Popularization of Chemistry

Chemistry—A Central Pillar of Human Culture**
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Little seems to have changed in the public image of chemistry and chemists, since Gabriel-François Venel depicted, in 1753, in Diderot's Encyclopedia, the “miserable state of the chemical community” as being “isolated in the midst of the greater people hardly curious of its business”. We are all painfully aware of the public image of chemistry and its status, in the media, as “the forgotten science”. Nevertheless, popularization of chemistry remains scant, and chemists themselves regard such attempts with ambivalence, if not disdain, as if admitting the verdict that foretold the position of chemistry as a central pillar of human culture.

While there may be difficulties to enchant the layman with chemistry, popularize we must! We just have to find new ways to tell the story of “the chemical universe” and project the position of chemistry as a central pillar of human culture.

This Essay shares with the readers my own experience of popularizing chemistry by delivering the following universal message of our science, that:

- Chemistry is the window given to Mankind to glimpse into its material essence.

It is through its relation to human characteristics such as love, addiction, sex, dream, and pleasure, that chemistry can be appreciated in its above universal sense. It is this universality that makes chemical knowledge a dictum and an enchanting story for the layman. Once this point is made, it paves the way to the introduction of concepts associated with “chemical matter” and how structure and interactions trigger human traits. Subsequently, a connection is made between the universal message of chemistry, and the system of thought of alchemists who considered that every material entity had also a spiritual manifestation and vice versa. The Essay is constructed along these lines, and its content can serve as an example either for an introductory lecture in freshmen chemistry or a popular-science talk to the general public.

Chemistry is the window given to Mankind to glimpse into its material essence

Love, Addiction, Psychological Balance, and More

Pheromones are molecules that control the “love life” and all communicative aspects of insects. This is true also for higher organisms, such as mammals; humans do not seem to be an exception. Thus, even though the chemical details of the emotional map are not yet worked out, it has become gradually evident that emotional life is written in an alphabet of genetically determined patterns and coded by specific brain chemicals. For example, a recent discovery reveals that individuals with different forms (alleles) of the gene, which encodes the transporter protein of the brain-chemical serotonin, exhibit different patterns of activity in the brain’s emotional center, the amygdala. A hyperactive amygdala is associated with permanent anxiety even in nonthreatening situations. Indeed, our brains are chemically wired. Some of these neurochemicals are neurotransmitters, others are neuromodulators that regulate the action of neurotransmitters, and others include hormones. These neurochemicals act sometimes on their own, other times with neuromodulators and other neurotransmitters, and sometimes by a cascade that leads to secondary molecules, which transduce the signal to the final trigger.

Research suggests that the brain-chemical 2-phenylethylamine (1; PEA, Scheme 1), is a neurotransmitter and neuromodulator of libido and interpersonal energy. Its administration to Drosophila and other insects, such as fruit flies, results in increased sexual activity and more successful mating. The chemical structure of PEA is similar to that of monoamines, such as dopamine and serotonin, except that in PEA the amino group is replaced by an ethyl group. This structural difference results in a variety of effects on the brain.

Dedicated to my students of the “second culture” who taught me that what is useful is not necessarily also enchanting!
tion increases emotional warmth, affection, sexuality, and the feeling of physical energy. It was even implicated in the “runner’s high”, which is the feeling of well-being that accompanies physical exertion. While PEA may function together with neurotransmitters (e.g., dopamine (2) and serotonin (3)), its action in the emotional domain is unique. Recently, it was discovered that PEA has indeed a specific receptor located mainly in the amygdala, the brain’s emotional command center. Unique also are the facts that PEA has a very short lifetime (minutes), and is degraded by a specific isoform of the enzyme MAO (monoamine oxidase), the MAO_{B} izyme. The short lifetime suggests that PEA has a special biodynamic role, possibly associated with excitatory effects triggered in a short space of time. By contrast, other neurotransmitters (serotonin (3), noradrenaline (5), and dopamine (2)) have long lifetimes (hours) and are degraded by the other isozyme, MAO_{A}.

The effects of PEA on human behavior have led to the hypothesis (henceforth the “psychochemical hypothesis”) that PEA is associated with the event of “falling in love” \cite{10}. Even though this connection is speculative, it is nevertheless interesting to learn of the psychochemical hypothesis, since it might contain some truth considering the role of PEA in regulating affect. Wahh \cite{10a} gives a vivid description of the action of PEA: When we meet someone who attracts us “the whistle blows at the PEA factory”. Unlike other mammals where “falling in love” is triggered by scent or touch, in humans the main trigger is sight. A mere glimpse is required to activate the sensation of romantic love. This is how the biblical story of David and Bathsheba begins: “From the roof he saw a woman bathing. The woman was very beautiful...”. The synthesis of PEA, in the brain, and its relay into the entire nervous system are implicated in the generation of excitement at the sight of the subject of love, and the great longing when the lover is not around. \cite{10a,11} PEA is also present in chocolate, Nutrasweet (for which the main ingredient is aspartame), and diet soft drinks, and its concentration rises with smoking of marijuana. \cite{10a} However, all these sources of PEA do not produce the kick of the brain-PEA. They fail to do so, in part because of their fast degradation by the enzyme MAO_{B}. Thus, even though PEA can cross the blood–brain barrier, most of it would be degraded without the addition of MAO_{B} blockers. \cite{12} Externally administered love potions may exist in Shakespeare’s Midsummer-Night’s Dream, while in reality our chemical system jealously safeguards the exclusivity of emotional response.

The psychochemical hypothesis \cite{10} assigns roles to other neurotransmitters, which figure in our psychobiological energy. One such family of neurotransmitters is the endorphins produced in the hypothalamus, the brain stem, and the pituitary gland. \cite{12} Endorphins are neuropeptides (β-endorphin, the most potent of the known endorphins, contains 31 residues) that serve as natural painkillers in the body. They act on specific opiate receptors, \cite{12} to produce analgesia and create a sense of well-being. However, according to the psychochemical hypothesis \cite{10d} they also play a major role in maintaining durable relationships. Thus, in the course of time after falling in love, the body requires larger doses of PEA to maintain the same initial kick, and we gradually “fall out of love” \cite{10b–c}. Had this been the entire story, love would have consisted by the sudden arrest of the endorphin mechanism.

PEA is only one of a few neurotransmitters that act as molecules of the emotions, which are shown in Scheme 1. The molecule dopamine (2) is manufactured from tyrosine in the Ventral tegmental area of the brain and is released in the frontal cortex. This molecule is involved in reward-seeking behavior, learning, drug addiction, and development of dependencies, including trained conditioning and willed control. \cite{10} According to the psychochemical hypothesis, \cite{10} dopamine regulates the desire to pursue pleasure, to seek danger, and is the motivator to achieve and to desire. With too little dopamine there is little joy of life, little sense of adventure and experience, \cite{10,13} while too large quantities or enhanced dopamine absorption by nerve cells lead to addictive behavior. It appears now that addictive behavior is associated with long-term potentiation (changes) in the synapses between the neurons, much like in memory and learning. \cite{16}

Serotonin (3) is formed (from tryptophan) in the raphe nuclei, deep in the brain stem, \cite{14} and is then transported to the nerve endings. It is the “mood molecule”, \cite{14} responsible for the psychological balance, and is the innate antidepressant. Problems in the serotonin cycle are associated with ailments, such as chronic pain, depression, Alzheimer’s diseases, strokes, and Parkinson’s disease. Serotonin deficiency is associated with aggression (including sexual), depression, schizophrenia, craving for carbohydrates and sweets. Normal levels cause a balanced personality, while excess is associated with anxiety. Serotonin can be found in bananas, tomatoes, and pasta. But again, this does not mean that eating any one of these foods increases serotonin levels in the brain, because of its fast degradation by the enzyme MAO_{A}.

Adrenaline (4) and noradrenaline (5) also known as epinephrine and norepinephrine are shown in Scheme 1. These are the stress hormones, which prepare the body for strenuous activity. Adrenaline, released from the adrenal medulla, acts to raise the level of glucose in the blood and thereby provides the surge of energy needed for performing demanding tasks or facing dangers. Noradrenaline is a neurotransmitter, which is also activated in stressful situations along with adrenaline. However, it is implicated (in conjunction with PEA and dopamine) in maintaining the sensation of vitality and focus. The molecule 6 (Scheme 1) is a hallucinogenic drug known as mescaline. The structural similarity of mescaline to the innate drugs is apparent. It raises thoughts about the “reality” of emotions, independent of their unique chemical motors.

A neuropeptide that figures in the psychochemical hypothesis \cite{10} is oxy-
Oxytocin (7, Scheme 2), a nonapeptide formed in the pituitary gland. Oxytocin was one of the first natural peptides to be synthesized in the laboratory and thereby demonstrated the chemical origins of psychobiological energy flow. In humans, oxytocin induces labor near the end of pregnancy, controls contraction of the uterine muscles, and stimulates the flow of milk during suckling. In laboratory animals, it was established that oxytocin promotes sexual behavior and pair bonding. By extrapolation, it has been proposed[10,14] that oxytocin is one of the molecules responsible for “pair bonding”,[14] and is behind the human urge to touch, caress, and assure. One can simply rub the back of one’s neck to feel the pleasing sensation caused by oxytocin secretion. The sensation gets much stronger when your partner does it for you, since this is an evolutionary chemical mechanism of seeking and getting addicted to “togetherness”. In women, oxytocin is thought to play additional important roles. During nursing, the surge of oxytocin causes pleasure and relaxation and thereby reinforces the mother–child bond. During lovemaking the surge of oxytocin causes the female’s orgasm. Oxytocin thus regulates our “chemical commitment” and its consequential well-being.

Male’s orgasm is geared towards ejaculation that was recently demonstrated[15] to be chemically triggered and controlled by a population of spinal neurons (lumbar spinothalamic (LSt)) and located in the two segments (L3 and L4) of the lumbar region. These neurons form part of the spino-thalamic tract that relay sensory information from the body to the thalamus area of the brain, which in turn uses a chemical relay that results in ejaculation. However ejaculation requires an initial erection, which is also chemically triggered, by the natural Viagra, nitric oxide (8; Scheme 2) which is an important neurotransmitter responsible for the regulation of blood flow.[16] It is so essential, that a special enzyme, called nitric oxide synthase (NOS), exists for the sole purpose of degrading l-arginine amino acid to generate NO in the endothelial cells.[16] The diffusion of NO (and its binding to the heme of the guanylate cyclase) to the smooth muscle cells, in the walls of the penile arteries of the erectile tissue, causes a cascade of chemical events, by the end of which the muscle cells are depleted from Ca\(^{2+}\) ions, the muscles then relax and thereby enable a blood flow into the penis and its eventual erection.

Nitric oxide is also involved in the mechanism of long-term memory (long-term potentiation-LTP) in the hippocampus.[6,17] In memory, NO acts as a neuromodulator that helps the l-glutamate receptor, NMDA (N-methyl d-aspartate), increase the concentration of Ca\(^{2+}\) ions within the cells. This results in repetitive firing patterns of the cell, which is the essence of LTP. One cannot avoid smiling at the recognition that erection and memory require opposite mechanisms of Ca\(^{2+}\) ion flow, outwards versus inwards.

The artificial compound sildenafil (9) better known under the trade name Viagra (Scheme 2), is simple enough to synthesize that a 2nd year undergraduate student who had completed a laboratory course of chemical synthesis may be able to produce homemade quantities of this molecule. The molecule interferes with the mechanism of the NO-induced Ca\(^{2+}\) ion depletion described above. The excitement caused by Viagra has barely subsided, and chemists are already utilizing their understanding of the mechanism of the erection-based NO mechanism to synthesize drugs that are “more than Viagra.”[18] The love elixir may well be within the reach of chemistry.

The discovery of the chemical neurotransmission in the late 1950s has led to a paradigm shift from an “electrical brain” to a “chemical brain”. Thus, it is the neurotransmitters that carry the information flow between nerve cells, and serve as the means by which the brain commands and receives information from the body and reacts to external stimuli. At any given time 100 billion (100 x10^9) nerve cells may be engaged in this “conversation”, which is conducted by two prototypical mechanisms—fast ion “firing” and the slow biochemical cascade—and combinations thereof.[16] Cell communication is an exceedingly rich and fast developing topic that cannot be elaborated in this popularizing essay.[6,19] Perhaps the easiest to illustrate, albeit very briefly, is the mode of cell communication that is triggered by a neurotransmitter molecule and mediated by an electrical impulse (“firing”).

At rest, the nerve cells are segregated by gaps, known as synapses.[19] The synaptic gap is the “off” position while the neurotransmitter is responsible for the “on” position by bridging this gap and enabling the transmission of the signal into the cell. The neurotransmitter molecules are stored in sacs in the nerve endings of a pre-synaptic cell. When an electrical signal (for example, a flux of Ca\(^{2+}\) ions) reaches the cell, it swells and its sacs release the neurotransmitter molecules that cross the gap and attach themselves to receptors of the next cell, the post-synaptic cell. The receptor is an ion channel, made from a bundle of a few proteins (for example, NMDA, the receptor of l-glutamate contains five proteins)[17] while the receptors of the amine neurotransmitters, in Scheme 1, belong to a special family of G-protein coupled receptors (GPCRs) which include seven helices[20]. The attached neurotransmitter opens the channel by causing a conformational change in the receptor. The opened channel then allows an ion flux that causes another neurotransmitter to cross the synaptic gap, leading another cell to fire (this may also activate intracellular biochemical pathways, e.g., as in LTP where persistent changes are induced in the post synaptic cell).

The neurotransmitter molecules, which completed their job, must then return to their nerve endings (the transporter cells) by recrossing the synaptic gap. Otherwise they generate radicals, by inhibition of superoxide dismutase, that lead to the death of the cell owing to its chemical degradation. In the case of neuroamines, the enzymes MAO\(_{A,B}\) degrade any stray neurotransmitter, not on a receptor or inside a sac in a transporter.
cell (neurotransmitters are replenished in the brain by specific biochemical pathways). A recent exciting discovery is associated with the mechanisms of return of serotonin molecules to their pre-synaptic cells.\[3\] Serotonin is assisted by making a tricyclic antidepressant\[2,3\] to recross the synaptic gap by trans-synaptic mechanisms and free choice as human characteristics that form the great divide from the rest of the animal world. I recently read that rats dream about themselves and their whereabouts during the day (running around their laboratory mazes)\[2,3\]. In this sense, a rat certainly has a form of self-cognition and awareness. In fact, the chemistry of emotions, memory, learning, is universal, much as are the genetic code and the synthesis of proteins. Thus, the great divide between humans and the animal world is not any form of self-cognition and free choice. It is rather the self-cognition gained as Mankind has journeyed through chemical matter in the unconscious process of self-introspection, we call chemistry. Thus, whereas the details of the above story are certainly simplistic and new facts will replace quite a few of them, the above lesson is with us to stay.

The Chemical Matter

Since Mankind is made of chemical matter, this is a good point to discuss some key features of the chemical matter that may pertain to this identity.

The central paradigms of chemistry are that:

- There exist atoms, which can form chemical bonds.
- The bonds are directed in space and determine the molecular architecture, the reactivity, and interactivity potentials of molecules.
- This in turn holds all the properties of inanimate and animate matter.

The atom is a neutral entity composed of electrons and protons, which are charged particles, and neutrons, which are neutral particles. The electron mass is 1/2000 of those of the proton and neutron. Scheme 3 shows dimensions of an average atom as a sphere (defined by a 99% probability of locating the electron), which is occupied in its center by a nucleus that packs together all the massive particles. The radius (R) of the atom is 1 Å. However, the radius of the nucleus is 10⁻³ times smaller. If we represent the atom as a football field, the nucleus will not even be the football, but rather a speck of dust on a shoe of the player standing in the center of the field. The chemical matter is empty and we, made from it, are sculpted voids.

Why doesn’t the void collapse unto itself? The architecture of the void is shaped by the behavior of this tiny, particle/not-particle, entity called the electron. In general, all chemical matter and its various interaction modes abide by the rules of the electron. In this sense,
chemical matter is unique because the electron is already an elementary particle and hence, chemical patterns cannot be further reduced or constructed from the bottom up (that is, from more elementary constituents). As an elementary particle, a few “laws” govern the electron behavior. The Heisenberg uncertainty principle forbids the electron to be located and have, at the same time, a definite energy (velocity). Therefore the electron is delocalized in space and “hovers” over the nucleus. In brief, the uncertainty principle gauges the size of the void in the atomic entity.

Accepting that atoms do not collapse, why then do they not all combine into a single giant molecule, making all of us pieces of the same material continuum (a material nirvana)? Here comes to play the Pauli exclusion principle, which when applied to electrons, imposes upon all atoms a specific connectivity that chemists discovered as early as the 19th Century and called it “valency”. It is the exclusion principle that underlies the division of matter into discrete molecules, and this is also the creator of the molecular diversity of the chemical matter.

The outcome of these two laws is that chemistry is a game of Lego with atoms and fragments, which have specified connectivities. The patterns of connecting two fragments form the architecture of the molecule, its electric and magnetic properties, and its modes of interaction, with other molecules and with light, to form new information and emergent properties. This, in a nutshell, is chemical causality. The magnum opus of the chemical matter and its emergent qualities are manifestations of the architecture of the molecule and the movements of its atoms.

**Molecular Architecture**

Figure 1 shows a demonstration of the transcendental function of architecture using diamond and graphite. Diamond and graphite are both made of carbon atoms. However, they differ in their architecture that is nascent from the degree of freedom in the four-connectivity of carbon. Diamond is hard and translucent, while graphite is opaque and brittle. The different architecture determines the outcome of the interaction of the two compounds with light. But much more than that: Diamond is “beautiful” and expensive while graphite “ugly” and cheap. Some people will murder for diamonds and scheme daring robberies, others will simply eulogize its beauty. No one will devote a single such thought to graphite. The architectural differences of diamond and graphite transcend into social and moral values and into poetry. This is a demonstration how information stored in the architecture of matter is mediated by light through molecular processes of the biosystem to evoke an emotional–mental response. This is an emergent property of the architecture of matter through the information created by its interaction with light, and through the specific evocation mediated by the chemical mechanisms of neurotransmitters and neuromodulators.

“Let there be light”

Indeed, our inner-visual world is shaped by the interaction of a molecule with light and by the ability of one molecule to exist in two definite states. The visual pigment is the rhodopsin receptor, a G-protein coupled receptor (GPCR),[20,24] that contains a chromophore called retinal. The retinal, in Scheme 4, has a cis configuration that gives the molecule a shape of a short curve. Upon light absorption, the molecule is isomerized to the trans configuration and thereby attains the shape of a lengthened chain. This architectural change modifies the structure of the membrane and activates a G-protein.[29] This event triggers an amplification of the initial signal, which is transmitted as a neural signal and onward to imaging.[24] Subsequently, another event of neurotransmission, yet to be elucidated, takes over and evokes an emotional response (oh diamonds are beautiful!). Our cognition of shape and the innate sense of beauty are outcomes of the interaction of matter with light and of the motions of the atoms of matter. This is reminiscent of the emotional–sensory system that is activated by the chemical mechanisms of the neurotransmitters and neuromodulators.
Chemistry and Its Emergent Expressions

Again and again one witnesses the same truism, that in the basis of the human attributes there lies chemical mediation. Molecules, weak molecular interactions and conformational energies harbor information that make us tick. This algorithm is everywhere; from the way “matter recognizes matter” by chirality recognition,[25] or lock-and-key fits, to the genetic code and protein synthesis that are based on the hydrogen-bonding templates. Chemistry provides infinite ways by which a few fundamental mechanisms and the power of numerous combinations can lead to a great variety of emergent qualities. This chemical machinery, its genetic origins, and its emergent emotional-sensory expressions form the “psychophysical connection” (body = chemistry; spirit = thinking, emotions, motivation) that is gradually unfolding.[6,c,f,19,26,27]

Dawn and Future

In the dawn of chemistry there was alchemy. The first alchemist was Hermes Trismegistus, shown in Figure 2.[28a,29] This legendary figure gave Mankind the “Hermetic Knowledge of the Divine Art”. The phrase Hermetic Knowledge evokes the sense of mysticism and magic, which is brushed off by modern chemists. However, we must recognize that alchemists were trying to do precisely what modern chemists are doing to day. The alchemists investigated matter in order to formulate a world viewpoint— as system of philosophy and cognition. In their system, spirit and matter were entangled,[28b] every material entity had a spiritual manifestation and vice versa.

Alchemists also practiced the manipulation of matter and left behind chemical tools, which are still in contemporary use.[28b] Maria the Jewess is considered to be the first alchemist in the Western world. The tools she invented for gentle warming and separation of matter serve chemistry to this day, and she may thus be credited as being the first to investigate the behavior of matter, something that chemists do to this day. The accumulation of chemical knowledge has taught us, however slowly, that behind the spectrum of human traits there lie chemical mechanisms of molecular motions and mutual interactions of molecules with each other and with the surrounding photonic field. We come full circle, to close a chasm between the old and modern worlds of chemistry. Chemistry is the intellectual adventure of Mankind in his excursion through his own material being. As this journey unfolds, so Mankind discovers the complex connection between matter and its emergent spiritual manifestations.[27]

Closing Remarks

Clearly, chemistry is the manifestation of the personal and universal cognition of Mankind of his own material being, and is also the intellectual matchmaker between this material being and Mankind’s rule over matter. On the one hand, with knowledge of chemistry we are Matter that possesses self-cognition and gnosiss, which have immense importance for progress and well being of Mankind. On the other hand, practicing our control over matter, we are constantly reminded of the warning to Mankind (represented by Cain) in the Old Testament, Genesis 4:7: “Sin is crouching at your door; it desires to have you, but you must master it.” Chemistry defines the limitation of the power over matter, and exemplifies this limitation by, for example, pollution and chemical warfare. Ruling over matter means also mastering the right ways of tinkering with it. We are still not there, and our chemistry has yet to fulfill the biblical dictum.

Bringing chemistry closer to the public is the duty of chemists, especially in these times when some of the world’s major problems are chemistry-laden. However, imparting knowledge is easy only if the topic is fascinating, which chemistry certainly is. In a way, chemistry is a practical form of introspection—an unconscious introspective analysis that has taken place as Mankind journeyed through Matter. Chemistry brings to life Mankind’s internal experience of change, of betterment, and the innate knowledge that changes are brought by the existence of opposites with great affinity. All in all, chemistry touches the human existence, well-being, and commitment to be a benevolent master of matter—our essential constituent. All these features make chemistry a central pillar of human culture.

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Counterpoint Press, Boulder, CO, 2000 (chemistry is mentioned once on p. 20 in association with pollution); c) see however, B. Werth, The Billion-Dollar Molecule, Simon and Schuster, New York, 1994 (the book creates however a wrong impression that chemistry is only the synthesis part, while the rest, even NMR spectroscopy or molecular modeling, is not).


[11] It was found in a study of medical students that at the early stage of “romantic love” they exhibited changes in serotonin transporter similar to the changes reported in obsessive–compulsive disorder. See: D. Marazziti, H. S. Aikisikd, A. Rossi, G. B. Cassano, Psychol. Med. 1999, 29, 741.


[20] These receptors activate guanine nucleotide binding proteins (G-proteins) in the interior of the cells. The G proteins are signaling molecules within the cell and they stimulate ion channel, and cause the synthesis of second messenger molecules. See descriptions and discussions of G proteins in, a) C. A. Parent, P.N. Devreotes, Science 1999, 284, 765; b) S. P. Neves, P. T. Ram, R. Iyengar, Science 2002, 296, 765.


[25] A beautiful metaphor for chiral recognition is the “Handshakes in the Dark”, described by Hoffmann on p. 40 in ref [38]. This can become very “handy” in a public talk—shake hands with your audience to illustrate chiral recognition.

[26] The drug “Ecstasy” (3,4-methylenedioxy-methamphetamine) was recently shown to cause huge amplification of serotonin neurotransmission. The drain of serotoninn causes depression, as well as permanent brain damage and profound dopaminergic toxicity (disruption of the axon of neurons, and vulnerability to Parkinson’s disease). See Science 2002, 297, 2185.

[27] Unlike chemistry that uses a very precise language, neurochemistry has been forced to use a much less precise language, because of the necessity to shift from the level of chemical-mechanical details (neurotransmission, brain re-
gions, etc) to the level of integrated experience (depression, love, motivation). The chasm between these levels can be likened to the relationship between the letters of alphabet and a poem. The letters are certainly the only constituents of the poem, but not every pile of letters makes a poem. Bridging this language gap in a manner that draws the relation between the whole and its parts is a great challenge that lies ahead. See e.g., “Whole-istic Biology” in Science 2002, 295, 1661–1682.


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