

Biological and Medical Physics, Biomedical Engineering

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Liquid Crystals in Biotribology

Synovial Joint Treatment

 Springer

Liquid Crystals in Biotribology

BIOLOGICAL AND MEDICAL PHYSICS, BIOMEDICAL ENGINEERING

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Preface

The book is given over to study of nature of abnormally low friction and wear of human and animal joints. Trends in joint function and lubrication, possibilities of rheological correction and cartilage mechanodestruction prophylaxis during arthropathies are generalized.

The complex researches of cartilage friction process in natural and artificial lubricants that lead to breakthrough understanding of joint boundary lubrication nature take a large part of the book. It has been proved that liquid-crystal state of synovial fluid, such as cholesteric-nematic crystals, plays an essential role in intra-articular friction decrease. The results of this discovery have fundamental and applied meaning. They greatly expand up-to-date understanding of the role of liquid crystal in biological tribosystem function and expose a completely new trend of joint lubrication properties research.

Creation of novel pharmaceuticals—artificial synovial fluid reproducing lubrication mechanism inherent to natural synovia—a new and important balance of the work.

Experimental and clinical data on chondroprotective efficiency of preparation are of practical interest for further research in the field. It should be noted that only a combination of biological, technical, physical, chemical and medical knowledge makes it possible to investigate the lubrication mechanism of joint cartilage and the prophylaxis methods of premature wear.

The book should be of interest to communities of scientific workers, practitioners and students of medicobiological and technical specialties. It will draw the attention of researches to problems of biotribology, chondroprotection, liquid-crystal biological environment function and creation high-performance materials for endoprosthetics.

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Acronyms and Nomenclature

ANS	8-aniline-1-naphthylsulphonate (fluorescent probe)
BS	Blood serum
C	Cholesterol
CE	Cholesterol ester
CL	Common lipids
DMSO	Dimethylsulfoxide
HUA	Hyaluronic acid
LC	Liquid crystal
LCCC	Liquid-crystal cholesterol compound
MP	Medicinal preparations
Na-CMC	Sodium carboxymethyl cellulose
NCID	Non-steroid counter inflammatory drugs
NSA	Non-steroidal anti-inflammatory drugs
PVP	Polyvinyl pyrrolidone
RF	Rheumatoid factor
RSR	Relative specific radioactivity
SAA	Surface active agent
SCMC	Sodium carboxymethyl cellulose modulus of tension
SF	Synovial fluid
SR	Specific radioactivity
TG	Triglycerides
E	Modulus of tension
F_a	Adhesion component of friction
F_c	Cohesion component of friction
F_f	Friction force
G	Coefficient of rigidity
I_{fl}	Fluorescence strength
K	Forces of action of body weight part

K_{22}	Elastic constant
M	Forces of action of lateral abductor muscles
P	Reliability
Q	Liquid volume flow
R	Resulting compressive forces
S	Liquid crystal order parameter
S_5	Body center of gravity
T	Temperature
W	Free energy of liquid crystal
W_s	Surface energy of liquid crystal
W_e	Elastic energy liquid crystal
a	Cholesterics molecular layer thickness
b	Extrapolative path
d	Thickness of liquid crystal
h	Thickness of lubricant layer
h_i	Range of sinusoidal relief
h_l	Thickness ratio of lubricant layer
Δh	The thickness of the specimen
k	The coefficient of permeability
Δl	Deformation
\vec{n}	Unit vector (director)
p	Pressure
\tilde{p}	Dimensionless pressure
Δp	Differential pressure
S	Pitch of the helically-coiled cholesteric
t	Time
v	Speed
Φ	Pressure in the fluid
Θ	Calorific endothermal effect
Ψ	Pressure in the articular cartilage
α	Angle
η	Viscosity
φ	The angle of molecular orientation in cholesteric
λ	Wave-length of sinusoidal relief
θ	The angle of director orientation \vec{n} relatively to the instantaneous direction of the cholesteric major molecule axis
ρ	The radial measure in the cartilage
τ	Dimensionless time parameter

Introduction

Synovial joints is a unique biological body of movement (motion). They can function under significant live loads, at high and low speeds for a long time and not wear for lifelong. A study that deals with the design, friction, wear and lubrication of interacting surfaces in relative motion is called tribology. In spite of considerable progress in tribology in recent years, neither technical unit exhibits the same friction characteristics as natural joints do. Therefore, synovial joints are of great interest to present and future tribology. Investigation of such complicated processes can be made at the intersection of disciplines about the physical and chemical properties of rub surfaces, the interaction of a solid phase and its field with atoms and molecules of various substances, mechanics of solids and liquids and others. Thus, tribology is an up-to-date cross-disciplinary science that encompasses various aspects of the world.

Biotribology is a medical-biological branch of tribology. It studies friction interaction of biopolymer composites having unique structure—cartilages in the synovial joint of humans and animals. Comprehension of joint tribology opens up great perspectives in the destruction pathogenesis during trauma and arthropathies. Thus, one can also speak of development of new methods for effective cartilage protection against premature destruction and wear.

Biotribology arose with swift advance in the past five decades. A significant amount of information about friction and wear features of joint cartilage in health and disease, importance of joint structure specificity, joint surface macro- and microgeometry, biochemical composition and rheology of synovial fluid for load transfer and decrease, joint kinematics and lubrication has been collected.

It is doubtless that the biotribology developmental pathway is closely associated with researches in frictional interaction of various materials and units in engineering. Simultaneously, researches in engineering cannot be automatically used in tribology of synovial joints. It is impossible to describe their abnormally low friction and wear nowadays.

Meantime, the authors think that abnormally low friction of joints is conditional upon synovial fluid lubricity. The last achievements in physics of liquid crystals and

the obtained data on their unique lubricant properties are very promising and encouraging.

It has been found that liquid-crystal state is inherent to a number of biological tissues and matrixes, but there were no similar evidence for synovial fluid. Therefore, research of cholesteric liquid crystals and definition of their role in natural lubrication is considered to be a brand new scientific approach to further knowledge of the nature of articulate cartilages abnormally low friction, and also to development of new arthropathy treatment mode.

Intensive biotribological researches are carried out mainly in England, the USA, Germany and some other countries in recent years. Similar works are also conducted at research institutes and laboratories in Gomel, Minsk, Moscow, Vilnius, Kiev and Ivanovo. The primary goal of this study is to create artificial synovial fluid for destruction prophylaxis and new effective biopolymer self-lubricating materials for joints endoprosthetics. However, the available scientific works and publications on biomechanics and tribology of the joint synovial have incidental character, and are insufficiently generalized.

In the work the authors made an attempt to analyze the available literature data on structure and function features of synovial joints, lubrication mechanisms, pathogenesis of cartilage mechanodestruction and opportunities of its prevention with known pharmaceuticals and physical factors.

Our own study of cartilage friction and wear, experimental and theoretical proofs of interfacial liquid-crystal state of synovial fluid, justification for new intraarticular friction decrease concept and a new scientific field for creation of artificial synovial fluid and new arthropathy treatment mode take up a large part of the book.

The authors hope that this study will be of interest and use for not only arthrology, biomechanical and tribology experts, but also the engineering, medical and biological communities.

Chapter 1

Biomechanics of Joint Synovia

Abstract In this section summarizes the results of research into the field of living synovial joints and structural elements of the environment. Construction features of synovial joints are analyzed as of kinematic pairs capable of operation under considerable loads. Molecular and supermolecular structural arrangements of cartilage matrix and their influence on the deformation properties of cartilage tissue are considered. The latter is underlined to act as a specific damper of dynamic loads which participates in uniform distribution of pressure in joints. An analysis is presented of synovial fluid both as a lubricating medium and an active structural element of joints performing important biomechanical functions together with the cartilage tissue.

Everyday life of human and animals is known to be continuous motion and it is inseparably linked with normal functioning of the synovial joints [1–3]. Exceptional reliability and durability of joints as natural friction elements depends directly on the nature of their structure, mechanical properties and principles of functioning. Their main structural elements are two mated bone contacts coated with hyaline cartilage that is enclosed in the articular lined with the synovial membrane and filled with the synovial fluid [1].

According to modern ideas, the entire of complex of structurally differentiated, yet morphologically integral and functionally combined tissues is conventionally termed as “the synovial medium in joints”. Only interaction and interdependence of the elements of the articulation medium, like the synovial membrane, synovial fluid, and articular cartilage, are capable to produce optimal biophysical conditions, perform metabolic processes between the articular cavity and blood vessels and frequently to maintain high performance of joints in extreme conditions and for prolonged periods. This idea about the synovial medium of as an integral organ specific system is fundamental in studying any matters of functioning of the joints.

1.1 Kinematics of Synovial Joints

At present, the anatomic structure of synovial joints is rather well known (Fig. 1.1). According to modern ideas, the synovial joints are dynamically loaded movable articular members of the skeleton in which (translational and rotational) motions take place various in scopes and degrees of freedom. The variety forms of joints of humans and animals makes it impossible to imagine their functional features by a single-unified model [4].

The hip joint is a classic example of the ball articular joint with three degrees of freedom. It is a compact union of the femoral head almost spherically shaped ball and the pelvic acetabulum shaped hemispherically that form a multiaxial system with an extensive scope of motions. Therefore, the joint in the average physiological position is capable to contract and extend in the sagittal plane within 140° , to retract and extend the extremity in the frontal plane within 50° , to rotate it around the hip longitudinal axis through 50° in the horizontal plane. The motions are limited by the tension in the capsule, ligaments and muscles and can vary considerably in response to the joint spatial position, e.g., when the hip is bent, moved away, etc.

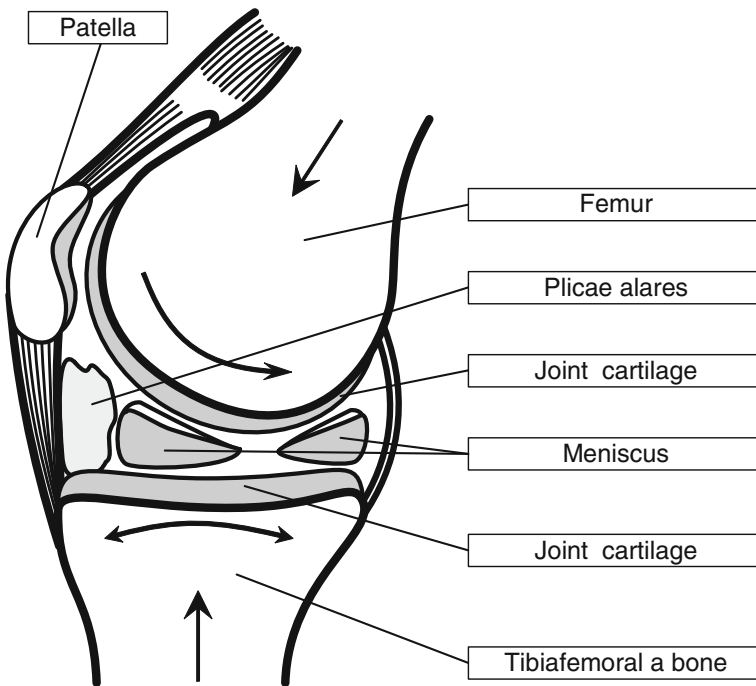


Fig. 1.1 Anatomic structure of knee joint

The knee joint performs two main independent motions: flexion-extension movements of the tibiofemoral joint within a sufficiently large range (up to 140°) in the sagittal plane and limited rotational movements (up to 10°) of the shinbone in the horizontal plane at the terminal extension stage. When deflecting the knee through over 45° , the shin relaxes and the limiting functions of the capsule joint apparatus can increase sizably.

In addition to these complicated joints, other joints almost coincide with a sheave. The talocrural joint can be likened to two cylinders resembling a well-fitted radial bearing with a single degree of freedom practically and limited rotation limited by the articular apparatus. The joint between the shoulder and elbow bones has a similar structure serving just to bend and extend the forearm in the elbow. In this case, the extra lateral movement of bones is impossible because the collateral ligaments are close to the axis of rotation and the sliding surfaces of this sheave-like “pivot” have a specific anatomic structure.

This different natural design of the joints is certainly dictated by their specific locomotor functions and simultaneously the need to maintain high mechanical properties [5]. Therefore, from the viewpoint of the mechanics, the joints of animal and human extremities are very effective kinematic pairs capable to withstand considerable loads during prolonged period.

Investigation of the principles of the structure and functioning of different elements of the human and animal locomotorium revealed that both the position and the resulting forces affecting on partial elements of joints and neighboring bones [6, 7] determine their physiological loading in natural conditions. The resulting force pressing on the head of the hip joint is composed of the body weight and muscles that stabilize the pelvis normally in case the body center of gravity displaces (Fig. 1.2).

The line of the resulting effect passes medially across the hip head and laterally to it at a vertical angle $15\text{--}20^\circ$. As a result, the diagram of loading of the hip joint has the peak loadings acting on the hip head and exceeding the body weight three to nine times, i.e. the order of magnitude of $700\text{--}6300$ N. These peaks appear at extreme amplitudes of oscillations, then the loading drops to the minimum in the sweep middle. Thus, the hip joint has to withstand during a year up to 2.5 million of cyclic loads and accomplish a considerable scope of movement, such as bending-unbending within a range of $45\text{--}60^\circ$, extension-contraction at the same time within a range of $11\text{--}12^\circ$, rotation through $6\text{--}14^\circ$, at a relative sliding speed of articular surfaces in different periods of a walking cycle $0.01\text{--}0.05$ m/s.

The biomechanics of other elements of the human and animal locomotorium have its own specific features [8, 9]. The hip joint bends to almost 160° [10, 11], however, during normal ambulation the bending ranges just within $60\text{--}67^\circ$ [12]. The shinbone in the unsupported phase is in the position of external rotation in respect to the hip condyle. At the moment the foot reaches support when the knee fully unbends, it acquires active and passive stabilization by the articular, capsular, and muscular apparatus. When the hip condyle reaches the terminal unbending stage the condyles rotate internally in respect to the tibial plateau.

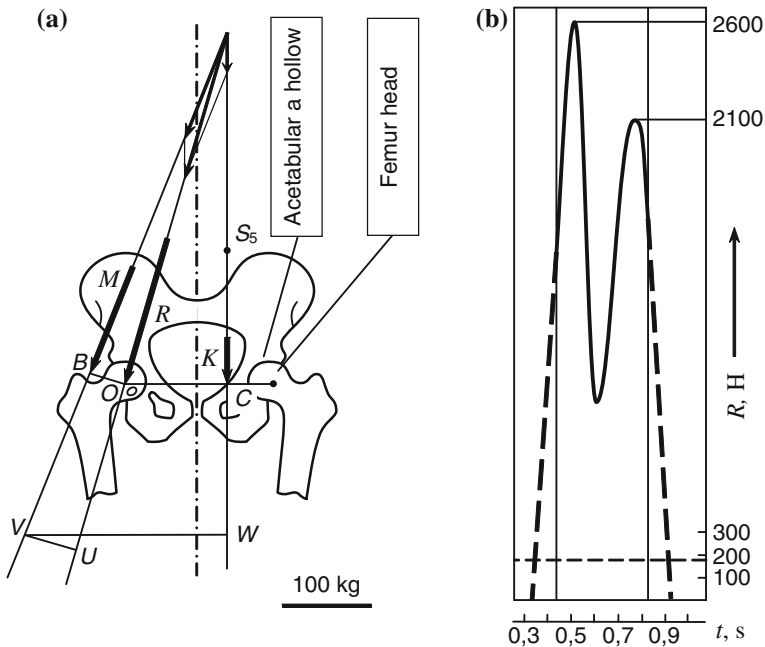


Fig. 1.2 Main elements of hip joint pivot unit **a** and diagram changes of compressive forces in hipbone head within step cycle **b** [8]. S_5 body center of gravity; K forces of action of body weight part; M forces of action of lateral abductor muscles; R resulting compressive forces

Rotation of the shinbone is limited by collateral joints actively and by a specific configuration of the articular surfaces passively [1, 13]. The sections show that axial compression is capable independently to stabilize the unbent knee after transversing all the ligaments, including the cruciform ones. The cruciform joints limit actively the displacement of mated articular surfaces in motion in the ventrodorsal direction. The posterior cruciform joint is the main knee stabilizer. Relaxation of all the ligaments during rotation in the terminal unbending stage is a prerequisite of the normal functioning of the knee joint because it reduces the contact pressure on the medial portions of the shinbone. It is noteworthy that unbending of the knee increases the curvature of the hip condyles, normally more of the internal always than the external one.

Moreover, the essential role in the knee stability belongs to the capsular-articular elements and meniscuses, especially in the retromedial portion of the joint [14].

As the knee joint motion is exposed to five forces: axial, ventrodorsal in the sagittal plane, medial lateral in the horizontal plane and two moments of rotation relatively to the shinbone bone axis in the ventrodorsal axis, the ventrodorsal and medial lateral forces play just a secondary role as compensating forces to balance movements in these directions. At the same time, the forces of rotation in relation to the shinbone axis bone and ventrodorsal axis can redistribute the forces of flow

from the lateral portion of the joint towards the medial portion. It is believed that the exterior hip condyle in the physiological conditions is loaded three or four times heavier than the interior condyle [14]. The knee joint may experience considerable forces that depend on the dynamic loading conditions. For example, it is noted in [15] that its elements when ascending a stairway may be affected by forces of the order of magnitude 150 Nm; when standing up after low crouching this joint can be exposed to the loading five times exceeding the body weight.

Nevertheless, the time dependence of the resulting forces in the knee joint can have a similar pattern to that in the hip joint: it is determined by a significant straining of muscles and ligaments in addition to the load bearing force.

The latter play quite an important role in the knee joint biomechanics, controlling the physiologically comfortable positions, redistributing and reducing the compressive forces affecting the articular contact [8]. The paper [16] that changes of the length of ligaments redistribute contact forces, while shifts in the points of attachment of muscles do not practically affect them.

The effects in motion of the knee joint due to the spatial position of the centers of its rotation contribute sizably to the biomechanical process. It is known that the knee due to the ellipsoid form of the hip condyles does not have any permanent center of rotation typical for common pivots. Therefore, when it unbends and the radii of curvature of the condyles grow the center of rotation moves along an arcuate line. However, the latter deviates from the line of arrangement of momentary centers of rotation of the joint. It can be traced vividly if one imagines the joint as a closed crossing four-link kinematic chain with two parts having the same degree of relative motion freedom, i.e. ignoring conventionally rotation of the shin bone in the terminal unbending stage and assuming that the cruciform joints are constantly stretched (Fig. 1.3). Modeling of rotation of links AD , BC (the cruciform joints) and AB (the tibial bone) around the fixed hip link DC enables to obtain a dorsal movement of momentary centers of rotation best reproducing the functional features of the natural knee joint. The diagram makes it ultimately clear how to interpret many features of functioning of joints in physiological norm and in pathology.

The analysis in [17] proves that application of a longitudinal compressive force via a joint to a joint boosts its stability, on the one hand, but limits its degrees of freedom and that can change the joint mechanical properties due to movement of the momentary centers of rotation in space. A position of the knee joint center of rotation depends on the extent of initial compression and can displace by over 0.02 m. An essential fact too that the momentary centers of rotation in the hip intercondyle pit (the fixed element) of the lie mutually closer than in the unloaded joint. As a result, the sliding speeds under these conditions differ little and their directions coincide with the articulation slot line. A significant scatter of the momentary centers of rotation, e.g., in case of injury of the meniscus, ligaments, or changes in the configuration of mating surfaces, induce extra forces with the speed vector different from the articulation slot line and directs it a certain angle to it. Friction in the joint intensifies joint, the cartilage is continuously microtraumatized, degeneration centers appear, and mechanodestruction follows.

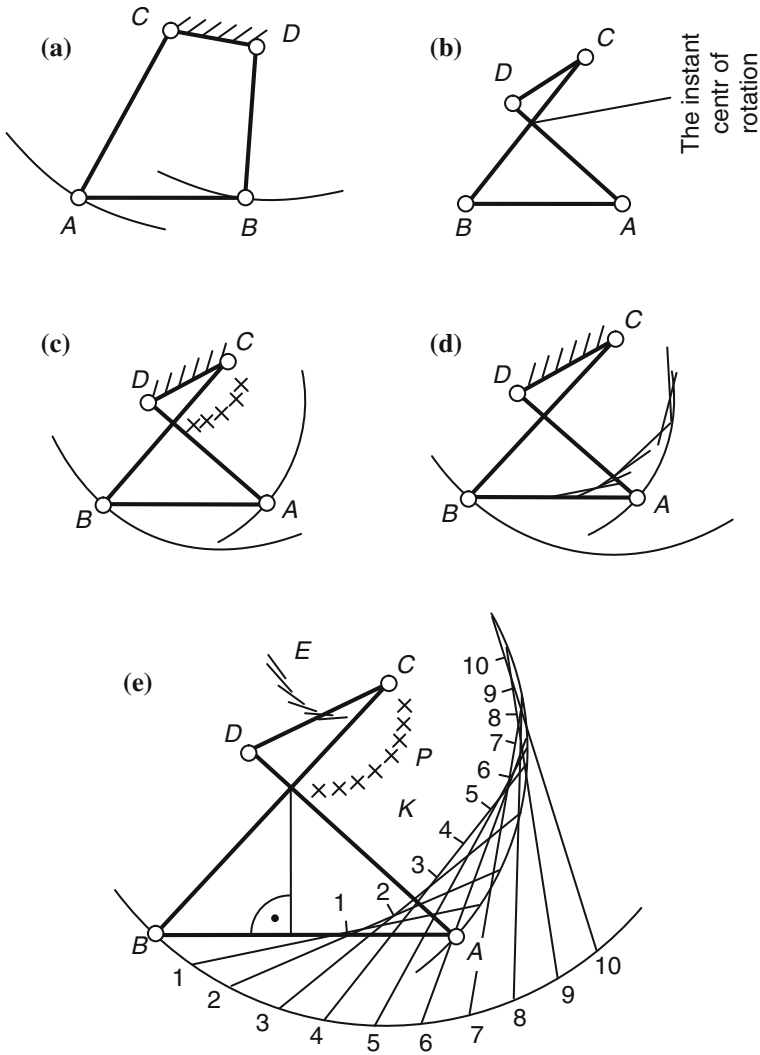


Fig. 1.3 Four-link knee joint kinematic chain: **a** closed Four-link kinematic chain; **b** crossed kinematic chain; **c** crossed kinematic chain showing passage of axis of motion of knee through momentary center of rotation in point of intersection of cruciform ligaments when hip component is fixed; **d** crossed kinematic chain showing curvature of contours of hip when shinbone moves; **e** crossed kinematic chain showing geometrical arrangement of tibiofemoral contact points during knee bending [13]. *AB* intercondyle shinbone hill; *BC* crossed kinematic chain of anterior cruciform joint; *AD* posterior cruciform joint

Therefore, operative interventions are biomechanically justified when it is necessary to correct the centers of rotation of pathologically altered joints and can restore their normal functioning in a number of cases.

From the viewpoint of transmission of the supporting loading the geometrical characteristics of joints are essential, such as forms of dynamically contacting surfaces and their mutual compliance (congruence) that determine the extent of mobility of articular ends, the amplitude of their motion and the number of axis around which they move. It is believed that working contact joints are fully loaded in only one position corresponding to transmission of the maximum force via the joint [18]. The articular contacts in other positions are incompatible, i.e. incongruent. As a result, loads of various magnitudes and directions in the hip joint can produce four contact types: a usual contact that occurs under inconsiderable loads; a contact in response to a position of joints; a contact in response to loading and occurring only under considerable loads; no contact between surfaces at all at any joint position and load.

The data about the actual contact area in different joints are controversial. Paper assumes that the actual contact area in each knee joint condyle under load is 1–2 cm². However the results in [12] show that the mean supporting area of the interior condyle of the unbent knee is 2.5–6.7 cm², that of the exterior condyle is 1.7–5.1 cm², i.e. 1.6 times less than that of the interior one. It is believed that the surface contact reaches 4 cm² in the hip joint under full loading. Thus, it is apparent that the articular surfaces have sufficiently high contact pressures of 60–70 kg/cm² under maximum loads exceeding the body weight three to nine times [19].

Mechanical interactions between articular surfaces are known to occur always through the layer of a compliant composite material—the hyaline cartilage of irregular thickness. The cartilage layer gradually thins away in contact zones in the direction towards the edges of articular surfaces. It is probable that the geometry of the articular cartilage in the contact zone that affect considerably the mechanism of transmission of mechanical forces in the joint. In fact, analysis of the contact interaction of one solid body with another through the elastic interlayer from a homogenous material shows that the geometric characteristics of the interlayer strongly affect both the specific pressure and the pattern of its distribution (Fig. 1.4).

Constant thickness of the elastic interlayer changes the specific pressure in response to the contact angle according to the sinusoidal law, meanwhile the thickness of the elastic layer is variable according to the law of mass and the specific pressure distribution in the contact region is regular. The fact that the cartilage layer in the contact zone between articular surfaces narrows towards the edges permits to assume a similar pattern of distribution of contact forces in joints. Hence, the thickness distribution of the cartilage in the joint is such that during ambulation the pressure on the articular surfaces distributes regularly in the contact region. Whence an essential conclusion is that the cartilaginous layer is a peculiar shock absorber of dynamic loads favoring regular distribution of pressure in the joint. Table 1.1 shows examples of the moduli of elasticity of some materials most frequently used for prosthetic arthroplasty.

Table 1.1 shows clearly that just few possess the mechanical properties comparable with the properties of the joint cartilage as a natural composite material.

Some human and animal joints have fibrous cartilaginous structures or the interarticular cartilage known as the meniscus in addition to the hyaline cartilage

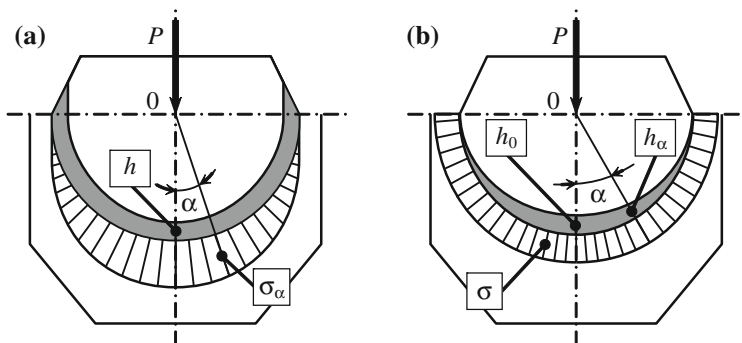


Fig. 1.4 Diagram of contact interaction between two solid bodies separated by an elastic interlayer of inhomogeneous material in response to angle of contact α : **a** specific pressure sinusoidal distribution; **b** regular specific pressure distribution

Table 1.1 Moduli of elasticity of composite materials [19]

Material	Modulus of elasticity $\times 10^3$, MPa
Joint cartilage	0.001–0.17
Natural rubber	0.0025–0.1
Silicon rubber	0.01
Super high-molecular polyethylene	0.5
Bone cement	3.0
Bone	10.0–30.0
Alloy Ti–Al–Va	106.0
Stainless steel	205.0
Alloy Co–Cr–Mo	230.0
Aluminium	350.0

coating the bone [1, 2]. For example, there is a medial meniscus and a lateral meniscus in the human knee joint. In the joint they balance the mismatch between the hip condyle and the shinbone, expand the actual contact area. Their configuration demonstrates it (Fig. 1.5).

The peripheral part of each meniscus is thicker and convex; the central part has a fine free edge. The sagittal section shows an edge-like shape. The medial meniscus resembles a hemisphere that arranges laterally over the entire circumference of the respective shinbone condyle. As a result, the external edges of the meniscus repeat the configuration of the external edges of the tibial plateaus. It is believed that a high congruence of articular surfaces provided by menisci strongly contributes to the joint stability, even if anterior cruciform joint is injured [20, 21].

The unique dumping properties of the cartilaginous tissue in the meniscus, their good adaptability to articular surfaces and extensive contact area with hip condyles play an essential role in undertaking and redistributing continuously variable

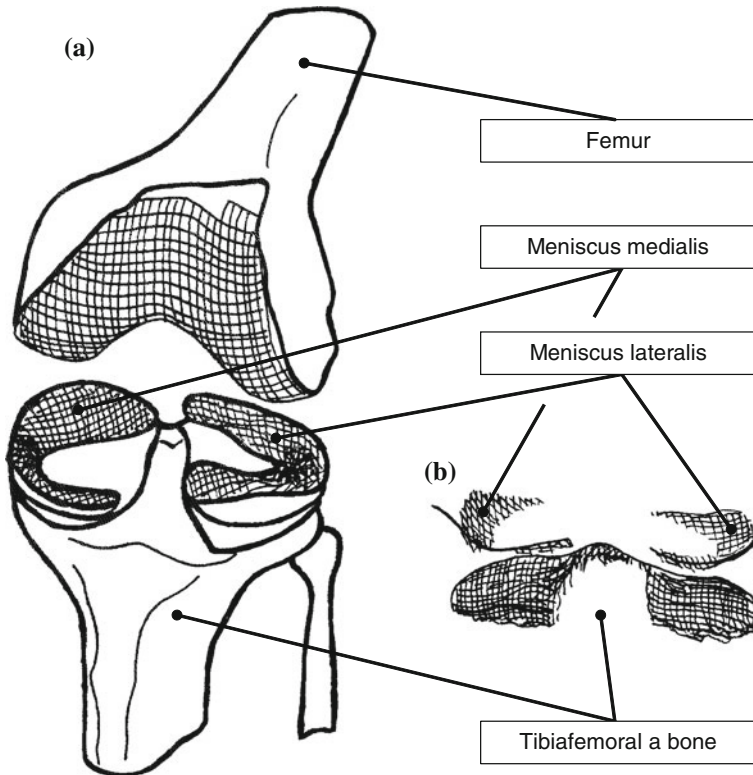


Fig. 1.5 Diagram illustrating contact interaction in knee joint, (a) and stereogram representing contact zones between hip condyles, tibial plateaus and meniscus, (b)

specific pressure in the joint [1]. According to [20], the meniscus bears up to 50 % of the compressive loading when the knee is unbent and up to 85 % when the knee is 90° bent. It is significantly because that the meniscus is capable to change its configuration in response to the angle of bending of the knee joint assisted by the joint capsule along the edges of the tibial plateaus that arrest the meniscus peripherally resisting the effect of the forcing out forces appearing under rather heavy axial loads [1].

A total or subtotal removal of the internal meniscus shrinks the contact in the medial portion of the joint by 50–70 %, hence, the specific pressure on jumps sharply [22]. It may lead to gradual impairment of the dumping properties, degeneration, and mechanical destruction of the cartilage. Numerous clinical observations confirm this fact [23]. A number of experimental models of the early osteoarthritis are based on the meniscus resection [21, 24]. It is noted that degenerative changes in the joint are pronounced and proportional to the area of the removed meniscus segment [20, 22]. That is why in recent years the concept of partial or so-called intermeniscus resection is gaining recognition in case meniscus

damage; the progress of the concept is due to adoption of modern arthroscopic medical surgical equipment [25].

The experiments have shown that partial meniscus ectomy leads in the majority of cases to a significant dysfunction of joints [25]. A probable explanation of this behavior of the locomotorium is that, if the cartilage is normal, and just a slight of the affected meniscus is removed, distribution of stresses in the joint remains practically unchanged and regular [1]. However, it is possible in such cases that arthrosis may reappear [26]. One of the causes of its development may be a disorder of the congruence of the articular surfaces after an operative intervention. It can produce zones the contact of cartilages is fully dependent of the loading magnitude and occurs only in case the forces are large and the zone also, where there is no contact at all under any load at any position of the joints. This boundary region between the zone of permanent contact and its absence is the most sensitive and vulnerable to appearance and development of really centers of degenerative changes in the cartilage. Other more detailed studies confirm it too [1, 22, 23].

Thus, the accomplished analysis of joints as versatile kinematic pairs capable to withstand significant variable loads shows that, alongside with their features, structure, functioning, and biomechanics, the articular cartilage plays an essential role in transmission of mechanical interactions between mated bone surfaces. To perform this function, the cartilaginous tissue should possess specific biomechanical properties that differ from those of other tissues [27]. Their unique structural arrangement in the cartilage can explain it.

1.2 Structure and Functions of Joint Cartilage

The first works in the sphere of chemical composition and structural organization of the cartilage matrix relate to the mid of the last century when J. Hunter studied the morphology of a pathologically altered cartilage in vivo. In 1837, E. Müller exposed the cartilage to heavy pressure and obtained a solution of a substance that he called chondrine [28]. Later K. Krukenberg separated the main chondrine component and identified it as chondroitin sulfate. In 1953 E. Davidson, K. Meyer, A. Linker and B. Weissmann discovered one more substance that they believed initially a constituent cartilage component and called keratan sulfate. In these years K. Meyer with his disciples showed that chondroitin sulfates were a variety of polysaccharides; their molecules were chains of disaccharide links alternating with the glucuronic acid and *N*-acetylgalactosamine—a sulfate derivative (Fig. 1.6a, b). Later it was established that keratan sulfate is the same polysaccharide, but it consisted of alternating molecules of galactose and the sulfate derivative *N*-acetylglucosamine (Fig. 1.6c).

Though certain results were achieved by the studies of the chemical composition of the constituent components of the cartilaginous tissue, the first full idea about its structure appeared only in 1969 when the methods used to study of nucleic acids were successfully applied to extraction of undamaged giant aggregates of