Mathematical Models for Bioengineering and Probabilistic Systems

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Preface

This really is the golden age of Mathematics. It has been said that half the Mathematics ever created has been in the last 100 years and that half the mathematicians who have ever lived are alive today. We have seen such achievements as the resolution of the four-colour problem and Fermat's last theorem, with the latter being a special manifestation of a much more general result!

It is befitting that the golden jubilee of the Indian Institute of Technology Kharagpur, happens to fall in the golden age of mathematics. As a senior professor in the Department of Mathematics, I felt encouraged to bring out a series of books covering all the major areas of Mathematical Sciences during this period of historic importance.

This book is an important member of the aforesaid series and consists of chapters devoted to the analysis of mathematical models for some important bio-engineering systems as well as some probabilistic systems. Mathematical Modelling may be looked upon as the art of applying mathematical methods to solve various problems in almost every aspect of technical development whatever be its level of sophistication. The methodology of mathematical modelling consists of carefully formulating the definitions of the concepts to be discussed, and of explicitly stating the assumptions that shall be the basis for the reasoning employed. The actual problem is formulated symbolically by these definitions and assumptions, while conclusions are drawn by employing the most rigorous logic, basing upon the observation of the mathematical analysis. Thus modelling primarily deals with recognizing the characteristics governing the observable and operating features; a model is supposed to be a prototype of the system under investigation.

It is now an well accepted fact that the flow of knowledge in science and technology owes to a great extent to the development of advanced mathematical tools. Mathematical methods are now a days being successfully applied to explore a variety of interesting information in Engineering, Biology, Psychology, Chemistry, Physics, Economics and many other subjects. A glance through any modern textbook or journal in the fields of ecology, genetics, physiology or biochemistry reveals that there has been an increasing use of mathematics which ranges from the solution of complicated differential equation in population studies to the use of transfer functions in the analysis of eye-tracking mechanisms.

The aim here has been to formulate various mathematical models on a fairly general platform and to perform the analysis in relatively rigorous terms. I hope, the choice and treatment of the problems will enable the readers to understand and evaluate detailed analyses of specific models and applications in the literature.

For over three decades I have been engaged in teaching and research at several well-known institutions of India, Germany and North America. Publication of the series of books has been the fruit of a long period of collaboration together with relentless perseverance. It has been our endeavour to make these books useful to a large section of people interested in mathematical sciences, professional as well as amateur. The volumes have been so designed and planned that illustrative examples and exercises as well as fairly comprehensive bibliography are included in the various chapters. This will help strengthen the level of understanding of the learners. Thus the books of this series will be of interest not only to graduate students but also to instructors, research scientists and professionals. The volumes of the series might not exactly serve as textbooks, but will definitely be worthwhile supplements. Our labour will be deemed amply rewarded if at least some of those for whom the volumes are meant derive benefit from them.

I am thankful to the members of the ICRAMS committee for their kind encouragement in publishing the mathematical science series. I feel highly indebted to the contributors of all the volumes of the series who have so kindly accepted my invitation to contribute chapters. The enormous pleasure and enthusiasm with which they have accepted my invitation have touched me deeply, boosting my interest in the publication of the series. Special care taken by Mr. N. K. Mehra of Narosa Publishing House and his team for producing this series of books with utmost efficiency is gratefully acknowledged.

I.I.T. Kharagpur J C Misra

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Modelling of Head Impact Problems

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It has been a common observation that in most of the accidents leading to fatality, head is the most vulnerable part of the human body. This information, all by itself, is more than enough to answer why, as a natural consequence of an unprecedented development of Biomedical Engineering, quite a few studies have been made in recent years, in order to have a proper understanding of the composition, functioning and possibilities for operational movement of the head. Even then our knowledge about the direct cause of brain dysfunction remains in a prenatal state (as is the case with many other biological tissues) as compared to our comprehension of the mechanical behaviour of technological structures. The difficulty is that since brain damage in most cases is macroscopically not detectable, its presence has to be speculated from physiological or neurological malfunction.

The facts that harmful experiments cannot be carried out on living human beings and that observations on the tests performed with experimental animals cannot always be readily used for the human system emphasize the importance of models in the study of human head impact. There are two principal types of models in use – physical ones based on experimental investigation and mathematical ones based on theoretical analysis. Although in most cases, physical models can be constructed more realistically than the mathematical models, their applicability has got limitations due to the difficulties faced while taking necessary measurements and due to the enormous amount of time required to collect the necessary data. On the other hand, a variety of cases can be explored quickly by means of mathematical models. Also the trends which are difficult or even sometimes impossible for experimentation can be investigated by the use of such models.

We intend to present here an overview of mathematical models in the realm of Biomechanics of Head Impact. In order to have a better understanding of the modelling of head impact problems and the mechanism of the physiological problem of brain injury it is essential to have some knowledge of the anatomy of the cranial vault, mechanical properties of different components of the head structure and associated matters. It is with this end in view, the relevant topics will be first discussed briefly.

Components of the Human Head

The human head consists of the scalp, the skull, the dura, the pia-archnoid complex, the brain (cf. Fig. 1), the blood vessels, the cerebrospinal fluid and the blood. The head-neck junction must also be taken into consideration inasmuch as its physical characteristics significantly affect the response of the head either to a direct impact or to accelerations induced in some other parts of the body.

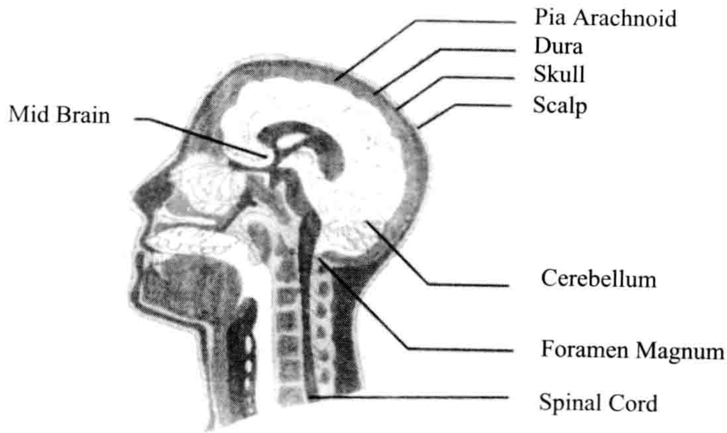

Fig. 1 : A Median View of the Human Cranial Vault

The **scalp** is the outermost component of the head; it is a combination of five different tissues overlaying the cranial bone. It has a leathery consistency and is under a constant low tension in the living human. This leathery layer is arranged in a descending sequential order as (i) the skin with its hairy covering, (ii) the layer tela subcutanea (loose fibrous connective tissue that binds the skin to the deeper structures), (iii) the aponeurotic layer (a fibrous structure representing very much flattened tissue that connects the frontal and occipital muscles), (iv) a very loose subaponeurotic layer of connective tissues and (v) the pericranium (a tough vascular membrane with a somewhat looser zone).

The **skull** rests upon the upper end of the vertebral column and its structure is divided into two parts – the cranium and the face. The cranium is composed of eight separate bones viz. one frontal, two parietal, two temporal, one occipital, one sphenoid and one ethmoid while the face is comprised of fourteen bones forming the skeleton of the face. As the face appears to have a negligible influence with respect to the production of brain injury, which is of prime concern in the present discussion, its further consideration for the subsequent treatment is deemed to be unnecessary.

Next inward skin is known as **dura**. It consists of two layers of dense fibrous tissues – the outer layer forming the lining of the skull while the inner layer provides a protective covering for the brain and the spinal cord. The venous blood from the brain is drained into venous sinuses, which are formed between the layers of dura matter. This matter continues downwards to line the vertebral canal and goes beyond the end of the spinal cord.

The next inward tissue, the **arachnoid,** a non-vascular membrane is separated from the dura by a narrow non-communicating capillary known as the **subdural space**, which is filled with a lymphlike fluid. There is another delicate membrane known as **pia** closely investing the brain and contains white fibrous tissues and the arachnoid is connected to it. The cerebrospinal fluid flows within the sub-arachnoid space where the arachnoid matter is separated from the pia matter by a definite space. It continues downwards to envelop the spinal cord and ends by merging with the dura matter at the level of the second sacral vertebra.

Composition of the Brain

The brain mass which is almost completely enclosed by the skull (except for the foramen magnum), consists of the cerebrum, the mid brain, the pons varolii, the medulla oblongata and the cerebellum. The **cerebrum** constitutes the largest part of the brain and is divided by a deep cleft named the longitudinal cerebral fissure into two distinct parts – the right and the left cerebral hemispheres. Both the hemispheres are connected by a mass of white matter or nerve fibers to the deep within the brain. The superficial part of the cerebrum is composed of nerve cells or gray matter forming the cerebral cortex. Each hemisphere of the cerebrum is divided into various lobes by means of superficial grooves viz. frontal, parietal, temporal, occipital, limbic and insula lobe. The midbrain occupies the region of the brain between the cerebrum above and pons varolii below. The fibers from the cerebrum and the spinal cord pass through the mid brain up to the cerebrum and descend from the cerebrum to the cerebellum and the spinal cord. The nerve cells act as relay stations for the ascending and descending nerve fibers. Two groups of nerve cells provide cell stations for the transmission of nerve impulses from the optic nerves and the vestibular portion of the auditory nerves to the cerebellum. These nerve impulses play a dominating role in the maintenance of balance of the body. The pons varolii is accommodated in front of the cerebellum below the midbrain and above the medulla oblongata. The nerve fibers of this region form a bridge between the two hemispheres of the cerebellum, which pass between the higher levels of the brain and the spinal cord. There are also a few groups of nerve cells within the pons which act as relay stations and some of these are concerned with cranial nerves. The medulla oblongata occupies the region between the pons varolii above and below the spinal cord, which lies just within the cranium above the foramen magnum. Grey matter or nerve cells lie at the centre of the medulla while a few of these cells constitute relay stations for sensory nerves ascending to the cerebrum. The next and the last constituent of the brain is **cerebellum** which occupies the region behind the pons varolii and immediately below the posterior portion of the cerebrum. It consists of two hemispheres separated by a narrow median strip. The gray matter is found forming the surface of the cerebellum while the white matter lies deeply forming a branched appearance.

Macroscopically, the egg-shaped brain is something like a gel and composed of (i) about 78% water, (ii) 10-12% phospholipids, esters containing phosphate, fatty acids and nitrogenous compounds, (iii) 8% protein, (iv) small amount of carbohydrates, (v) some inorganic salts and (vi) soluble organic substances. The length and transverse diameter of the human brain are about 165 mms and 140 mms respectively. The average adult brain is 1200 c.c. by volume and 1500 gms by weight.

Mechanical Properties of the Different Components of the Human Head

The experimental observations reported by Advani and Owings[1] and Gurdjian[2] indicate that the outermost component of the head, viz. the scalp possesses viscoelastic properties. The average value of the bulk modulus has been reported to be approximately 2 GPa while the ultimate tensile strength and elongation are reported to be around 0.46 MPa and 54% respectively. Moreover, the scalp is anisotropic and inhomogeneous; its thickness varies from 6.5 mms to 13 mms.

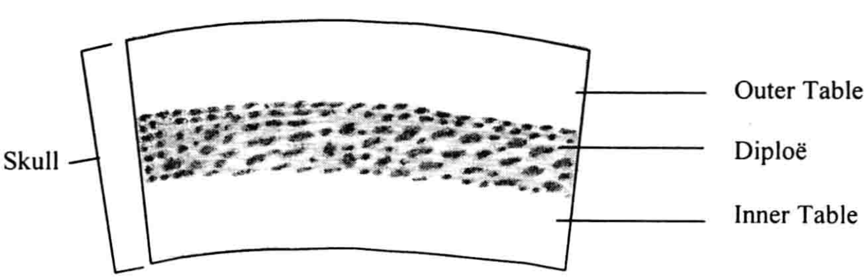

Fig. 2 : Three Layers of the Skull Bone

The skull consists of an outer and an inner table of solid bone (cf. Fig. 2) separated by a trabecular domain (diploë) with a total thickness ranging between 6.5 mms and 7.9 mms. As mentioned earlier, the skull consists of eight separate bones, their junctions in an adult specimen are so calcified that it composes a single structural unit. Thus mechanically the skull material is non-homogeneous and non-isotropic. The mechanical properties of skulls reported by various researchers (Haynes et al.[3], Hubbard[4], McElhaney et al.[5], Melvin et al.[6,7], Robbins and Wood[8], Roberts and Melvin[9]) seem to vary widely; it appears that the properties vary according to the sites of a given skull specimen. The different conditions (e.g. biopsy, autopsy, frozen, embalmed etc.) also contribute to the determined physical constants of the tested specimen. For unembalmed compact skull bone the average isotropic values of the tensile and compression modulus have values around 14 MPa while the tensile and compressive strength are approximately 70 and 165 MPa respectively. The tensile failure strain seems to lie in the range 0.55 – 0.70%. The average value of the compressive strength of the diploë is 34 MPa. When the skull is treated as a composite structure possessing transverse isotropy, the average radial compression modulus ranges from 0.4 to 2.6GPa while the compression modulus ranges between 2.6 GPa and 5.6 GPa. Also the modulus in tangential tension varies between 5.4 GPa and 8.8 GPa. The Poisson's ratio ranges from 0.19 to 0.22. Corresponding to a structural Young's modulus of 10.2 GPa, Hubbard[10] determined the bending stiffness of the skull as nearly 2.75 Nm^2. The equivalent shear modulus was found to vary in the ranges 138-745 MPa and 138-690 MPa for the composite and for the core respectively. Melvin and Evans[11] as also Wood[12] reported the values of the ultimate strength in the ranges 71-145 MPa and 50-97 MPa when the samples were tested in radial compression and in tangential compression respectively, the value in tangential tension being 43 MPa.

Piekersky[13], Pope and Outwater[14] as also Wright and Hayes[15] observed that the stress intensity factor (S.I.F.) of cranial bones varies with the density of cranial bone; for a specimen of density 2 Kg/m^3, the S.I.F. has got the value 4.0 $MN/m^{3/2}$, the corresponding strain-energy release rate being reported to be 1600 $N\text{-}m/m^2$.

Vibration modes in living humans have been found by Gurdjian[2] and Gurdjian et al.[16] at about 300 (antiresonance) 600 and 900 Hz (resonance), with some variability depending upon the location of the driving force and topography of the individual. Below 200 Hz, the skull moves as a rigid body and will so respond to impacts of more than 5 ms duration. The quasistatic elastic modulus and ultimate shear strength of dura were found to be 42 MPa and 2.3 MPa while its complex Young's modulus has been determined as 32.8 + 3.45 i MPa from free vibration tests at a particular frequency of 22 Hz by Galford and McElhaney[17].

Experiments show that brain exhibits viscoelastic properties. Its bulk modulus is around 2 GPa (almost equal to that of water). Jamison et al.[18], Galford and McElhaney[17] and Goldsmith[19] reported that for a direct shear at 10 Hz, if the complex modulus G* be represented as $G^*_1 + iG^*_2$, the ranges for G^*_1 and G^*_2 are respectively 550-1100 Pa and 225-655 Pa. But the corresponding ranges for torsion tests executed from 2-400 Hz were found to be 827-137, 900 and 345-82, 700 Pa respectively. Mertz et al.[20] carried out experiments on animal brain and observed a decrease in modulus with time after death. Completely different values ranging between 0.46 and 50 poises were reported by various investigators for the viscosity of brain, at normal body temperature, the difference being attributed to the method of measurement. It was remarked that an average value of around 40 poises near 20°C might be taken for practical purpose.

The blood vessels of the cranial vault are nonlinearly viscoelastic. It was reported by Yamada[21] that the ultimate tensile strength of a carotid artery is around 115 KPa and the ultimate elongation is approximately 36%. These values correspond to human specimens of the age group of 20-29 years; of course both of these values decrease with increasing age.

Yamada[21] also found that the average ultimate tensile strength and ultimate elongation for cervical vertebrae are around 0.33 MPa and 0.8%. Also stress-strain curves for vertebrae, discs and skeletal muscle exhibit concave upward trends.

The main mechanical properties of dura which represents the interior lining of the skull, are anisotropy and inelasticity.

The pia-arachnoid complex is made up of a gossamer tissue whose strength characteristics are ignorable. The cerebrospinal fluid contained in the subdural space is a colourless fluid having specific gravity of 1.004 – 1.008 and can be approximately represented as a Newtonian fluid.

Experiments on Skulls of Cadavers, Live and Dead Animals and Use of Experimental Models

All the experimental studies referred to in the preceding section were made for the determination of the mechanical properties of different components of the cranial vault. In the present section, an attempt is made to briefly review some of the important experimental investigations which were performed on the skulls of embalmed and unembalmed cadavers, live and dead animals and artificial head forms in order to ascertain causes of head injury and to collect enough pathological information to establish tolerance limits.

Evans et al.[22] studied the relationship of energy, velocity and deceleration with skull fracture in their experimental investigation. The intact human heads from adult embalmed cadavers were taken in their free and guided fall tests with an automobile instrument panel and they came to the conclusion that not only the magnitude of the available energy but also its rate of absorption is important to study the mechanism of skull fracture. Lissner et al.[23] investigated whether or not the body weight augmented the impact of the head in the sense that whether the body attached to the head produced a more severe impact to the head than if the head alone were dropped on the panel. By making a gelatin-filled head strike a thin steel plate, an automobile panel and a large steel block they tried to establish a relationship between the acceleration and the intracranial pressure. Gurdjian et al.[24] observed the areas of different stress levels in the skull subjected to blows in various locations on the skull surface and finally correlated their observations with clinical skull fractures. Gurdjian and Lissner[25] investigated the relationship between intracranial acceleration and impact velocity in their experiments in which the heads of human cadavers struck laminated tempered safety glass panels.

Mertz and Patrick[20] observed the kinematics of rear-end collisions based on known acceleration pulses of actual car-to-car collisions on a crash simulator using anthropomorphic dummies, human cadavers and a volunteer. The responses of both the dummies used were not comparable with those of cadavers or the volunteer or to each other. Based on their observations, they arrived at a conclusion that the head torque rather than the neck shear or axial forces is the major factor in producing neck injury. Ommaya et al.[26] tried to illustrate the possible injury mechanisms occurring in whiplash and head impact. From their experimental observations on monkeys they concluded that multiple mechanisms are involved in cerebral concussions; among them rotational acceleration of the head, flexion-extension-tension of the neck and intracranial pressure gradients are perhaps the most significant. Patrick[27,28] performed an experiment impacting cadavers with automobile windshields to investigate the potential head and neck injury.

Hodgson et al.[29] measured the force input by using a force generator directly to the skull of an embalmed human cadaver and obtained the effective mass and stiffness in the frequency range 5 - 500 Hz with the help of a linear simple degree of freedom model. The driving point impedance characteristics of the human and monkey heads over the frequency range 30 - 5000 Hz was determined by Stalnaker et al[30]. In vitro experiments on a fresh human cadaver as also both the in vivo and in vitro experiments on monkeys were carried out. Using a linear two-degree of freedom model, the results were presented with appreciable accuracy.

Holbourn[31], in his experimental study with a gelatin-filled model, illustrated the stress patterns generated between the brain and the skull owing to an input angular acceleration. He also observed that the shear strains produced by linear acceleration are found mainly in the neighbourhood of the foramen and in the neighbourhood of the ventricles due to slight differences in density between the cerebro-spinal fluid and the brain tissue. He further concluded that the shear strains produced by linear acceleration could be neglected compared to those produced by rotational acceleration. Gurdjian and Lissner[25] observed that the generation of pressure gradients arising from acceleration or deformation of the skull may cause shear stresses in the brain stem area. They used a two-dimensional photoelastic model to show that the region of the craniocerebral junction is an area of high shear stress concentration.

Unterharnscheidt and Sellier[32] pointed out that head acceleration and skull deformation produce intracranial pressure changes in sufficiently reduced form which result in cavitation at the antipole and points of skull outbending. They claimed that this cavitation hypothesis is the principal cause of brain damage. Gross[33] produced experimental cavitation by impacting water-filled flasks. By taking a water-filled human skull, the pressure gradients were measured in three mutually perpendicular directions by Roberts et al.[34] and the regions of negative pressure were pointed out. Gurdjian and Lissner[25] also concluded that the foramen magnum of the model is a region in which an external blow to the skull responds in the development of shear strains in the fluid. A plastic model of a sagittal section of the skull including foramen magnum filled with 1.5% solution of milling yellow was used for their experiment.

Head Injury Mechanics, Different Types of Head Injuries

That the behaviour of a head during and immediately after the application of a blow can be studied by employing Newton's laws of motion through the use of the physical properties of the various components of the head, indicates that there exists a mechanics of head injury.

An injury to the head may occur due to damage of its various components, viz.

(i) **Scalp damage** : A damage to the scalp may occur owing to an impact with a sliding object, which may result in denuding the superficial skin or due to a cut of the skin by a sharp object. The injury to the scalp may also involve leakage of blood from the broken vessels into surrounding tissues below the skin.

(ii) **Skull damage** : There may be various reasons for skull damage. It may be in the form of a depression of the skull due to a high speed projectile or a heavy falling object (e.g. bricks or stones) or interior vehicular structures under crash conditions, which may lead to perforation of the skull bone and fracture. The depression may also be caused due to a missile, which may lead to fragmentation of the bone. A damage to the skull may also occur due to a static or quasi-static loading on it, produced by a relatively long time crushing of a heavy object. In the case of young children where the skull is a bit softer, there may be a permanent deformation of the skull without fracture.

(iii) **Brain damage** : The two types of damages to the head, described above are invariably due to a direct impact or a blow, whereas a direct impact or an impulsive load due to a sudden acceleration (or deceleration) of a considerable magnitude can cause brain injury. The injury may be in the form of concussion, contusion, laceration or intercerebral hematoma. In most cases, an injury to the brain can not be easily detected. This is why, the occurrence of brain injury has to be speculated by neurological or physiological malfunction. Based upon the observations of past experimental as well as theoretical investigations on intracranial trauma, three different, relatively independent, postulates have been put forward, which help understanding the growth and development of neurological damage.

Hypotheses on Brain Damage

The first hypothesis for explaining the mechanism of brain injury, usually described as the **cavitation hypothesis**, illustrates the contrecoup lesions, which are usually observed at the pole opposite to the point of impact. According to this postulate, following an impact on the head, an area of negative pressure is developed at the contrecoup site and this causes capillary rupturing in this region. The pressure in the contrecoup region is described as 'negative' by Unterharnscheidt and Sellier[32] in the sense that the pressure is less than that before the impact has occurred. They examined