Introductory—Coordination of the Simple Reflex*

SIR CHARLES SHERRINGTON

ARGUMENT: The nervous system and the integration of bodily reactions. Characteristics of integration by nervous agency. The unit mechanism in integration by the nervous system is the reflex. Coordination of reflexes one with another. Coordination in the simple reflex. Conduction in the reflex-arc. Function of the receptor to lower for its reflex-arc the threshold value of one kind of stimulus and to heighten the threshold value of all other kinds of stimuli for that arc: it thus confers selective excitability on the arc. Differences between conduction in nerve-trunks and in reflex-arcs respectively. These probably largely referable to the intercalation of synaptic membranes in the conductive mechanism of the arc. Latent time of reflexes. Reflex latency inversely proportional to intensity of stimulation. Latency of initial and incremental reflexes. None of the latent interval consumed in establishing connexion between the elements of a resting arc. After-discharge a characteristic of reflex reactions. Increase of after-discharge by intensification of the stimulus, or by prolongation of short stimuli. ‘Inertia’ and ‘momentum’ of reflex-arc reactions.

Nowhere in physiology does the cell-theory reveal its presence more frequently in the very framework of the argument than at the present time in the study of nervous reactions. The cell-theory at its inception depended for exemplification largely on merely morphological observations; just as these formed originally the almost exclusive tests for the Darwinian doctrine of evolution. But with the progress of natural knowledge, biology has passed beyond the confines of the study of merely visible form, and is turning more and more to the subtler and deeper sciences that are branches of energetics. The cell-theory and the doctrine of evolution find their scope more and more, therefore, in the problems of function, and have become more and more identified with the aims and incorporated among the methods of physiology.

The physiology of nervous reactions can be studied from three main points of view.

In the first place, nerve-cells, like all other cells, lead individual lives—they breathe, they assimilate, they dispense their own stores of energy, they repair their own substantial waste; each is, in short, a living unit, with its nutrition more or less centered in itself. Here, then, problems of nutrition, regarding each nerve-cell and regarding the nervous system as a whole, arise comparable with those presented by all other living cells. Although no doubt partly special to this specially differentiated form of cell-life, these problems are in general accessible to the same methods as apply to the study of nutrition in other cells and tissues and in the body as a whole. We owe recently to Verworn and his co-workers advances specially valuable in this field.

Secondly, nervous cells present a feature so characteristically developed in them as to be specially theirs. They have in exceptional measure the power to spatially transmit (conduct) states of excitement (nerve-impulses) generated within them. Since this seems the eminent functional feature of nerve-cells wherever they exist, its intimate nature is a problem coextensive with the existence of nerve-cells, and enters into every question regarding the specific reactions of the nervous system. This field of study may be termed that of nerve-cell conduction.

But a third aspect which nervous reactions offer to the physiologist is the integrative. In the multicellular animal, especially for those higher reactions which constitute its behavior as a social unit in the natural economy, it is nervous reaction which par excellence integrates it, welds it together from its components, and constitutes it from a mere collection of organs an animal individual. This integrative action in virtue of which the nervous system unifies from separate organs an animal possessing solidarity, an individual, is the problem before us in these lectures. Though much in need of data derived from the two previously mentioned lines of study, it must in the meantime be carried forward of itself and for its own sake.

The integration of the animal organism is obviously not the result solely of any single agency at work within it, but of several. Thus, there is the mechanical combination of the unit cells of the individual into a single mass. This is effected by fibrous stromata, capsules of organs, connective tissue in general, for example, of the liver, and indeed the fibrous layer of the skin encapsulating the whole body. In muscles this mechanical integration of the organ may arrive at providing a single cord tendon by which the tensile stress of a myriad contractile cells can be additively concentrated upon a single place of application.

Integration also results from chemical agency. Thus, reproductive organs, remote one from another, are given solidarity as a system by communication partum in all the transaction of it between the pec organs we find glands, and the digestive glands reaching the py on reaching the which absorbed pancreatic juice substances initio 1905. Again, circulation of surface of the t unit in the body organs is brou

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communication that is of chemical quality; lactation supervenes post partum in all the mammary glands of a bitch subsequent to thoracic transection of the spinal cord severing all nervous communication between the pectoral and the inguinal mammae (Goltz). In digestive organs we find chemical agency coordinating the action of separate glands, and thus contributing to the solidarity of function of the digestive glands as a whole. The products of salivary digestion on reaching the pyloric region of the stomach, and the gastric secretion on reaching the mucosa of the duodenum, make these substances which absorbed duly excite heightened secretion of gastric and of pancreatic juice respectively suited to continue the digestion of the substances initiating the reaction (Bayliss & Starling, 1899; Edkins, 1905). Again, there is the integrating action effected by the circulation of the blood. The gaseous exchanges at one limited surface of the body are made serviceable for the life of every living unit in the body. By the blood the excess of heat produced in one set of organs is brought to redress the loss of heat in others; and so on.

But the integrative action of the nervous system is different from these, in that its agent is not mere intercellular material, as in connective tissue, nor the transference of material in mass, as by the circulation; it works through living lines of stationary cells along which it dispatches waves of physicochemical disturbance, and these act as releasing forces in distant organs where they finally impinge. Hence it is not surprising that nervous integration has the feature of relatively high speed, a feature peculiarly distinctive of integrative correlation in animals as contrasted with that of plants, the latter having no nervous system in the ordinary sense of the word.

The nervous system is in a certain sense the highest expression of that which French physiologists term the milieu interne. With the transition from the unicellular organism to the multicellular a new element enters general physiology. The phenomena of general physiology in the unicellular organism can be divided into two great groups; namely, those occurring within the cell, intracellular, and those occurring at the surface of the cell, in which forces that are associated with surfaces of separation have opportunity for play at the boundary between the organism and its environment. But in the multicellular organism a third great group of phenomena exists in addition; namely, those which are intercellular, occurring in that complex material which the organism deposits in quantity in the intercellular interstices of its mass as a connecting medium between its individual living units.

When the intercellular substance is solid, for example, in many connective tissues, the physiological agencies for which it affords a
field of operation are mechanical rather than chemical. The organism obtains from it scaffolding for supporting its weight, levers for application of its forces, etc., and in this degree the intercellular material performs an integrative function. Where the intercellular material is fluid, as in blood, lymph, and tissue juice, it constitutes a field of operation for agencies chemical rather than mechanical. The intricacy of the chemistry of this *milieu interne* is shown by nothing better than by the specificity of the preciptins, etc., the intercellular media for each separate animal species yielding its own particular kinds. The cells of a multicellular organism have therefore in addition to an environmental medium in which the organism as a whole is bathed, and to which they react either directly or through the medium of surface cells, an *internal medium* created by their organism itself, and in many respects specific to itself.

But the internal interconnexion of the multicellular organism is not restricted to intercellular material. Intercellular material is, after all, no living channel of communication, delicately responsive to living changes though it may be. An actually living internal bond is developed. When the animal body reaches some degree of multicellular complexity, special cells assume the express office of connecting together other cells. Such cells, since their function is to stretch from one cell to another, are usually elongated; they form protoplasmic threads and they interconnect by conducting nervous impulses. And we find this living bond the one employed where, as said above, speed and nicety of time adjustment are required, as in animal movements, and also where nicety of spatial adjustment is essential, as also in animal movements. It is in view of this interconnecting function of the nervous system that that field of study of nervous reactions which was called at the outset the third or integrative, assumes its due importance. The due activity of the *interconnexion* resolves itself into the coordination of the parts of the animal mechanism by reflex action.

"It is necessary to be clear as to what we understand by the expression 'reflex' action.

In plants and animals occur a number of actions the initiation of which is traceable to events in their environment. The event in the environment is some change which acts on the organism as an exciting *stimulus*. The energy which is imparted to the organism by the stimulus is often far less in quantity than the energy which the organism itself sets free in the movement or other effect which it exhibits in consequence of the application of the stimulus. This excess of energy must be referred to energy potential in the organism itself. The change in the environment evidently acts as a releasing force upon the living energy set free is transferred to the living organism, and these are of high power consequence of the external from internal point of view. For example, amoeba, is an organism that changes form in its reaction, and the reaction occurs in one and the same separable part of the organism.

Sudden light. Large also large fields of particular certain stimulus is, so to say, of a nervous impulse cut out of part of the *movement* on appliable to enter into the application of its exclusive (in this ii) retinal receptors. In for the three processes. These reactions, an end-effect reaches incapable either of the inception of the reason. Usually the spaces are quite large, and excesses, especially in the case of action where the response may involve some degree specific physiologically as a source not to apply the term for the reactions empirically and morphological understanding.
force upon the living machinery of the organism. The source of energy set free is traced to chemical compounds in the organism. These are of high potential value, and in immediate or mediate consequence of the stimulus decompose partly, and so liberate external from internal energy. It is perfectly conceivable, and in many undifferentiated organisms, especially in unicellular, for example, amoeba, is actually the case, that one and the same living structure not only undergoes this physicochemical change at the point at which an external agent is applied, but is subject to spread of that change from particle to particle along it, so that there then ensue in it changes of form, movement. In such a case the initial reaction or reception of the stimulus, the spatial transmission or conduction of the reaction, and the motor or other end-effect, are all processes that occur in one and the same living structure. But in many organisms these separable parts of the reaction are exhibited by separate and specific structures. Suppose an animal turn its head in response to a sudden light. Large fields of its body take part in the reaction, but also large fields of it do not. Some of its musculature contracts, particularly certain pieces of its skeletal musculature. The external stimulus is, so to say, led to them by certain nerves in the altered form of a nervous impulse. If the neck nerves are severed the end-effect is cut out of part of the field; and the nerves themselves cannot exhibit movement on application of the stimulus. The optic nerve itself is unable to enter into a heightened phase of its own specific activity on the application of light. Initiation of nervous activity by light is the exclusive (in this instance) function of cells in the retina, that is, retinal receptors. In such cases there exist three separable structures for the three processes—initiation, conduction and end-effect.

These reactions, in which there follows on an initiating reaction an end-effect reached through the mediation of a conductor, itself incapable either of the end-effect or, under natural conditions, of the inception of the reaction, are ‘reflexes.’ The conductors are nerve. Usually the spaces and times bridged across by the conductors are quite large, and easily capable of measurement. Now there occur cases, especially within the unicellular organism and the unicellular organ, where the spaces and times bridged are minute. In them spread of response may involve ‘conduction’ (Poteriodendron, Vorticella) in some degree specific. Yet to cases where neither histologically nor physiologically a specific conductor can be detected, it seems better not to apply the term ‘reflex.’ It seems better to reserve that expression for reactions employing specifically recognizable nerve-processes and morphologically differentiated nerve-cells; the more so because the process of conduction in nerve is probably a specialized one, in
which the qualities of speed and freedom from inertia of reaction have been attained to a degree not reached elsewhere since not elsewhere demanded.

The conception of a reflex therefore embraces that of at least three separable structures—an effector organ, gland cells or muscle cells; a conducting nervous path or conductor leading to that organ; and an initiating organ or receptor whence the reaction starts. The conductor consists, in the reactions which we have to study, of at least two nerve-cells—one connected with the receptor, the other with the effector. For our purpose the receptor is best included as a part of the nervous system, and so it is convenient to speak of the whole chain of structures—receptor, conductor, and effector—as a reflex-arc. All that part of the chain which leads up to but does not include the effector and the nerve-cell attached to this latter, is conveniently distinguished as the afferent arc.

The reflex-arc is the unit mechanism of the nervous system when that system is regarded in its integrative function. The unit reaction in nervous integration is the reflex, because every reflex is an integrative reaction and no nervous action short of a reflex is a complete act of integration. The nervous synthesis of an individual from what without it were a mere aggregation of commensal organs resolves itself into coordination by reflex action. But though the unit reaction in the integration is a reflex, not every reflex is a unit reaction, since some reflexes are compounded of simpler reflexes. Coordination, therefore, is in part the compounding of reflexes. In this coordination there are therefore obviously two grades.

THE SIMPLE REFLEX

There is the coordination which a reflex action introduces when it makes an effector organ responsive to excitement of a receptor, all other parts of the organism being supposed indifferent to and indifferent for that reaction. In this grade of coordination the reflex is taken apart, as if separable from all other reflex actions. This is the simple reflex. A simple reflex is probably a purely abstract conception, because all parts of the nervous system are connected together and no part of it is probably ever capable of reaction without affecting and being affected by various other parts, and it is a system certainly never absolutely at rest. But the simple reflex is a convenient, if not a probable, fiction. Reflexes are of various degrees of complexity, and it is helpful in analysing complex reflexes to separate from them reflex components which we may consider apart and therefore treat as though they were simple reflexes.

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In the simple reflex there is exhibited the first grade of coordination. But it is obvious that if the integration of the animal mechanism is due to coordination by reflex action, reflex actions must themselves be coordinated one with another; for coordination by reflex action there must be coordination of reflex actions. This latter is the second grade of coordination. The outcome of the normal reflex action of the organism is an orderly coadjustment and sequence of reactions. This is very patently expressed by the skeletal musculature. The coordination involves orderly coadjustment of a number of simple reflexes occurring simultaneously, that is, a reflex pattern, figure, or 'complication,' if one may warp a psychological term for this use; orderly succession involves due supersession of one reflex by another, or of one group of reflexes by another group, that is, orderly change from one reflex pattern or figure to another. For this succession to occur in an orderly manner no component of the previous reflex may remain which would be out of harmony with the new reflex that sets in. When the change from one reflex to another occurs it is therefore usually a far-reaching change spread over a wide range of nervous arcs.

This compounding of reflexes with orderliness of coadjustment and of sequence constitutes coordination, and want of it incoordination. We may therefore in regard to coordination distinguish coordination of reflexes simultaneously proceeding, and coordination of reflexes successively proceeding. The main secret of nervous coordination lies evidently in the compounding of reflexes.

**COORDINATION IN THE SIMPLE REFLEX**

It is best to clear the way toward the more complex problems of coordination by considering as an earlier step that which was termed above, the first grade of coordination, or that of the simple reflex. From the point of view of its office as integrator of the animal mechanism, the whole function of the nervous system can be summed up in the one word, conduction. In the simple reflex the evidence of coordination is that the outcome of the reflex as expressed by the activity induced in the effector organ is a response appropriate to the stimulus imparted to the receptor. This due propriety of end-effect is largely traceable to the action of the conductor mediating between receptor and effector. Knowledge of the features of this 'conduction' is therefore a prime object of study in this connection.

But we have first to remember that in dealing with reflexes even experimentally we very usually deal with them as reactions for which the reflex-arc as a whole and without any separation into constituent
parts is laid under contribution. The reflex-arc thus taken includes the receptor. It is assuredly as truly a functional part of the arc as any other. But, for analysis of the arc's conduction, it is obvious that by including the receptor we are including a structure which, as its name implies, adaptation has specialized for excitation of a kind different from that obtaining for all the rest of the arc. It is therefore advantageous, as we have to include the receptor in the reflex-arc, to consider what characters its inclusion probably grafts upon the functioning of the arc.

Marshall Hall (1850) drew attention to the greater ease with which reflexes can be elicited from receptive surfaces than from afferent nerve-trunks themselves; and this has often been confirmed (Eckhardt, Biedermann). Steinach (1899) has measured the lowering of the threshold value of stimulation when in the frog a reflex is elicited by a mechanical stimulus applied to skin instead of to cutaneous afferent nerve. The lowering is considerable. There are numerous instances in which particular reflexes can be elicited from the receptive surface by particular stimuli only. Goltz (1869) endeavoured in vain to evoke the reflex croak of the female frog by applying to the skin electrical stimuli. Mechanical stimuli of non-noxious kind were the only stimuli that proved effective. By direct stimulation of the afferent nerve itself the reflex could but rarely be elicited at all. Later Goltz's pupil Gergens (1876) succeeded in provoking the reflex by applying to the skin a mild discharge from an influence machine.

A remarkable reflex (Sherrington, 1905) is obtainable from the planta of the hindfoot in the 'spinal' dog. The movement provoked is a brief strong extension at knee, hip, and ankle. This is the 'extensor-thrust.' It seems obtainable only by a particular kind of mechanical stimulation. I have never succeeded in eliciting it by any form of electrical stimulation, nor by any stimulation applied directly to an afferent nerve-trunk.

Again, a very characteristic reflex in the cat is the pinna-reflex. (Sherrington, 1905) If the tip of the pinna be squeezed, or tickled, or in some cases even touched, the pinna itself is crumpled so that its free end is turned backward, as in Darwin's (1872) picture of a cat prepared to attack. The afferent nerve of this reflex appears to be in part at least not the cranial fifth nerve, but the foremost cervical. The reflex emerges very early from the shock of decerebration and is submerged very late in chloroform narcosis. This reflex, easily elicitable as it is by various mechanical stimuli to the skin, I have never succeeded in provoking by any form of electrical stimulation.

The same sort of difference, though less marked in degree, is exhibited by the scratch-reflex (Goltz, 1881; Haycraft, 1890; Sherrington, 1905; St reflex is one stimulation (back behind movement) of stimuli elicitable, va elicibility, of electrical: elicitable ele suitable met vigorously.

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cludes the reflexes evoked by the skin. The skin reflex, in particular, has been extensively studied (Eckert, 1905; Sherrington, 1904a; Sherrington & Laslett, 1903). This reflex is one in which various forms of innocuous mechanical stimulation (rubbing, tickling, tappin\-\-g) applied to the skin of the back behind the shoulder evoke a rhythmic flexion (scratching movement) of the hind-limb, the foot being brought toward the seat of stimulation. This reflex in the spinal dog, although usually elicitable, varies much under various circumstances in its degree of elicitability. When easily elicitable it can be evoked by various forms of electrical stimulation as well as by mechanical; but when not easily elicitable electrical stimuli altogether fail, while rubbing and other suitable mechanical stimuli still evoke it, though not so readily or vigorously as usual.

A question germane to this is the oft-debated sensitivity of various internal organs. Direct stimulation of various afferent nerves of the visceral system is itself well known to yield reflexes on bloodpressure, etc. But in regard to the sensitivity of the organs themselves we have, on the one hand, the passage of bile-stones, renal calculi, etc., accompanied by intense sensations, and on the other hand the insensitivity of these ducts and various allied visceral parts as noted by Haller (1752) and observed by surgeons working under circumstances favorable for examining the question. The stimulation which excites pain in these internal organs is usually of mechanical kind, e.g., calculus, and the surgeon's knife and needle provide mechanical stimuli, and Haller and his co-workers in their research employed multiform stimuli, many of them mechanical in quality. But though mechanical, the latter are remote in quality from the former; the former are distensible. The action of a calculus can be imitated by injecting fluid of itself innocuous. Marked reflex effects can then be excited (Sherrington, 1899) from the very organs (Fig. 2.1), the cutting and wounding of which remain without effect. For Haller's and the surgical experience to be harmonized with the medical evidence from calculi, etc., all that is necessary is that the mechanical stimulation be adequate, and to be adequate it must be of a certain kind. Thus we see that when the mechanical stimulation employed resembles that occurring in the natural accidents that concern medicine, the experimental results fall into line with those observed at the bedside.

Therefore we may infer provisionally—for the facts justify only a guarded judgement—that the part played by the receptor in the reflex-arc is in the main what from other evidence it is inferred to be in the case of the receptors as sense-organs, namely, a mechanism more or less attuned to respond specially to a certain one or several of the agencies that act as stimuli to the body. We may suppose this
special attuning acts as does specialization in so many cases, namely by rendering more apt for a certain kind of stimulus and at the same time less apt for stimuli of other kinds. The main function of the receptor is therefore (Sherrington, 1900) to lower the threshold of excitability of the arc for one kind of stimulus, and to heighten it for all others. This is quite comparable with the low threshold for touch-sensation under mechanical stimulation applied to a hair (v. Frey, 1897) contrasted with the high threshold under electrical stimulation of the skin. Adaptation has evolved a mechanism for which one kind of stimulus is the appropriate, that is, the adequate stimulus: other stimuli than the adequate not being what the adaptation fitted the mechanism for, are at a disadvantage. Electrical stimuli are in most cases far the most convenient to use for experimental work, because of their easy control, especially in regard to intensity and time. But electrical stimuli not being of common occurrence in nature, there has been no chance for adaptation to evolve in the organism receptors appropriate for such stimuli. Therefore we may say that electricity never constitutes the adequate stimulus for any receptor, since it is always an artificial form of stimulus, and every adequate stimulus must obviously be a natural form of stimulation. It is therefore rather a matter for surprise that electrical stimuli applied to receptor organs are as efficier particularly if attuned speci do local dam effective. But peculiar; and later.

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are as efficient exciters of reflexes as they in fact prove to be. It is particularly in regard to a class of reflexes whose receptive cells seem attuned specially to react to nocuous agents, agents that threaten to do local damage, that electrical stimuli are found to be excellently effective. But the conditions of adaptation to stimuli appear here peculiar; and there will be better opportunity of considering them later.

We infer, therefore, that the main contribution made to the mechanism of the reflex-arc by that part of it which constitutes the receptor is selective excitability. It thus contributes to coordination, for it renders its arc prone to reply to certain stimuli, while other arcs not having that kind of receptor do not reply, and it renders its arc unlikely to reply to certain other stimuli to which other arcs are likely to respond. It will thus, while providing increase of responsiveness on the part of the organism to the environment, tend to prevent confusion of reactions (incoordination) by limiting to particular stimuli a particular reaction.

On the whole, we may regard the receptor as being concerned with the mode of excitation rather than with the features of conduction of the reflex-arc, and may now return to that conduction, which itself has important coordinative characters.

Nervous conduction has been studied chiefly in nerve-trunks. Conduction in reflexes is of course for its spatially greater part conduction along nerve-trunks, yet reflex conduction in toto differs widely from nerve-trunk conduction.

Salient among the characteristic differences between conduction in nerve-trunks and in reflex-arcs respectively are the following:

Conduction in reflex-arcs exhibits: (1) slower speed as measured by the latent period between application of stimulus and appearance of end-effect, this difference being greater for weak stimuli than for strong; (2) less close correspondence between the moment of cessation of stimulus and the moment of cessation of end-effect, that is, there is a marked 'after-discharge'; (3) less close correspondence between rhythm of stimulus and rhythm of end-effect; (4) less close correspondence between the grading of intensity of the stimulus and the grading of intensity of the end-effect; (5) considerable resistance to passage of a single nerve-impulse, but a resistance easily forced by a succession of impulses (temporal summation); (6) irreversibility of direction instead of reversibility as in nerve-trunks; (7) fatigability in contrast with the comparative unfatigability of nerve-trunks; (8) much greater variability of the threshold value of stimulus than in nerve-trunks; (9) refractory period, 'bahmung,' inhibition, and shock, in degrees unknown for nerve-trunks; (10) much greater dependence
on blood-circulation, oxygen (Verworn, Winterstein, v. Baeyer, etc.); (11) much greater susceptibility to various drugs—anaesthetics.

These differences between conduction in reflex-arcs and nerve-trunks respectively appear referable to that part of the arc which lies in grey matter. The constituents of grey matter over and above those which exist also in nerve-trunks are the nerve-cell bodies (perikaryon) (Foster & Sherrington, 1897) the fine nerve-cell branches (dendritic and axonic nerve-fibres), and neuroglia.

Neuroglia exists in white matter as well as in grey, and there is no good ground for attributing the above characteristics of conduction in reflex-arcs to that part of the arcs which consists of white matter. It is improbable, therefore, on that ground that the features of the conduction are due to neuroglia. Indeed, there is no good evidence that neuroglia is concerned directly in nervous conduction at all. As to perikaryon (nerve-cell bodies) the experiment of Bethe (1897a) on the motor perikaryon of the ganglion of the second antenna of Carcinus, and the experiments of Steinach (1899) on the perikaryon of the spinal-root ganglion, also the observation by Langley (1901) that nicotine has little effect when applied to the spinal-root ganglion, though breaking conduction in sympathetic ganglia, all indicate more or less directly that it is not to the perikaryon that the characteristic features of reflex-arc conduction are referable. Similarly, the experiments of Exner (1877) and of Moore and Reynolds (1898) detecting no delay in transmission through the spinal-root ganglion—though observations by Wundt (1876) and by Gad & Joseph (1889) had a different result—withdraw from the perikaryon the responsibility for another feature characteristic of reflex-arc conduction.

Again, histological observations by Cajal, van Gehuchten and others, indicate that in various cases the line of conduction may run not through the perikaryon at all, but direct from dendrite stem to axone.

As to the nerve-cell branches (dendrites, axones, and axone-collaterals) which are so prominent as histological characters of grey matter, they are in many cases perfectly continuous with nerve-fibres outside, whose conductive features are known by the study of nerve-trunks; they are also themselves nerve-fibres, though smaller in calibre than those outside. It seems therefore scarcely justifiable to suppose that conduction along nerve-fibres assumes in the grey matter characters so widely different from those it possesses elsewhere as to account for the dissimilarity between reflex-arc conduction and nerve-trunk conduction respectively.

In this difficulty there rises forcibly to mind that not the least fruitful of the facts which the cell-theory rests upon and brings together is the existence at the confines of the cells composing the

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of the nervous system. In certain syncytial cases such surfaces are not apparent, but with most of the cells in the organism their existence is undisputed, and they play an important role in a great number of physiological processes. Now in addition to the structural elements of grey matter specified above, there is one other which certainly in many cases exists. The grey matter is the field of nexus between neurone and neurone. Except in sympathetic (autonomic) ganglia, the place of nexus between neurone and neurone lies nowhere else than in grey matter. We know of no reflex-arc composed of one single neurone only. In other words, every reflex-arc must contain a nexus between one neurone and another. The reflex-arc must, therefore, on the cell-theory, be expected to include not only intracellular conduction, but intercellular conduction. But on the current view of the structure of the nerve-fibres of nerve-trunks the conduction observed in nerve-trunks is entirely and only intracellular conduction. Perhaps, therefore, the difference between reflex-arc conduction and nerve-trunk conduction is related to an additional element in the former, namely, intercellular conduction. If there exist any surface or separation at the nexus between neurone and neurone, much of what is characteristic of the conduction exhibited by the reflex-arc might be more easily explicable. At the nexus between cells if there be not actual confluence, there must be a surface of separation. At the nexus between efferent neurone and the muscle-cell, electrical organ, etc., which it innervates, it is generally admitted that there is not actual confluence of the two cells together, but that a surface separates them; and a surface of separation is physically a membrane. As regards a number of the features enumerated above as distinguishing reflex-arc conduction from nerve-trunk conduction, there is evidence that similar features, though not usually in such marked extent, characterize conduction from efferent nerve-fibre to efferent organ, for example, in nerve-muscle preparation, in nerve-electric-organ preparation, etc. Here change in character of conduction is not due to perikarya (nerve-cell bodies), for such are not present. The change may well be referable to the surface of separation admittedly existent between efferent neurone and effector cell.

If the conductive element of the neurone be fluid, and if at the nexus between neurone and neurone there does not exist actual confluence of the conductive part of one cell with the conductive part of the other for example, if there is not actual continuity of physical phase between them, there must be a surface of separation. Even should a membrane visible to the microscope not appear, the mere fact of non-confluence of the one with the other implies the existence of a surface
of separation. Such a surface might restrain diffusion, bank up osmotic pressure, restrict the movement of ions, accumulate electric changes, support a double electric layer, alter in shape and surface-tension with changes in difference of potential, alter in difference of potential with changes in surface-tension or in shape, or intervene as a membrane between dilute solutions of electrolytes of different concentration or colloidal suspensions with different sign of charge. It would be a mechanism where nervous conduction, especially if predominantly physical in nature, might have grafted upon it characters just such as those differentiating reflex-arc conduction from nerve-trunk conduction. For instance, change from reversibility of direction of conduction to irreversibility might be referable to the membrane possessing irreciprocal permeability. It would be natural to find in the arc, each time it passed through grey matter, the additive introduction of features of reaction such as characterize a neurone-threshold (Goldscheider, 1898). The conception of the nervous impulse as a physical process (du Bois Reymond) rather than a chemical, gains rather than loses plausibility from physical chemistry. The injury-current of nerve seems comparable in mode of production (J. MacDonald, 1902) with the current of a ‘concentration cell,’ a mode of energy akin to the expansion of a gas and physical, rather than chemical, ‘volume-energy.’ Against the likelihood of nervous conduction being pre-eminently a chemical rather than a physical process must be reckoned, as Macdonald well urges, its speed of propagation, its brevity of time-relations, its freedom from perceptible temperature change, its facile excitation by mechanical means, its facilitation by cold, etc. If it is a physical process the intercalation of a transverse surface of separation or membrane into the conductor must modify the conduction, and it would do so with results just such as we find differentiating reflex-arc conduction from nerve-trunk conduction.

As to the existence or the nonexistence of a surface of separation or membrane between neurone and neurone, that is a structural question on which histology might be competent to give valuable information. In certain cases, especially in Invertebrata, observation (Apathy, Bethe, etc.) indicates that many nerve-cells are actually continuous one with another. It is noteworthy that in several of these cases the irreversibility of direction of conduction which is characteristic of spinal reflex-arcs is not demonstrable; thus the nerve-net in some cases, for example, Medusa, exhibits reversible conduction (Romanes, Nagel, Bethe, and others). But in the neurone-chains of the grey-centred system of vertebrates, histology on the whole furnishes evidence that a surface of separation does exist between neuro secondary degen strictly a bound transgress it. It and neurone i vertebrate, inv neurone; and must be in characters dist conduction mi delicate transw.

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Sherrington’s began by cutting the spinal mecha mediated by the the system, so th could be obser simplified his pr the limb itself or held a pen (or mounted on a re
between neurone and neurone. And the evidence of Wallerian secondary degeneration is clear in showing that that process observes strictly a boundary between neurone and neurone and does not transgress it. It seems therefore likely that the nexus between neurone and neurone in the reflex-arc, at least in the spinal arc of the vertebrate, involves a surface of separation between neurone and neurone; and this as a transverse membrane across the conductor must be an important element in intercellular conduction. The characters distinguishing reflex-arc conduction from nerve-trunk conduction may therefore be largely due to intercellular barriers, delicate transverse membranes, in the former.

In view, therefore, of the probable importance physiologically of this mode of nexus between neurone and neurone it is convenient to have a term for it. The term introduced has been synapse (Foster & Sherrington, 1897).

The differences between nerve-trunk conduction and reflex-arc conduction are so great as to require for their exhibition no very minute determination of the characters of either; but we may with advantage follow these differences somewhat further. In doing so we may take the reflexes of the hind-limb of the spinal dog as a field of exemplification.

### SHERRINGTON'S EXPERIMENTS

Following the introductory overview Sherrington passed on to a lengthy presentation of experimental data. Sherrington's immense influence derives in appreciable measure from the way in which he illustrated his findings with experimental records showing reflex limb movements as a function of time since the onset of a stimulus or series of stimuli. I have extracted from the rest of the book experimental records that illustrate several of the 11 experimental findings enumerated by Sherrington (on p. 27).

Sherrington's method was the same in all of his experiments on reflexes. He began by cutting through the spinal cord just below the brain so as to remove the spinal mechanisms from the influence of the more complex processes mediated by the brain itself. In other words he began by radically simplifying the system, so that the operation of the basic mechanisms of the spinal cord could be observed without an overlay of higher activity. Having thus simplified his preparation, Sherrington attached the distal extremity of either the limb itself or an individual muscle to the lever of a kymograph. The lever held a pen (or other marking instrument) pressed against chart paper mounted on a revolving drum (see Fig. 2.2). Thus, time is represented along
the abscissa of the records and movements of the limb are represented by rises and falls in the line of the chart. The times at which Sherrington delivered the stimuli are indicated by appropriate markings on the chart (see caption to Fig. 2.3).

Figure 2.3 illustrates Sherrington's first point, namely, that conduction through a reflex arc is relatively slow. In the fastest case (Fig. 2.3a), one second elapses between the onset of the stimulus and the initial movement of the leg. The latency between stimulus onset and initial leg movement also depends quite a lot on stimulus strength (compare Fig. 2.3a to Fig. 2.3b). Sherrington took this finding to mean that somewhere in the pathway from the sensory neurons to the motor neurons there must be a "conduction process" whose dynamic properties (rates of rise and fall) were very different from the dynamic properties of the processes involved in conduction along nerve trunks. Extensive work by others had already shown that conduction along sensory a...
along sensory and motor nerve trunks was much faster than the conduction rates implied by the data in Fig. 2.3. And the speed of nerve trunk conduction is little affected by stimulus intensity; whereas the comparison between panels (a) and (b) in Fig. 2.3 shows that stimulus intensity greatly affects the speed of conduction in a reflex arc. The latency of a reflex contraction gets shorter as stimulus intensity increases.

FIG. 2.3. Records of the scratching movement elicited by a stimulus whose onset(s) and offset(s) is indicated on the graphs. The intensity of the stimulus in Panel b was less than in Panel a. Note that this weakening of stimulus intensity results in a much longer latency between stimulus onset and the onset of scratching. (From Sherrington, 1947, Fig. 2, p. 20)
FIG. 2.4. Flexion reflexes (bending of the leg in response to a painful stimulus to the foot). The vertical arcs labeled S and S’ show the onset and offset of the stimulus. Responses I–III were elicited by progressively stronger stimuli. Note that in the response to the strongest stimulus (response III), the reflex contraction outlasted the stimulus by more than 7 seconds. (From Sherrington, 1947, Fig. 5, p. 26)
In Fig. 2.4 is a record showing the lack of close correspondence between the cessation of a stimulus and the cessation of the reflex activity caused by that stimulus. The leg whose movement is recorded in Fig. 2.4 had not fully returned to its resting position several seconds after the stimulus ceased. One could not produce such a long after-effect by stimulating the motor nerve itself. Therefore the stimulus must have given rise (somewhere in the spinal cord) to a process that continued to excite the motor nerves long after the stimulus had ceased to act on the sensory nerves. Sherrington called this phenomenon "after-discharge" (see his point #2, p. 27).

Figure 2.5 illustrates Sherrington's third point, namely, that the temporal structure (rhythm) of the movements caused by the stimulus may be independent of the temporal structure of the stimulus. In a long series of

![Diagram of movements](image)

**Fig. 2.5.** The rhythmic scratching movements elicited by three different stimuli: (a): The eliciting stimulus was light rubbing of the skin behind the shoulder. (b) & (c): The eliciting stimulus was a train of weak shocks (marked at top of panels). Note that the rhythm of the scratching movement was the same (about 4/sec) even though the temporal characteristics of the eliciting stimuli were very different. (From Sherrington, 1947, Fig. 14, p. 48)
experiments, Sherrington showed that the rhythm of the scratching movement of the dog’s hind leg is about 4 scratches per second regardless of the rhythm of the stimulus that elicits the scratching. A continuous stimulus (rubbing the skin) elicits a four-per-second scratch and so does an intermittent stimulus consisting of a brief electric shocks delivered at rates from 10–100 shocks per second. When one stimulates the motor nerve itself, the temporal structure of the muscle response closely follows the temporal structure of the stimulus. Hence, Sherrington concluded that somewhere in the spinal part of the reflex arc there must be a process that can generate a rhythmic output with a frequency that is independent of the frequency of the stimulus.

The “refractory period” referred to in Sherrington’s tenth point was not really an experimental finding, hence it cannot be illustrated. Sherrington’s concept of a refractory period in the central part of the reflex arc derived from his attempt to infer the nature of the processes that gave rise to the rhythmic autonomy of the scratch reflex. As we shall see later, Sherrington’s attempt to explain the autonomous rhythm of this output in terms of a refractory period in the synapses of the reflex arc was in all probability wrong. There are neurons and/or neural circuits in the spinal cord that produce rhythmic bursts of firing in the motor nerves that leads to the muscles. In Chapter 4 such neurons or neural circuits will be termed oscillators. An oscillator, by definition, produces an output whose rhythmic structure is independent of whatever temporal pattern there may be in the input to the oscillator. There are, for example, oscillator neurons, which produce bursts of signals at regular intervals even when they are divorced from any neural input. There are other oscillator neurons that fire rhythmic bursts in response to a steady neural input, an input signal that does not have any rhythmic structure. Even when the input has a rhythm, that rhythm is not seen in the output. Oscillator neurons are like bell-clocks. The bell-clock rings every hour provided only that it is wound from time to time. The rhythm of the input (winding) does not affect the rhythm of the output. The hourly rhythm of its ringing is the same whether the clock is wound every 24 hours, every 48 hours, or haphazardly, whenever the winder remembers to do it. The mechanisms underlying the rhythmic output of oscillators in the central nervous system are still not well understood, but refractory periods at synapses play no role.

Sherrington’s explanation of the rhythmic structure of some reflexes reveals how thoroughly he was committed to the view that the nervous system conducted activity rather than generated activity on its own. The nervous system reacted to the world; it did not act spontaneously.

Figure 2.6 illustrates another rhythmic reflex—the “stepping” movements of the dog’s hindleg. This rhythmic output is elicited by stimulating the paw of the contralateral leg with brief electric shocks at a high frequency (25–100 shocks/sec). The rhythm of this reflex is about 5 steps in 2 seconds (2.5Hz)—about half the frequency of the scratch reflex for the same limb in the same animal. Again, the frequency. It is int reading von Holst’s (Chapter 4). Von frequently seen as Sherrington would surmised from the ton’s reference to mechanism under reflexes:

It is clear that a refractory phase:

Refractory pha primitive Medus fundamental imp higher forms (dc muscular organ,
animal. Again, this rhythm is independent of stimulus strength and frequency. It is interesting to keep these two rhythmic "reflexes" in mind in reading von Holst's paper on the role of central oscillators in coordination (Chapter 4). Von Holst's emphasis on the role of central oscillators is frequently seen as standing in opposition to Sherrington's ideas. That Sherrington would not necessarily have insisted on this opposition may be surmised from the following passage. In the passage that follows Sherrington's reference to "refractory phase" refers to his conception of the mechanism underlying the autonomous rhythms he observed in some reflexes:

It is clear that an essential part of many reflexes is a more or less prolonged refractory phase succeeding nervous discharge.

Refractory phase appears ... at the one end [in mantel movements of the very primitive Medusa] and at the other [end] of the animal scale as a factor of fundamental importance in the coordination of certain mobile actions .... in higher forms (dog) refractory phase occurs ... not in the peripheral neuromuscular organ, but in the centers of the nervous system itself [p. 69].
Fig. 2.7. The crossed-extension reflex (extension of the contralateral leg in response to a painful shock to the toe of a hindfoot) in response to stimuli of increasing strength (Panel a, weakest; Panel f, strongest). Note the tremendous increase in the amplitude and duration of the response from Panel d to Panel e. One characteristic of synaptic action in reflex arcs is this non-linear relation between the strength of the stimulus and the strength of the response: the first few increases in stimulus intensity produce only slight increases in the response (Panels a-d). The increase in the response at the fifth step (Panel e) is out of all proportion to what has gone before. (From Sherrington, 1947, Fig. 27, p. 76.)
In other words, the spinal cord contains mechanisms that produce rhythmic outputs. Sherrington attributed these rhythmic outputs to refractory phases at synapses. In this he was in all probability mistaken. But he was very much in line with modern thinking when he recognized that oscillatory mechanisms in the central nervous system are a significant aspect of coordination in animals throughout the phylogenetic scale.

Figure 2.7 illustrates to some extent the highly variable amplification characteristics that Sherrington observed in reflex conduction. In other words, Fig. 2.7 illustrates Sherrington’s fourth point—the “less close correspondence between grading of intensity of the stimulus and the grading of intensity of end-effect [p. 27].” The availability of processes whose amplification characteristics (relation between strength of input and strength of output) may vary is of great importance in the design of machinery that must organize the timing and relative strengths of its outputs. We make repeated use of this property in subsequent chapters.

Sherrington realized that the highly variable relation between stimulus strength and response strength was closely related to two other properties of the reflex arc. The first of these was the “considerable resistance of the passage of a single nerve impulse; but a resistance easily forced by a succession of impulses” (point 5 on p. 27). The second was the great variability in the threshold value for a stimulus (point 8, p. 27). What follows is his succinct discussion of the observations upon which these claims rest:

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SUMMATION

SUMMATION of subliminal stimuli so that by repetition they become effective is practically unknown in nerve-trunk conduction. But it is a marked feature of reflex-arc conduction (Setschenow, 1863; Stirling, 1874). Nor is it attributable to the muscles whose contraction may serve as index of the reflex-response, since summation of this extent is not known for vertebrate skeletal muscle; though found by Richet (1882) in the claw-muscle of the crayfish.

We find striking instances of the summation of subliminal stimuli given by the scratch-reflex. The difficulty in exciting a reflex by a single-induction shock is well known. A scratch-reflex cannot in my experience be elicited by a single-induction shock, or even by two shocks, unless as physiological stimuli they are very intense and delivered less than 600 milliseconds (msecs) apart. Although the strongest single-induction shock is therefore by itself a subliminal stimulus for this reflex, the summating power of this reflex
mechanism is great. Very feeble shocks, each succeeding the other within a certain time—summation time—sum as stimuli and provoke a reflex. Thus long series of subliminal stimuli ultimately provoke the reflex. I have records where the reflex appeared only after delivery of the fortieth successive double shock, the shocks having followed each other at a frequency of 11.3 per sec, and where the reflex appeared only after delivery of the forty-fourth successive make shock, the shocks having followed at 18 per sec. A momentary stimulus, for example, a break shock of fair physiological strength applied by a stigmatic pole (needle point) to a skin-spot in the receptive field of this reflex, produces in the nervous arc a change which though, as just said, unable of itself alone to produce the reflex movement, shows its facilitating influence (bahnung) on a subsequent stimulus applied even 1400 msec later. The duration of the excitatory change induced by a momentary stimulus is therefore in this mammalian arc (scratch-reflex) almost as long as that noted in the frog by Stirling, namely, 1500 msec.

With serial stimuli of the same frequency of repetition the latent time of the scratch-reflex is shorter the more intense the individual stimuli. Stirling (1874) conclusively traced length of latency to dependence on spinal summation of successive excitations. In accord with this in the 'scratch-reflex,' when the serial stimuli follow slowly, the reflex ceteris paribus is prolonged. A single brief mechanical stimulation of the skin (rub, prick, or pull upon a hair) usually succeeds in exciting a scratch-reflex, though the reflex thus evoked is short; but there is nothing to show that these stimuli, though brief, are really simple and not essentially multiple. A striking dissimilarity, therefore, between reflex-arc conduction and nerve-trunk conduction is that in reflex-arc conduction considerable resistance is offered to the passage of a single nerve-impulse, but the resistance is easily forced by a succession of impulses; in other words, subliminal stimuli are summed.

It follows almost as a corollary from this that the threshold excitability of a reflex mechanism appears much more variable than that of a nerve-trunk, if the threshold excitability be measured in terms of the intensity of the liminal stimulus. The value will be more variable in the case of the reflex mechanism, because there the duration of the stimulus is a factor in its efficiency far more than in the case of the nerve-trunk. In the scratch-reflex a single stimulus which is far below threshold intensity is found, on its fortieth repetition and nearly 4 sec after its first application, to become effective and provoke the reflex.
NONLINEAR SUMMATION

Sherrington's fourth and fifth points (variable amplification and response only to the cumulative effect of several stimuli) are both traceable to his eighth point (the variable threshold). Both phenomena are instances of nonlinear summation, a process of summation in which the effect of several stimuli acting together or in rapid succession is not equal to the sum of the effects of the individual stimuli acting in isolation. For example, a single electric shock elicits no scratch reflex. If the summation of stimuli in reflex conduction were linear, then repeating the shock a number of times would likewise fail to elicit a reflex, since $0 + 0 + \ldots + 0 = 0$. The fact that a number of stimuli delivered together will elicit a reflex even though no one of them elicits anything when acting alone indicates nonlinear addition of stimuli somewhere in the course of the reflex pathway (or, in Sherrington's terms, the summation of subliminal stimuli).

The phenomena that reflect nonlinear summation in reflex pathways were the focus of much interest in 19th century neurophysiology. The English termed such phenomena facilitation, because the first few stimuli in a train of stimuli were not themselves conducted to the effector organ, but seemed to make the passage easier for later stimuli. The German workers referred to this as Bahnung ("path-making"). Since most workers of the time tended to think of the nervous system as a structurally continuous passive conduction network, the ability of nerve signals to "change the resistance in a nervous pathway" seemed quite mysterious. This mystery inspired a good deal of complex and/or vague theorizing, despite the fact that Richet had offered a simple explanation as early as 1871.

Richet suggested that nonlinear summation phenomena (such as facilitation or Bahnung) implied the existence somewhere in the conduction pathway of excitation processes that were sluggish: These processes responded to a neural message with a relatively slow increase followed by a prolonged subsidence back to their original level. The effects of fairly widely spaced stimuli could partially summate through the agency of these slowly rising and subsiding excitation processes. Richet suggested that the sudden appearance of an observable response from the effector organ after some number of stimuli had been delivered implied that the summation excitation had to exceed some threshold before it could excite the next stage in the conduction pathway (see Fig. 2.8). The nonlinearity of the summation—the fact that the combined effect of several stimuli is not equal to the sum of their individual effects—is due to the presence of a high and/or variable threshold. Sherrington (1947, p. 156ff) offered a similar interpretation of at least one kind of nonlinear summation—irradiation (see Chapter 3).

Sherrington realized that the capacity for nonlinear or subliminal summation had far-reaching functional significance. In modern terms,
nonlinear summation permits "decision processes" that have the characteristics of logical AND gates. AND gates are devices that produce no output except in response to the conjoin occurrence of at least two inputs. They respond only to \( x \) and \( y \) in combination. They do not respond to either input alone. AND gates can be used in such a way that a complex spectrum of events must occur in order for a particular reaction to occur on the part of the organism. (For illustration, see Chapter 6, Fig. 6.9, and accompanying discussion).

As regards his sixth point—the irreversibility of conduction in a reflex arc—Sherrington again provides no illustrative experimental records, but he summarizes the evidence succinctly.

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**IRREVERSIBILITY OF DIRECTION OF CONDUCTION**

Another remarkable difference between reflex-arc conduction and nerve-trunk conduction is the irreversibility of direction of the former and the reversibility of the latter. Double conduction as it has been termed, is efferent. It wa roots, for perig great single el sympathetic nerve myself (1897) f. The nerve-fib course, condu stimulated; th directions open as conductive.

From the B that reflex-arc central end of (1811) and M excitation of t of reflex actic afferent chan conduction fr afferent. The case which fo the neural sys direction' (W. in nerve-fibre spinal roots dendrites of direction only however, be t synapse. The may lie in a than in the o is reversible i.

Chain-cell majority of a higher anim nervous circu nerve-net of reversibility effected by o When the contracts, its it is expelled in the reves
been termed, is well established for nerve-trunks both afferent and efferent. It was shown by du Bois Reymond, for the spinal nerve roots, for peripheral nerves by Kuhne’s gracilis experiment, for the great single electric fibre of Malapterurus by Babuchin (1876), for sympathetic nerve-cords by Langley & Anderson (1894), and by myself (1897) for certain fibres of the white tracks of the spinal cord. The nerve-fibres in all these cases, when excited anywhere in their course, conduct nerve-impulses in all directions from the point stimulated; that is, in their case both up and down, the only two directions open to them. Their substance may therefore be regarded as conductive in all directions along their extension.

From the Bell-Magendie law of the spinal nerve-roots we know that reflex-arcs conduct only in one direction. The stimulation of the central end of a motor-nerve remains without obvious effect. Bell (1811) and Magendie (1822) and their followers established that excitation of the spinal end of the severed motor root evokes no sign of reflex action or sensation. Evidently the central nexus between afferent channel and efferent is of a kind that though it allows conduction from afferent to efferent, does not allow it from efferent to afferent. The path is patent in one direction only. This is the special case which forms the first foundation of the law that conduction in the neural system proceeds in one direction only, the ‘law of forward direction’ (W. James, 1880). When the property of double conduction in nerve-fibres had been ascertained, the Bell-Magendie law of the spinal roots became more instructive. Gad (1884) argued that the dendrites of the motor root-cell are capable of conduction in one direction only, namely, toward and not away from the axone. It may, however, be that the irreversibility of the conduction is referable to the synapse. The explanation of the valved condition of the reflex circuit may lie in a synaptic membrane more permeable in one direction than in the other. In other words, though intraneuronic conduction is reversible in direction, interneuronic may be irreversible.

Chain-cells of polarized conduction form the basis of the great majority of all the nervous reactions of the cerebrospinal system of higher animals. It appears, however, that not all pluricellular nervous circuits exhibit irreversible direction of conduction. The nerve-net of Medusa is a pluricellular conductor which exhibits reversibility of direction of conduction. In Medusa locomotion is effected by contraction of a sheet of muscle in the swimming-bell. When the swimming-bell, which resembles an inverted cup, contracts, its capacity is lessened, and some of the water embraced by it is expelled through the open end, the animal itself being propelled in the reverse direction by recoil. The mechanism is like that of the
heart, but the heart propels its contents, the swimming-bell propels itself against its contents. The contractions of both recur rhythmically, though Medusa, unlike the heart, has periods of prolonged diastolic inactivity. At such a period an appropriate stimulus restarts the swimming-bell. The contractile beat begins from the point stimulated and spreads thence over the whole muscular sheet (Romanes, 1877). It spreads rapidly enough for the contraction not to have culminated at the initial point before it has set in at the most remote part. The beat is thus not only everywhere in progress at the same time, but is practically in the same phase of progress everywhere, and similarly synchronously passes off.

The arrangement of the nervous system of Medusa, *Rhizostoma*, is, according to Bethe (1897b), of the following kind (Fig. 2.9). The nerve-cell has on one side a sub-umbrella, and the sheet of connective tissue has also longitudinal nerve-cells. The nerve-cells form a network throughout the sheet. From this network there are threads to the acicular nerve-cells.

The circular and continuous field reveals no muscular sheet across which the muscular contraction spreads. The spread of Conchocelis is due to the spread of impulses in the nerve-cells to a neural action over the nervous sheet. So long as the acicular nerve-cells are stimulated, the nerve-impulses enter the nerve-fibres in the sub-umbrella-shaped disk, and the band of nerve fibres to the other end of the free nerve sheet. Therefore, direction only. 1 Arthropods and other sub-umbrella-shaped nerve-fibres—the plus conductor, contain two kinds of nerve impulses, a microscopic for the difference in the two well-known in their free nerve ends.
cell has on one hand threadlike arms that extend to the surface of the sub-umbrella, and on the other hand others which stretch down to the sheet of contractile cells on the underside of the bell. Each nerve-cell has also long side threads which join similar side threads from other nerve-cells. By virtue of these lateral connexions the nerve-cells form a network of conductors spreading horizontally through the bell in a layer of tissue between a receptive sheet and a contractile sheet. From this nerve-net, throughout its extent, there pass nerve-threads to the adjacent muscle; it also receives at many points of its extent nerve-threads from specially receptive areas of surface.

The circularly arranged sheet of muscle does not form a continuous field toward the center of the disk; there are wide radial gaps in it. Across the gaps the 'conduction' passes: the microscope reveals no muscular tissue in these gaps, but the nerve-net can be seen to spread across them (Bethe, 1902). The presence of the nerve-net explains the conduction across them. It is therefore argued by Bethe that the spread of the contraction over the muscular sheet in Rhizostoma does not imply conduction of the contraction from one muscle-cell to another, but is the result of the spread of nervous action over the nerve-network. In its progress along the nerve-net, the nervous discharge, as it reaches each part of the nerve-net, spreads down the nerve-threads, descending thence to the underlying musclesheet. So long as the nerve-cell network is intact, wherever the point stimulated, the ensuing contraction is of the whole bell, that is, the nerve-impulses started at one point of the receptive surface, on entering the nerve-network, spread over it in all directions. When the bell-shaped disk is spirally cut into a long band, to whichever end of the band the stimulus be applied, the conduction spreads from that end to the other and over the whole strip (Romanes, 1877). The nerve-net therefore conducts nerve-impulses in both directions along its length. Therefore it is not a polarized conductor, conductive in one direction only. In the chains of nerve-cells of higher animals, such as Arthropods and Vertebrates, although the conduction is reversible in each nerve-cell—at least along that piece of it which forms a nerve-fibre—the pluricellular chain in toto constitutes a polarized conductor, conductive in one direction only. In such cell-chains the individual nerve-cells are characterized morphologically by possessing two kinds of cell-branches, which differ one from another in microscopic form, the one kind dendrites, the other axones. The difference in appearance between dendrites and axones is marked enough for recognition by microscopical inspection. Since in many well-known instances the dendrites conduct impulses away from their free ends, while the axone conducts towards its free end, it is
possible on mere microscopic inspection of nerve-cells of this type to infer by analogy the normal direction of the conduction through the nerve-cell. But in the nerve-cells forming the nerve-network of Medusa there seems no such distinct differentiation of their branches into two types. Their cell-processes are not distinguishable into dendrites and axones.

Moreover, microscopic examination of the nerve-net of Medusa reveals another difference between it and the nerve-cell chains of higher animals. In these latter the neuro-fibrils of one nerve-cell are not found unbrokenly continuous with those of the next cell along the nerve-chain. Although the union may be close, there is not homogeneous continuity. The one nerve-cell joins another by synapsis. But in the nerve-net of Medusa the neurofibrils pass, according to Bethe, uninterruptedly across from one cell to another. Even if we admit the neuro-fibrils to be in a measure artifacts, the appearance of their continuity from one cell to another in one type, and of their discontinuity from one cell to another in the other type remains significant of a difference between the conduction-process from cell to cell in the two types. The nerve-net of Medusa appears an unbroken retiform continuum from end to end. Each nerve-cell in it joins its neighbors much as at a node in the myelinated nerve-fibre the axis-cylinder of each segment joins the next. Reversibility of conduction may be related to this apparent continuity of structure, and irreversibility to want of it. This points to the latter being referable to the synapse; if the synaptic membrane (Lecture I, p. 31) be permeable only in one direction to certain ions, that may explain the irreversibility of conduction. The polarized conduction of nerve-arcs would be related to the one-sided permeability of the intestinal wall, for example, to NaCl (Cohnheim).

The functional significance of the unidirectionality of conduction revealed by the study of reflexes is not readily appreciated unless one has some experience in the construction of organized signal systems, for example, relay or solid-state programming circuits. When a given control point ("common path" in Sherrington's terms) receives command signals from two different sources, one must always take measures to insure that the command signal from one source is not conducted back up the path from the other source. In electrical circuits one uses diodes, elements that allow current to flow in only one direction. In electronic circuits one uses elements called OR gates in order to prevent multiple inputs to the same point from generating "wrong 'way" signals in one another. Sherrington's emphasis on the unidirectionality of conduction is another instance of his deep insight into the properties of the central nervous system the functionally organized ou

The last finding that he inhibition mentioned in important physiological a of little significance in the stimulates motor nerves t the further stimulation sir progress. Except under v nerves never inhibits or c one turns to the study of that is, by the stimulation of one sensory area very been or are being elicited.

Figures 2.10 and 2.11 stimulus can inhibit the

![Image](https://via.placeholder.com/150)

**FIG. 2.10.** Reflex inl stimulus) elicits a reflex stimulus to the foot of relaxation. In other wc (Modified from Sherri
central nervous system that are important from the standpoint of producing a functionally organized output.

INHIBITION

The last finding that has important organizational consequences is the inhibition mentioned in Sherrington's point #9. (Points 10 and 11 have important physiological and pharmacological consequences but are probably of little significance in the organization of outputs.) In vertebrates, when one stimulates motor nerves that are already being excited by some other means, the further stimulation simply accentuates whatever contraction is already in progress. Except under very specialized circumstances, stimulation of motor nerves never inhibits or cancels the excitatory effects of other stimuli. When one turns to the study of the muscular contractions that are elicited reflexly, that is, by the stimulation of sensory nerves, this is no longer true. Stimulation of one sensory area very often inhibits the muscular contractions that have been or are being elicited by stimulation of some other area.

Figures 2.10 and 2.11 illustrate the striking way in which one reflex stimulus can inhibit the effect of another reflex stimulus. In Fig. 2.10,

![Diagram showing reflex inhibition](image)

**FIG. 2.10.** Reflex inhibition. A painful stimulus to the foot (the excitatory stimulus) elicits a reflex contraction of a muscle that flexes the leg. A painful stimulus to the foot of the opposite leg (the inhibitory stimulus) elicits a reflex relaxation. In other words, the second stimulus partially counteracts the first. (Modified from Sherrington, 1947, Fig. 32, p. 99)
stimulation of one foot elicits a sustained contraction of the hamstring muscle in the leg of that foot (the "homonymous" leg, or "leg of the same name"). Stimulation of the contralateral foot (the foot on the opposite side) then produces an abrupt, albeit incomplete relaxation of the hamstring muscle. This abrupt relaxation may be thought of as a "negative contraction," an effect opposite in sign to the effect of an excitatory stimulus. In Fig. 2.11 we see what might be called a "negative twitch," that is, a very brief relaxation of an extensor muscle in response to a brief stimulus to the homonymous foot delivered at a time when the muscle was contracting.

In summary, stimuli delivered to the motor nerves of vertebrates always have an excitatory effect. They cause the muscle to contract. Stimuli delivered to the sensory receptor areas may have effects of opposite signs; some cause the muscle to contract, others cause the muscle to relax. Sherrington saw that the relaxing effect of some of these stimuli gave rise to processes that antagonize or inhibit the signals that argue against the homonymous reflex signal, which drives the muscle to contract. This interaction between the afferent (sensory) and efferent (motor) pathways is a fundamental aspect of neural integration.

These, then, are the kind of phenomena that Sherrington termed "the system is regarded in its entirety as the reflex was the element in the organism that was constructed. Once one of the functional units was achieved. He identified a series of functional stages. In his analysis of the problem, every sense a modern physiological approach to the processes of the nervous system was treated as a psychophysical phenomenon. He drew on recent advances in neuroanatomy to explain how the general nature of the Sherrington's inference was beautiful and was relayed from the sensory to the motor systems through a series of junctions. At these junctions, there was no fiber-like structure but rather a complex network of connections. "Nowhere in physiology is there a more frequent study of nervous mechanisms at the level of the synapse, between the afferent and the efferent neural cells. Since Sher..."
the relaxing effect of some reflex stimuli must mean that signals produced by these stimuli gave rise somewhere in the spinal part of the reflex pathway to processes that antagonize the excitatory process. Sherrington termed this antagonistic process inhibition. Thus, the spinal part of the reflex pathway can integrate both the signals that argue for the contraction of a given muscle and the signals that argue against the contraction of that muscle. The motor neuron signal, which drives the muscle, will increase or decrease as the arguments pro and con fluctuate in strength. All stimuli have excitatory effects on the afferent (sensory) pathways, but central processes can “invert” these effects, so that a stimulus may inhibit a motor process rather than excite it.

SUMMARY

These, then, are the kinds of central processes revealed by the study of what Sherrington termed “the unit mechanism of the nervous system when that system is regarded in its integrative function” [p. 22]. In Sherrington’s view, the reflex was the elementary unit of behavior, from which all coordinated action was constructed. Although it will emerge below that the reflex is only one of the functional units in the construction of coordinated sequences of action, this in no way detracts from the magnitude of Sherrington’s achievement. He identified and experimentally characterized processes of far reaching functional significance.

In his analysis of the processes underlying reflex action, Sherrington was in every sense a modern psychologist. He was attempting to specify the general nature of the processes underlying integrated behavior. That he is known today primarily as a physiologist is owing in part to the fact that he was able to draw on recent anatomical advances to infer the locus of the processes whose general nature he had determined from behavioral study. Sherrington’s inference was beautiful in its simplicity: He knew that the neural signals were relayed from the sensory nerve to the motor nerve over pathways that were fiber-like throughout most of their length except at a few points, namely, at the junctions between neural cells. At these junctions between neural cells there was no fiber-pathway to conduct the signals. So important was this fact in Sherrington’s thinking that he opened his book with the sentence: “Nowhere in physiology does the cell-theory reveal its presence more frequently in the very framework of the argument than at the present time in the study of nervous reactions [p. 17].” The cell theory was embedded “in the very framework of the argument” because Sherrington attributed all of the differences between nerve-fiber conduction and reflex conduction to the only part of the reflex pathway that did not involve conduction along a fiber, namely, to the junction between cells. Here, the nervous signal had somehow to be transmitted across the barrier imposed by the walls of the two opposed neural cells. Since Sherrington attributed such far reaching significance to the
transmission process at this locus, he coined a special word for the signal-transmitting junction between two cells—the synapse. It was, he inferred, the transmission process at the synapse that made the phenomena of reflex conduction so different from the phenomena of conduction in nerve trunks.

The last seventy years of neurophysiological work have richly supported most but not all1 of Sherrington's inferences about the nature of the processes that occur at synapses. We now can explain the nature of synaptic transmission in terms of more molecular events such as the release of excitatory and inhibitory transmitter substances from the prejunctional membrane, the depolarizing and hyperpolarizing effects of these transmitter substances at the post-junctional membrane, the nonlinear conversion of the resulting depolarization into a conducted action potential, and so on. But this more molecular work need not concern us further. It has added little of functional significance to Sherrington's characterization of the process of synaptic transmission. Nearly all of the presently known aspects of synaptic transmission that play an important role in the construction of integrated sequences of muscular movement are clearly described in *The Integrative Action of the Nervous System*. These aspects are:

1. The capacity to integrate signals occurring over time intervals measured in seconds to minutes. This capacity derives from the wide range of rise times and decay times characteristic of excitation and inhibition at synapses.
2. The nonlinear summation of inputs so that several inputs acting together may produce an output even though any one input acting alone produces no output.
3. The control over the direction of signal flow so that signals arriving at a common point do not penetrate back up other input pathways.
4. The widely adjustable amplification characteristics that permit a strong signal to have no effect under some circumstances, while a weak signal may have a strong effect under other circumstances.
5. The ability to "invert" signals so that a signal from a given source can be used to excite one action and inhibit another.

For someone who is interested in the design of a system with complex adaptively organized outputs the above list is an exceedingly useful set of properties to work with. The question now becomes what sort of combinatorial principles does the system use? That is, given a functional unit, the reflex, that manifests the above list of useful properties, how does the system combine these units to form complexes of units acting in coordination. Here too, Sherrington had many important insights.

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1The most notable lack of support concerns Sherrington's inference of a long lasting synaptic refractory period.