thrown in or out or be finely modulated in excitability in response to other requirements, a step up in the degree of adaptability.

Immanent Teleology

This concept has been discredited by a taint of vitalism suggesting knowledge of ultimate causes. Vitalism has been dead for over half a century (although one still finds authors engaged in heaping disaster on its carcass.) But a purpose-seeking attitude to "immanence" as such can hardly be justified. We are after all accustomed to many immanent or ultimate properties of matter that are unexplained. There is immanent gravity and immanent magnetism; why not then immanent purposiveness in the biological realm of knowledge? There is no need for the biologist to hedge from speaking of an immanent teleology in the world he is studying. It is but a way of stating that one is dealing with biological processes from this highly pertinent point of view.

3
Exploring Adaptabilities

The dog not only walks but it walks to greet its master. In a word the component from the first—but it directs the character of the motor act from one of generality of purpose to one of narrowed and specific purpose fitting a specific occasion. The change is just as if the motor act had suddenly become correlated with the finite mind of the moment. (C. S. Sherrington in *Man on His Nature*. London: Macmillan, 1941.)

A systematic analysis of adaptability as such has not been much of a recognized problem in the study of the central nervous system, though numerous papers implicitly deal with mechanisms by which adaptability is achieved. It is interesting for a change to look at some of them in a more general perspective. Such questions have come to the fore lately and are destined to occupy a central place in future research dealing with degrees of pliability to environmental challenges. The largest field requiring exploration is the [illegible] between Nature and Nurture. So far experimenters have been mainly interested in discovering and [illegible] fixed functions to be analyzed and quantified. But now, after 150 years of experimentation, insight and methods have reached a degree of maturity that permits investigating physiological mechanisms of adaptability from the developmental point of view as well.

The introductory quotation from Sherrington emphasizes the point raised in Chapter 2, that the conscious brain represents the final stage in the development of our capacity to adjust ourselves to external demands. The dog shares with us some of this talent. An adaptation—the dog walks—has become adaptable by being subjected to cerebral control—it walks to greet its master.

However, to start studying adaptability at that level of [illegible] is to begin from the end, the top level of dog performance. Pavlov did this when he trained dogs to salivate in a tone by the [illegible] of [illegible] a reward of food in repeated trials [illegible] the tone. To appreciate the role of purposiveness in creating such conditioned reflexes one must only imagine that the reward had been given before sounding the tone instead of afterward. Perhaps after an excessive number of trials an association might have

been established, but not as easily as in Pavlov's well-known version of the experiment. The tone was not essential. The dog could just as well have been trained to salivate to something as abstract as the length of time after a warning signal. Purpose, meaning, motivation, and reinforcement are terms that in different ways show what made sense of the undertaking. Then it becomes another matter that pure associative learning also exists—to the extent that it serves some sensible purpose.

Problems of adaptability assume a different aspect at the cellular level. For instance, can we change a normal response of a single cortical cell (or a number of them) by impressing on them properties at cross-purposes with an ingrained purposive adaptation? This points the way to means of measuring the degree and range of adaptability by its resistance to change. The new and antagonistic environmental challenge is used as a test of the operation of the genetic instructions. The conscious brain behaves as if it had been genetically instructed to be maximally open to environmental modifications.

Adapting to Change of Purpose

A case of failure to adapt is provided by an experiment (Sperry) in which the optic nerve of a frog was cut, the eye bulb turned around by 180° in its socket, and regeneration of the nerve allowed to take place.[38] It was found that by some kind of chemically determined specificity the nerve fibers grew into their original sites in their station in the optic tectum. The result meant that the images of the surgically reversed eye were projected the way they had been before the operation and that they were misdirected with reference to the postoperative orientation of the eye bulb.

Although the animal might have been expected to adjust itself to the dislocation of the image, it never did. A fly in the upper field of vision excited the frog to catch it in the lower field. Once established, the ingrained adaptation was too resistant to allow any adaptability.

This experiment demonstrates inherently open genetic instructions that have been closed—almost certainly by a chemical marker—but it can be shown that originally they were open in the early stage of amphibian development.[39] If at this stage the eye was experimentally rotated (Jacobson), a normal purposive visual reflex arose.[40] Jacobson's analysis (with Hunt) showed the critical period for the operative rotation of the bulb to be between 39 and 40 hours of amphibian life, the retinal ganglion cells being born at about 31 hours and their nerve fibers reaching the optic tectum 15 hours later. Some—ultimately chemical—processes sanctioned by purposive function then operated to close the genetic instructions for good.

Kittens have a postnatal period of optimum adaptability lasting between 24 and 36 days (Hubel and Wiesel).[41] Two independent experiments by Hirsch and Spinelli, and Blakemore illustrate this in a new and interesting manner.[42] They presuppose knowledge of the discovery of Hubel and Wiesel that single cells in the striate visual cortex of the cat are sensitive to the orientation of oblongs or lines shown to the eye within the retinal receptive field of the particular cortical cell that has been isolated for recording by a microelectrode.[43] In the cat an assembly of such cortical cells in the striate visual cortex represents orientations of visual stimuli in a comprehensive manner. I shall describe the new experiment in Blakemore's version.

Young kittens are provided with a stiff collar that checks head movements and then reared in a vertically or hori-

zontally striped environment. The individual cortical cells adapt to the new environment and now respond preferentially to the direction to which they have been exposed. Blakemore's finding is rather exciting—that no more than an hour's exposure to such visual experiences suffices to modify the preferred orientation of most cellular units in the kitten's striate cortex, provided that this is followed by a minimum of two weeks in the dark. But if the kittens had had more than five hours of such abnormal experience, the effect became virtually ineradicable by other visual stimuli. Nothing else distinguished these cortical units from normal ones. For a modification of this experiment by Maffei and Fiorentini, see Chapter 5, section on contrast and spatial frequency.[44]

What about ourselves? Prisms, inversion spectacles, or even colored filters have been used in a very large number of experiments to create a visual world at cross-purposes with the one ingrained by prewiring and experience in combination. The oldest experiment was carried out by Stratton (1896).[45] "Stratton studied vision without inversion of the normally inverted retinal image. The experiments were done monocularly with an inversion lens, the other eye being covered. He wore this lens for eight consecutive days. Physiologically this amounted to a blatant clash between the information from the sensory fields representing the body (surface, muscle, joints, etc.) and those organized to deal with visual space, in which now [the picture was upside down] . . . On the second day of his experiment the room was upside down but the body was represented in preexperimental terms and was felt as a standard. . . . On the fifth day the new visual space had established itself so well that there was no anticipatory drawing in of the chin and chest when a solid object passed

through the visual field in the direction which in normal vision would have meant a blow." [46] Thus the perceived world as well as the reflex motor response to it had adapted to the new experience at cross-purposes with the old one.

From work on monkeys we are entitled to conclude that directionally sensitive cells exist also in our own visual cortex. An average response of such cells can actually be studied objectively by measuring the amplitude of electrical potentials evoked on the scalp in response to visual stimuli of variable orientation (Chapter 6). Vertical and horizontal targets are better resolved by our eye than oblique patterns, and evoked potentials by their amplitude indicate these preferential sensitivities.

Maffei and Fiorentini investigated what happened when several adult subjects wore tilting prisms continually for several days. The prisms produced a tilt of the target of 30° or 40° from the vertical, and the angle between the apparent vertical and the real vertical was measured and compared with the amplitudes of their evoked potentials to find the degree of perceptual compensation. Perceptual adaptation to the tilt occurred in all subjects in the first hours, and compensation was virtually complete on the second day. The adaptive effects were accompanied by a decrease of the mean difference between the amplitudes of evoked potentials for the vertical and oblique patterns.[47] [illegible] this faculty was localized by the outcome of this experiment to the sensory apparatus at some point between the retina and the cortical visual area. We are no more conscious of adjusting for a new direction of verticality than the kitten or the tadpole in comparable experiments. The perceptual net result of all the silent ongoings comes as a surprise.

The open instructions in these examples worked well

enough for the tadpole and the kitten but not for the frog or the cat. There must be some basic difference between cat and man to make us capable of "repurposing" against an ingrained purpose. At least one reason for our greater adaptability can be discerned—the greater complexity of our wiring diagrams. It is difficult to quantify this statement with figures because no methods are as yet available for measuring connectivity. Some figures can be given merely to indicate its nature. Cragg has made a rough estimate from his own work and concluded that 56 neurons are interconnected with each neuron in the monkey visual cortex and 600 in its motor cortex. On his own data these are minimal values, yet they represent a connectivity [illegible] of that in any man-made computer.[48] The average number of synapses on a cortical cell is of the order of 35,000. There are about 50 million cells per cubic centimeter in the human visual cortex, as against 10 million in the motor field, which has larger neurons. For the cat visual cortex Sholl found the territory of the branches of one neuron (stellate type) to spread within reach of 4,000 other neurons.[49] We do not know the full relevance of the enormous figures for synaptic densities, up to 60,000 on large cortical cells (Cragg). Recent work by Marotte and Mark has shown that normal looking synapses can be inactive;[50] however, these are synapses projecting to muscle fibers. His results, though not convincingly proved, raise the idea that neuronal adaptability may be based also on activation and deactivation of preexistent synapses. [illegible] keep a reserve of passive synapses in preparation for various emergencies, this would further extend the [illegible] in adaptability in the [illegible] system.

For the moment let us remain with the general notion of superabundance of linkages and greater redundancy in

the main distinction between our very much larger cortex and that of the cat and begin by considering the question of repurposing in organizational terms. Basically the desired neural organization can be described as an error-detecting mechanism capable of feeding back its information to the perceptive process. The visual perception of the distorted verticality is an illusion, but an important one, as very much of our sensory input is entering through our 2 million fibers in the optic nerves. In the experiments, on the other hand, powerful messages from other sources contradicted it, gravity being particularly relevant. Impulses from the vestibular organs record balance and head position, and sense organs in the ligaments and muscles of the neck support them. Furthermore, sense organs in the soles of the feet, legs, joints, and around the spine record any deviation from the responses required by the existence of gravity. Their presence is reflected in Stratton's description of his experiences as well as in an observation Kohler made while looking at a pendulum through inversion lenses: it swung upside down, but reverted to normal as soon as he touched its fixed end to swing it himself.[51]

Adaptability to prismatic goggles has lately excited much interest. A decisive experiment favoring error correction by feedback was carried out by Held and Hein when they demonstrated that an animal must be allowed to move about and see the deviations from normality reflected in its own movements to be able to correct for the visual distortion.[52] Moved about passively, it fails to adjust to the prismatically induced displacements. Man is likely to do better on purely sensory information, as shown by the experiments by Maffei and Fiorentini.

In following up one series of experiments in vision from frog to man, I have neglected much work on development

tal aspects of adaptability that is necessary for filling out the picture. Thus, for instance, the greater plasticity of the developing nervous system is found throughout the vertebrate kingdom. Man is no exception. It is known that if Wernicke's area in the left hemisphere of the brain responsible for comprehending language is destroyed in a child below about age 12, the right hemisphere takes over and full restoration ensues.[53] Later destructions of that same region leave a child incapacitated forever.

This of course raises the question of why another talent, readjusting to visual verticality, is retained in adults. I would like to link the answer with an attractive hypothesis by Jacobson. What I have called the closing of originally open genetic instructions, he speaks of as "specification" of originally unspecified connections. In Jacobson's theory "some neurons are highly specified and all their connections are fully determined, but there are also some incompletely specified neurons with indeterminate connections" (p. 388). The early developing neurons tend to be large, with long axons. They form the primary afferents, are somatotopically organized and specified at an early date in embryonic development, and later are unmodifiable. The unspecified neurons, retaining the property of openness, are small interneurons of various kinds. They have short axons, variable connectivity, and develop late—even postnatally in some parts of the brain. In contrast to the former type, they require stimulation for their development and for maintenance of their function.

In this view the visual cortex of man should be characterized by an abundance of small interneurons with short axons, which indeed is the case. On the whole the great expansion of our cortex, the "roof brain," is an expansion in terms of interneurons. And when I said that the conscious

brain behaves as if it had been genetically instructed to be maximally open to environmental modifications, the cellular substrate realizing this property is its bulk of unspecified small cells with short axons, long known as Golgi type II cells. These cells correspond to the small B-lymphocytes in the immune system, numerous enough to take a chance on chance and to remember what they did.

Chemical Specification by Motor Neurons

To most of us everything sensory including consciousness is always more interesting than a motor act. But the understanding of adaptability in chemical terms is at a more advanced level in the motor field in which we deal with long axons (motor nerve fibers) and synapses accessible in the muscles they innervate. Even if we do not fully understand how chemically traceable modifications in muscles are brought about, the road of advance has been opened. The adaptability to be discussed concerns muscle fibers influenced by their motor axons. Each axon divides to innervate a large number of muscle fibers. The motor cell (or motoneuron) *plus* its axon *plus* the muscle fibers that the axonal branches innervate by synapses is known by the technical term "motor unit."

With regard to environmental factors, muscles, like so many other tissues, show a general adaptability to use and disuse but are stable in their organization. Thirty years ago Sperry surgically cross-united nerves to antagonistic muscles in rats and monkeys and found a persistent lack of adaptation to the reversed tasks.[54] Even in young animals the reflexes failed to become reorganized, in rats not at all, and in monkeys with notable deficiencies.

Contrary to this experience, neurosurgeons operating to

restore lost function in disabled limbs of patients report that any muscle and tendon in the hand and the forearm, when transferred to a new site, can carry out any desired motion. Thus, in Bunnell's *Surgery of the Hand* it is stated that "a wrist extensor can act as a digital extensor, a digital flexor, a wrist flexor or a motor for opposition and adduction of the thumb."[55] As with adaptation to verticality, here, too, our internal computer seems to be of a superior type. But repurposing has to be checked by internal feedback, within the brain itself, as well as by external feedback delivered by the sense organs. A lot of adaptability is needed when a lost part of an arm is supplanted by a prosthesis. In this case it has been found (Moberg) that maintained skin sensitivity of the stump is decisive for establishing control by feedback over the mechanical instrument.[56]

The motor units of the legs in many mammals are gathered into "heads" or muscles of dominantly tonic or phasic nature. The tonic ones contract slowly and are capable of long-lasting steady efforts of limited strength; the phasic muscles are capable of handling heavier loads and of acting rapidly but are more fatigable than the tonic ones. In newborn kittens there is an incipient differentiation into two types, but both are still slowly contracting. If at that stage the nerves to two leg muscles, one phasic and the other tonic, are exchanged, what will happen? (Buller, Eccles, and Eccles)[57] Will the slow nonfatigable muscle become fast when provided with the axons of motoneurons for the fast muscle and will the fast muscle remain slow when innervated by axons destined for a slow muscle?

The experimental reply was that within considerable limits they would exchange properties. In the first instance this implies that the motoneuron exercises a decisive influence on the contractile properties of the muscle fibers on

which it synapses (motor end plates). Thus, in a recent experiment, on cross-innervation of the slow soleus and the fast extensor digitorum longus muscles in the leg of the rat, it was found that reciprocal changes took place in contractile properties and in the concentration of the enzyme acting on the muscle substance myosin (Bárány and Close).[58] The myosin of the crossed extensor digitorum longus was now found to be very similar to that of the normal slow soleus, while the myosin of the crossed soleus was very similar to that of the normal fast extensor digitorum longus.

There are many histochemically traceable differences between slow and fast motor units. The fast ones, for instance, make more use of glycogen, a kind of sugar broken down anaerobically by glycolytic enzymes; the slow ones are richly provided with oxidative enzymes for enduring maintenance of function. The demonstration by Romanul and Van Der Meulen that cross innervation leads to a corresponding reversal of the histochemical profiles of slow and fast muscles has been confirmed many times.[59]

The powerful effect of a motoneuron upon the muscle fibers on which it has synapses is of the greatest interest in the present connection as a living model of how a substrate can be labeled by chemical transposition across a synapse. It illustrates a principle also available for explaining other aspects of adaptability of central neurons influenced by other neurons—the existence of "markers" conducted across synapses, though, thinking of neurons, we do not know if they merely penetrate to the synapse, or as far as the subsynaptic receptor within the cell membrane, or perhaps even into the interior of the cell.

Processes of chemical labeling conducted through nerve fibers are being hotly pursued today by the experimenters engaged in the study of axoplasmic flow.[60] Slow transport

along nerve fibers of such material as neurohormones and enzymes is well established, and this process at least partly explains the transformations muscle fibers undergo in cross-innervation experiments. The other conducted event, the nerve impulse, apparently plays a role too. The influence of the nerve impulse on contractile properties stems from the rate and duration at which a discharge is emitted from the motoneuron. The impulse in motor fibers of different mammals is conducted at rates from 40 to 90 m/sec, while axoplasmic flow takes place at rates from about 1 to 540 mm a day.

Concluding Remarks

What has been said so far does not exhaust the subject of adaptability in the nervous system. Every adaptation to environmental factors can in fact be treated from the point of view of adaptability. My aim is not completeness but rather to introduce the subject of adaptability by a few examples based on developmental neurobiology. This also illustrates how testing of the phenotype works out in cases in which it has been possible to entertain some well-founded notions as to how repurposing might be achieved. They underline my basic argument that teleological purposiveness cannot be neglected in genetics if so that science claims the testing of mutations and recombination takes place in the phenotype.

It has been shown that the phylogenetic development of adaptability reaches its climax in parallel with the expansion of the cortex or roof brain up to its greatest size in man. Even leaving out consciousness, this whole development of adaptability is one of the most remarkable phenomena that biology is called upon to explain. The ex-

amples were chosen to indicate the nature of some biological explanations that deserve to be ranked high.

The organizational explanation based on error correction by feedback places rules of repurposing in the realm of cybernetics, the science of regulation.[61] This attempt at rationalizing the problem is translatable into experiments. But general regulating principles do not absolve us from trying to understand the nature of the specific biological processes obeying the constraints of cybernetic theory. It is well known that regulated, interconnected mechanical, electrical, and biological events conform to the same general rules of cybernetics.

In looking for cellular substrates serving adaptability as well as its complement, specification, or fixation of a response, I chose to embrace Jacobson's view according to which the Golgi II cell types with short processes are "unspecified" and the Golgi I types with long axons are once and for all "specified." The former are numerous enough for their task. Methods of counting the total number of neurons in the cortex of man may not be very precise, but the range of figures from 2.6×10^9 to 14×10^9 is likely to be an estimate of the right order of magnitude. Some figures have been given for synaptic density and connectivity. The cellular mass of small neurons is not amorphous; on the contrary, it is structurally organized in conjunction with the larger cells.

The experiments on cross innervation provide evidence for a conducted process of chemical labeling. A number of synaptic transmitter substances are known, but in addition the small cells may be chemically differentiated in the manner of the lymphocytes of the immune system. We have no information on this point. We do know, however, that intercellular separation can be modified by growth and dis-

traction. Such phenomena are of particular importance for understanding the effects of use or disuse, which are being studied a great deal in developmental neurobiology today.[62] It seems entirely possible that in the act of repurposing a path could be expanded to reach new contacts by use while the original connection is disconnected and so "depurposed" from its original role by disuse.

Purpose, chance, and causality concern points of view rather than the actual hardware. The total causality involved in a purposive response can be subdivided into an inside complex (such as memory, genetical instructions, or fixed circuits), which only rarely will be fully known, and an external component relating the response to the environmental stimulus. Purpose or no purpose, the physics of the stimulus is the same and decisive, up to the point when it is taken care of by the cellular operator, of whose resources we now have caught a glimpse. At the moment purposiveness comes closest to a role of practical usefulness in the error-detection and feedback-correction hypothesis outlined. An important consequence of this hypothesis is its requirement for communication in at least two and often more directions. But the essential [illegible] well preserved by the adaptable or plastic small cells that are modifiable in connectivity by experience. Their exceedingly great number, while indicating their importance, is also a serious obstacle for the analyst. Because induced changes persist, at least as long as some environmental conditioning is being maintained, the small cells have a history and what they remember has also been influenced by unpredictable chance factors. They can never be neglected in discussing memory. But then what does memory involve, how creative is chance, and to what extent are single cells individualized? Questions of this sort could be multiplied if

my intention had been to expose our ignorance rather than to present some means and ways of approaching these exciting problems.

4
Encephalization, Cortical Maps, and Redundancy

If we refuse to admit that discrimination is in some way based on different anatomical mechanisms differently located in the brain, we may as well give up altogether. (Another, in his Silliman Lectures, published as *Reception and Sensory Perception*, by Yale University Press, 1956.)