveal a preferential pathway from the oropharyngeal cavity to the brain. There was no evidence for preferential distribution within the brain parenchyma itself, although those portions of the brain which are closest to the oropharynx generally exhibited greatest uptake of the isotope.

Approximately half of the animals receiving the labeled glucose orally provided autoradiograms similar to Fig. 1. The autoradiograms of the remaining animals showed less activity, including some in which no activity could be detected in the brain. This variability of our results may be related to technique, the character of the saliva, the physiological condition of the animal, or other factors.

In other radiotracer studies (*4*), sodium chloride and the insecticide phosphamidon were used with whole brain assay techniques (*1*). The results suggest that in both rats and blackbirds the isotope may reach the brain as we describe here. The chemical nature of the radioactivity which travels this more anatomically direct pathway from the oropharynx to the intracranial cavity is unknown.

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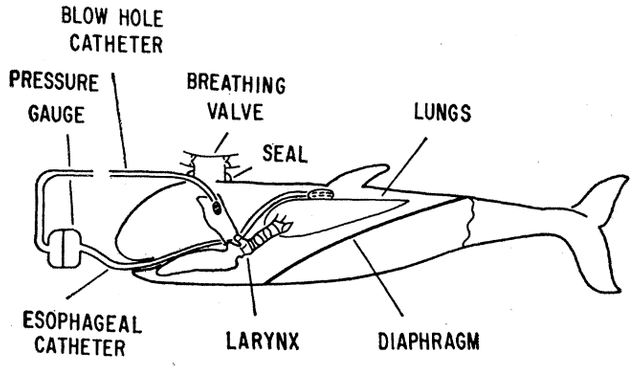
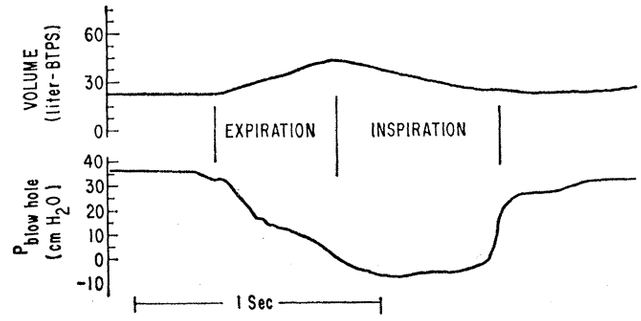
"Blow" of the Pilot Whale

Abstract. *A captive pilot whale emptied as much as 88 percent of lung gas passively, without the aid of expiratory muscles. Level or decreasing pressures in the esophagus during expiration, and in the blowhole at the onset of expiration, revealed the driving force of expiration to be solely elastic recoil. Active muscular reexpansion of the lungs ensued immediately. Expiration and inspiration were completed in about 1 second.*

Scholander has proposed that, as a special adaptation to the marine environment, whales may more completely deflate their lungs than terrestrial mammals do (*1*). Such is the case for porpoises (*2*). This mechanism would lessen frequency and duration of surfacing and would permit more effective exchange of respiratory gases during recovery after a dive.

A young adult female pilot whale *Globicephala scammoni* (3 m long, 450 kg) was kept in seawater pools of a marine mammal facility at Scripps Institution of Oceanography. The holding facility included a channel through which the animal could swim into an inside laboratory. The whale was trained to enter this channel on command, at which time the channel could be closed off by wooden gates from the adjacent pools.





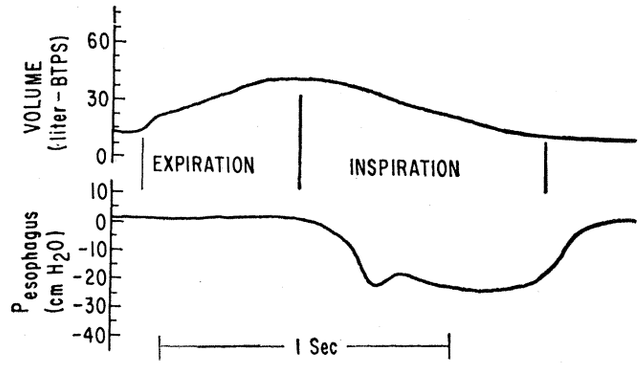


Fig. 1 (top left). Positions of blowhole, larynx, trachea, lungs, diaphragm, pressure-recording catheters, and breathing valve. Fig. 2 (top right). Expired volume on the upper tracing comes out in approximately 0.5 second while esophageal pressure remains slightly greater than atmospheric pressure. At the beginning of inspiration esophageal pressure becomes subatmospheric and sweeps to -20 cm H_2O. Esophageal pressure remains subatmospheric until after the end of inspiration. Fig. 3 (left). Expired volume on the upper tracing and pressure inside the blowhole on the lower tracing. The slightly subatmospheric pressure in the hole during inspiration is a result of both the resistance across the blowhole and the impedance of the spirometer, as well as probable Bernoulli effect within the blowhole.

For the experiments, the whale was placed in a canvas sling which could then be used to hoist her to any desired level. Although some measurements of esophageal pressures were made when she floated freely, she usually was elevated from 10 to 20 cm above a free-floating position in order to restrain her from swimming and to allow the placement of a respiratory valve on the blowhole.

To determine the mechanics of ventilation it was necessary to measure pressures across the lungs and volumes and flows of gas at the blowhole. One catheter in the midesophagus measured pressure changes on the dorsal surface of the lung; another catheter in the blowhole measured pressures in the airway (*3*).

To measure expired and inspired volume we built a one-way valve into each side arm of a sheet-metal T. The bottom of the T was rimmed by a rubber seal and placed over the blowhole. Each side arm of the T connected to large-bore corrugated tubing that formed a circuit to Krogh spirometers of either 20- or 60-liter capacity.

The esophageal and blowhole catheters were connected to opposite sides of a differential pressure gauge by tygon tubing (Fig. 1). Presures in each catheter were measured individually by opening the opposite side of the pressure gauge to atmospheric pressure. There were no lags between recordings of pressures across a pure resistance and of changes in spirometer volume during sinusoidal flows in and out of the spirometer up to frequencies of 2 per second (twice the ventilatory cycle of the whale).

Lung volumes were determined by helium dilution. The whale inspired a measured volume of air containing a concentration of helium which was determined by thermal conductivity. After the whale's usual retention of breath of 20 to 40 seconds she exhaled, and the helium concentration in the expired gas was measured. From the calculated volume we substracted the "dead space" of the breathing valve to obtain the inspiratory lung volume and then subtracted the volume inspired to obtain expiratory lung volume. In some studies we stimulated ventilation by either introducing carbon dioxide into the inspired air or permitting the animal to rebreathe expired gases (*3*).

In each of the 112 blows with simultaneous measurements of esophageal pressure and ventilation, the whale passively expired and actively inspired. Between blows esophageal pressure remained at or slightly greater than atmospheric pressure (0 to 7 cm of H_2O) both when the animal was partially suspended in the sling and when floating free. During expiration, esophageal pressure did not increase (Fig. 2) as it would if expiration were forced by active muscular effort. Even during the increased ventilation in response to carbon dioxide or rebreathing, esophageal pressure did not increase during expiration. During inspiration, a decrease of esophageal pressure to approximately 20 cm of H_2O below atmospheric pressure (Fig. 2) indicated that inspiration was active. Pressure in the esophagus remained subatmospheric until after closure of the blowhole.

Further evidence against active muscular force in expiration was seen in failure of pressure inside the blowhole to increase before expiration or in early expiration as the blowhole opened (Fig. 3). Between blows, pressure in the blowhole usually remained between 15 and 35 cm of H_2O above atmospheric pressure. During expiration it decreased steadily as expired flow decreased.

Between blows, the whale sometimes opened her blowhole; then the pressure in the blowhole fell to atmospheric pressure. When this occurred she must have contained the air and elastic recoil of her lungs behind a closed airway (possibly the larynx), because esophageal pressure did not decrease as it would have if inspiratory muscles held the lungs expanded. Before the next blow she closed the blowhole, and the pressure at that site increased again to the usual plateau of 15 to 35 cm of H_2O.

The average volume of gas remaining in the lungs at the end of expiration was 5.6 liters (range 2.1 to 9.6 liters in ten measurements). Taking this average expiratory lung volume and her largest tidal volume of 39.5 liters, we calculated a lung capacity of 45.1 liters; the whale could renew as much as 88 percent of

the lung gas by a single passive expiration and inspiration.

We interpret a constant esophageal pressure during expiration to mean that the lungs and surrounding chest walls are moving in at the same rate with respect to each other. With active expiration, muscles "push" the lung and pressures on surfaces of the lungs increase. With passive expiration, recoiling lungs may "pull" the chest wall in and cause pressures on surfaces of the lungs to decrease. When pressure on a surface of the deflating lungs remains constant, muscles are not "pushing" lungs nor are lungs "pulling" the chest walls.

Pressures on different surfaces of the lungs probably vary, and esophageal pressures reflect changes in pressure more accurately than absolute pressures on the lungs. When a whale surfaces, the esophagus and lungs lie dorsally near the water level. Laterally the water pressure may be absorbed partly by ribs. Ventrally some of the buoyant force on the abdominal surface may be transmitted through the diaphragm to the lungs.

There appears to be little advantage to active blowing since the lungs nearly empty themselves in 0.5 second. This whale passively expires even when hyperventilating in response to carbon dioxide. She increases ventilation, as does man, by inspiring more deeply and thereby creating greater recoil pressures to drive the next expiration. Morever, she could hyperventilate to 30 times the resting levels through increased frequency of breathing alone. By contrast, man lacks this reserve in frequency and must use his muscles to augment expiration when hyperventilating beyond six or eight times the resting levels (*4*).

Immersion in water should favor passive deflation of the lungs (*5*). Anatomical features that may facilitate emptying of as much as 88 percent of lung gas are cartilaginous supports of bronchi that maintain patency of small branches (*6*) and a diaphragm which, lacking a central tendon and being positioned horizontally (*7*), probably moves easily toward the spine between the buoyed-up abdomen below (*8*) and the recoiling lungs above.

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Operant Conditioning of Cortical Unit Activity

Abstract. *The activity of single neurons in precentral cortex of unanesthetized monkeys* (Macaca mulatta) *was conditioned by reinforcing high rates of neuronal discharge with delivery of a food pellet. Auditory or visual feedback of unit firing rates was usually provided in addition to food reinforcement. After several training sessions, monkeys could increase the activity of newly isolated cells by 50 to 500 percent above rates before reinforcement.*

Neural mechanisms of motor activity can be investigated by recording the activity of single neurons in unanesthetized animals performing a specific behavioral response. In such experiments, subjects are trained to a behavior pattern designed to test hypotheses concerning the function of the cells investigated (*1*), or to provide a well-timed motor response to which cell activity can be related (*2, 3*). When the response was overtrained until it recurred in a repeatable, stereotyped manner, its variability was reduced, and correlations between cell and muscle activity were enhanced. However, such correlations are not sufficient to establish functional relations when many elements of the motor system are activated in synchronized patterns. Indeed, the relations revealed in such repetitive situations sometimes disappeared during more random behavior (*1*).

To test the functional relations between neurons and muscles, it seemed desirable to study a more flexible situation in which the animal could be trained to activate specific cells or muscles directly. Reports that individual motor units can come under voluntary control (*4*) and Olds' original work on operant conditioning of neuronal activity (*5*) encouraged this approach. This report describes a technique for conditioning the activity of individual cortical cells in awake mulatta monkeys by direct operant reinforcement of high rates of unit activity.

Unit recording techniques described by Luschei *et al.* (*3*) were used to record from single neurons in precentral "motor" cortex of unanesthetized *Macaca mulatta.* A stainless steel bone plug, permanently implanted over the precentral cortex and sealed with a thin sheet of Silastic rubber, held a removable Trent Wells hydraulic microdrive, which advanced tungsten microelectrodes (*6*) through the Silastic and intact dura into the cortex. Signals recorded by the microelectrode were relayed by a field-effect transistor source follower on the microdrive to a Grass preamplifier (at 0.5 to 30 khz bandpass) and were displayed on a Tektronix 565 oscilloscope. When a single-unit spike was well isolated from background activity, the oscilloscope sweep was triggered from the rising phase of the action potential and was set sufficiently fast to display the action potential over the entire screen (usually 0.1 msec per division). Such continuous observation of the expanded action potential provided assurance that the same single unit was monitored throughout the session. The electrode penetrated the cortex at different points each day, which made repeated observation of the same cell unlikely; all cells were located within a circle 5 mm in diameter over the precentral hand area.

High rates of cortical unit activity