

# General Introduction

## The universe

1) Cosmogony reconstructs through backward extrapolation the earliest physical conditions of the cosmos. From a singularity at a finite point in space-time about  $14 \times 10^9$  years ago, a state of extreme density of radiation energy, approaching Planck's time  $h_t$ , it exploded, cooled and developed into the present geometry with a multitude of material formations.

### 2) Cosmology

2,1) The macro-cosmos is a coherently gravitation bound, isotropic, homogeneous, accelerating inflationary Riemann geometry with asymptotic Minkowski properties towards infinite. It developed stable single and groups of galaxies, clusters, nebula, stars and planetary systems.

2,2) The meso-cosmos constitutes the validity range of classical, non-relativistic physics. Its phenomena of abiotic matter are described by physics, chemistry and their fields of study.

2,3) The micro-cosmos enfolds according to the standard model out of 3 classes of elementary particles, point like spin  $\frac{1}{2}$  particles, field particles of the 4 forces and Higgs particles, preserving symmetries. It is ruled predominantly by strong, weak and electro-magnetic forces, unified in a single theory. It is described by Quantum Mechanics, Electro-, Chromo- und Flavordynamics.

3) Eschatology projects through forward extrapolation future physical conditions of the cosmos for the next  $10^{27}$  years as a continuing, entropy gaining, spatial expansion, dispersion of matter and emission of radiation to leave black dwarfs, neutron stars and black holes.

## Environments

Environments are long term variables, comprising natural and man made living areas.

1) The Heliosphere, a star of medium size and luminosity, about  $4.5 \times 10^9$  years old, generating by nuclear fusion electro-magnetic radiation, a gravitational and geometrical center of nine orbiting planets, allows a long, stable developmental time span for evolution of organic life. Planetary preconditions to support life in a moderate climate are:  $\alpha$ ) an adequate mass, size and structure,  $\beta$ ) an adequate distance to the source of radiation,  $\gamma$ ) an approximately circular orbit,  $\delta$ ) an approximately perpendicular rotation axis,  $\epsilon$ ) a medium rotation frequency,  $\zeta$ ) a chemical composition, containing all essential elements,  $\eta$ ) a magnetic field and atmosphere, shielding high energy radiation.

2) The Biosphere describes all single factors enclosed by the atmosphere.

2,1) The atmosphere of the earth, reaching about 10 km upwards, consists out of 78%  $N_2$ , 21%  $O_2$ , 0,03%  $CO_2$  and in its lower layers up to 4% of  $H_2O_{VAP}$ . It dampens by circulation temperature and pressure differences, carries precipitation inland and serves as a metabolic fuel.

2,2) The hydrosphere in forms of gas, ice and liquid, found to 99,7 % in the oceans, supplies with sweet water the largest component of plants and animals and is indispensable in their metabolism.

2,3) The lithosphere, the outer, firm, plate layered mantle of the earth, reaching about 100 km deep, has as its crust the pedosphere with rocks, stones, sands and soils of various qualities.

2,4) The biotic environment includes all living organisms in water, land and air.

2,5) Ecology describes individual, population, environmental abiotic and biotic forces and conditions of life with their multifaceted interdependencies in the development over geological time spans. Local ecological environments often form out self-organizing, semi-closed systems with energy-metabolic cycles along an ascending food chain in a dynamic, labile balance.

2,6) Man causes major, often irreversible environmental changes, substitutions, destructions and climatic shifts through persistent, large scale technological applications with pollution of air, water and soil and eradication of entire biotopes and species.

3) Boundaries are universal natural, mental and spiritual limits between man, society, nature and God. They can be expanded with improved cognition by contemplative, artistic, scientific research and applications to open up new fields of study and correct, refine, add to and spread present knowledge.

## First stages of evolution

The earliest forms of life appeared about  $3.7 \times 10^9$  years ago. Development of life on earth (biogenesis) was first a chemical, abiotic evolution, taking place in the oceans in the presence of phosphates ( $XPO_4$ ), silicates ( $XSiO_4$ ), metal ions, an atmosphere of nitrogen ( $N_2$ ), ammonia ( $NH_3$ ), carbon dioxide ( $CO_2$ ), methane ( $CH_4$ ), sulfur hydrogen ( $H_2S$ ), hydrogen ( $H_2$ ) and energy sources of heat, radiation and electric discharges. Formed were mixtures of amino acids, proteinoid microspheres with first forms of a membrane, metabolism, growth by budding.

Biological evolution with nucleic acid chains capable of reproduction progressed in self-organization of matter with basic forces of the evolutionary drives of mutation, recombination, divergent development of structures and forms with specialization of functions, adaptation and selection. Formed were protobiontes, containing a short DNA strand, which differentiated stepwise an improved metabolism, protein production, a multifunctional membrane. The first prokaryotes of blue algae and bacteria appeared. Following in the first evolutionary line were eukaryotes with differentiated organelles within the cell and a membrane enclosed nucleus, containing a chromosome set to control cell division by mitosis (start of phylogenesis). Their oldest known chalky fossils found in oceanic sediments are about  $1.5 \times 10^9$  years old. The spreading one cell organisms took up mainly carbon and hydrogen containing molecules in exchange for nitrogen and oxygen to radically change the composition of the atmosphere, starting  $2 \times 10^9$  years back, into the one we know today. During the Upper Precambrium of about  $9 \times 10^8$  years ago the evolutionary rate of the diverse aquatic one cell organisms accelerated, forming multi cellular eukaryotes with specialized cell functions. The branches of plants and animals separated about  $1 \times 10^8$  years back, introduced was sexual reproduction, further accelerating the evolutionary rate, and set up was a heterotrophic food chain with plants at the base, before the first forms of plant life appeared on land.

The first evolutionary line is continuously traceable in the development of genetic materials, their proteins (phylogenetic topology) and ensuing forms of life. The first nucleic acid chains grew by processes of base pair changes, addition, deletion, inversion, duplication, rearrangements, activation, deactivation, in later stages by production of catalyzing enzymes, by interaction of these factors, mostly enlarging the overall DNA material. The development of function specific genes and proteins is graphically demonstrated by a polygenetic tree (molecular phylogram), by branch order and lengths, indicating their degree and distance of relation, the evolutionary steps and the corresponding evolutionary rates. The molecular tree of lineage delineates copy true the evolutionary tree of comparative anatomy of all plant and animal species, stating a common ancestry of all living organisms in the biochemical building blocks, the genetic code, the bio-synthesis of proteins, the catalysis by enzymes and an energy metabolism with glycolysis.

The phylogenetic theory of descent serves as basis for description, denotation and categorization (taxonomy) of all organisms. As a result of evolutionary processes, there exist in discontinuous variability today about 500 000 plant and 2000 000 animal species. The degree of relationship between groups, traced in a hierarchical, monophyletic tree of lineage, is measured by singular, homologous, derived traits in descent of corresponding original traits (taxon, pl. taxa). The taxonomic categories are rooted in four kingdoms (regnum) of one cell organisms, prokaryotes, eukaryotes and mushrooms.

## The cell nucleus

The human genetic material, the genome, is stored on 2 sets (diploid) of 23 homologous chromosomes (22 autosome and 1 sex chromosome) and like all eukaryotes confined in a cell nucleus. The hereditary information is passed on as coded sequences and lengths, triplets or codons, of Desoxyribonucleic acids, DNA, selected from two purine bases guanine (G), adenine (A) and two pyrimidine bases cytosine (C), thymine (T). The codons, yielding  $4^3 = 64$  possibilities, encode for regulative signals and 20 essential proteins, the base group, accounting for about 200 000 proteins of the human body. The codons are arranged commaless, non-overlapping. They constitute a universal transcription code for all living organisms. About  $6 \times 10^7$  bases, one the primary structure, are joined by addition polymerization to form out a single macromolecular, chromosomal strand. Two complementary strands are arranged to a right handed, antiparallel double helix, the secondary structure. The interwinding strands are held together by hydrogen bonds between opposite C-G and A-T base pairs (bp). Each chromosome carries about 50 000 genes, one the functional unit, forming out a trait that is being passed on by Mendelian inheritance, consisting of single copy sequences with about 1 000 bp or polygenetically of repetitive, multicopy sequences with 2 – 10 gene copies with 20 – 500 bp each or of interspersed, with non-functional groups (intron) alternating, multicopy sequences. The double helix with a diameter of  $2 \times 10^{-9}$  m coils itself on nucleosomes, the tertiary structure, compressing the entire genome (chromatin) into a cell nucleus of  $6 \times 10^{-6}$  m in size.

## Proteins

Proteins, polymeric amino acids, containing a peptide bond in the repeat unit  $-(\text{RCH}(\text{NH}_2)\text{COOH})-$  with a molecular mass of  $10^4 - 10^6$  and a chain length of 50 – 1000 units, constitute the basic building blocks of all organisms. They represent up to 50% of structural cell material and serve as regulative, storage, immune active proteins. They are synthesized mainly in two steps, a process called gene expression, by transcription within the nucleus and after transport by translation in the cytoplasm of the cell, both proceeding over the phases of initiation, elongation and termination. In transcription, realizing the encoded genetic information, a gene sequence of a locally unwound chromosome string, the template, is copied base by base onto a single stranded messenger RNA (mRNA), the matrix. In translation, assisted by ribosomal binding sites, the matrix directs bio-synthesis, the produced amino acid units being polymerized by addition, unidirectionally to a polypeptide chain, followed by folding, function specific modifications and transport.

## Growth processes

An organism's life cycle over the stages of zygote, embryo, youth, adult, death (biology of development) in regular succession of generations is fueled by species specific, somatic (non-germ) cell growth, quantitative increase of cell tissue and by differentiation, qualitative expression of specific cell functions and organs. The morphological changes (morphogenesis), development and arrangement of cell populations in precise positioning and organized manner, are regulated by temporal genes for cell specific initiators, transcriptional and translational control and by external factors like intercellular signals, often hormones, in equilibrium with anabolic and catabolic metabolism. Growth of a cell type is achieved by cell division and subsequent increase of cytoplasmic volume. The periodic cell cycle proceeds in the steps of cell division (mitosis (M)), gap (G1), synthesis (S), gap (G2). In nucleus (karyokinesis) and cell division (cytokinesis) the chromosome set is separated to distribute the two homologous halves to the daughter nuclei. In synthesis, the haploid sets in each nucleus are replicated over 10 000 replication units per chromosome simultaneously for a copy true, continuous passing down of the genetic information to the next cell generation.

## Sexual reproduction

Animal cell hybridization takes place in the sexual replication process in purpose of reproduction, the production of new living organisms to guarantee the continuity of the species. It proceeds in the sexual cycle in three successive stages: The male (spermatozoa) and female (ova) germ cells grow in germ cell production (gametogenesis) mainly out of meiosis, two cell divisions of meiosis I, proceeding in 9 phases and meiosis II, a mitotic division, proceeding in 5 phases, achieving random assortment of chromosomes in the germ cells and a reduction of the diploid chromosome set to one half. In cell fusion (karyogamy, conjunction of nuclei in copulation) the gametocytes with their haploid chromosome sets are brought together to form a fertilized egg cell (zygote), a randomly recombined diploid chromosome complement, preserving a constant number of chromosomes. In the third, diploid phase, the zygote develops into the embryo, the daughter generation (ontogenesis), by successive cell divisions and development to an adult with formation of sex organs to complete the sex cycle.

## Hereditary traits:

The genotype of an organism, the complete set of genes, determines the hereditary traits and forms out in steps of species specific development the phenotype of the organism (phenogenesis), the visible and empirically verifiable manifestation of a morphological form. The phenotype is codetermined by a multitude of competing factors like the organism's environment, by humans also by anthropological conditions, especially social and personal environments, which change repeatedly over a life span. A genetically hereditary trait is based on an organism's identical replication and distribution of alleles to daughter cells, on a selected bio-synthetic pathway (gene expressivity or penetrance), on timing of gene expression of the required gene at the required time of development from the complete genome present in each cell (totipotency). Growth and differentiation of functions over the stages of embryo, youth, adult (ontogenesis) form out the full complexity, capacity, coordination and flexibility of the phenotype's hereditary traits. In humans, least determined by its genotype are behavioral traits, because of the enormous variety of developmental pathways of the central nervous system.

## Laws of inheritance

Mendel's laws of inheritance (1865) describe the genetic recombinations of allele pairs in sexual reproduction over successive generations, visible as hereditary traits, where the parent generation P differs in one allele on their diploid chromosome set with a pure homozygote wildtype  $a^-a^-$  and a pure homozygote mutagenic type  $a^+a^+$ . The variability of the genome is passed on in new combinations, where the progeny's ratio of genotypes is statistically predictable. Mendel's laws therefore serve as the genetic basis for breeding technologies.

1<sup>st</sup> law of uniformity: Crossing of two pure bred homozygote strains P with the allele combinations  $a^-a^-$  and  $a^+a^+$  results in a first daughter generation  $F_1$ , which is uniform heterozygote in genotype  $2a^-a^+$ . The trait expressed allele is called dominant, the unexpressed recessive, codominant alleles will form out an intermediate quality or intensity.

2<sup>nd</sup> law of segregation: Crossing of the heterozygous  $F_1$  generation results in a second daughter generation  $F_2$  with randomly distributed allele pairs, in average a relation of genotypes of 1:2:1 or  $a^-a^- : 2a^-a^+ : a^+a^+$ . The phenotypes split correspondingly 3:1 with a trait dominant allele, 1:2:1 with trait codominant alleles.

3<sup>rd</sup> law of independent assortment: Crossing of polyhybrid  $F_n$  strains with the non-linked allele combinations  $ab$  and  $cd$  results in a daughter generation  $F_{n+1}$  with a free combination of allele pairs, where the gene loci separate and new genotypes and phenotypes may arise that are not present in the  $F_n$  generation.

### **Breeding technologies:**

Breeding techniques have been employed since prehistoric times of about 10 000 years. Improving plant and animal traits of quality and form like nutritional content, yield, adaptability, resistivity, freshness, has given a major contribution to human civilization. Selection, crossing and cultivation, utilizing genetic variability and hereditary traits, reduce the genetic reserves, which are also depleted by destruction of biotopes of wildtypes. Breeding (mating) systems today describe all essential factors aside from mutation, which control population structure and evolutionary divergence.

Breeding of a phenotype is determined by the breeding value of the trait: on the morphological level by the kind of sex organs present, mostly dioecious, where a partner is required to contribute the second nucleus; on the genetic level by fertilization factors to inactivate cell specific restrictions for gametes to fuse; by contribution of the number of genes, chromosomes and nuclei to karyogamy; by allele frequencies; and by gene expressivity.

Main plant and animal breeding techniques comprise selection, cross, heterosis and bio-engineered breeding:

In selection breeding a phenotype is mass selected according to its desired trait from a mixture of a larger population for further cultivation. Directed (positive) selection improves the degree of efficiency of a trait by picking out one extreme, shifting the average of the character within the population. Stabilizing (negative) selection eliminates deviant individuals from the population, narrowing the range of genetic variability. Disruptive selection of specific extremes leads to greater variability and to polymorphism. Through line breeding by selection over successive generations a group of identical pure bred individuals is obtained and the chosen trait then multiplied.

In mono- and polyhybrid crossbreeding of genetically different organisms a fusion of alleles, surpassing incompatibility barriers, achieves in the daughter generation the combined, desired traits in one heterozygous genotype. Genetic hybrids are mixoploid combinations (mosaics) from different genera, leading to new species (chimera). Through convergence breeding by recurrent selection and intercrossing the new trait is stabilized in uniformity and consistency.

In heterosis breeding also a crossing of strains takes place, not to obtain a constant genotype, but for the heterosis effect, where the heterozygous mix in the genome is superior in a desired trait, which may be lacking in the P generation (hybrid vigor). The hybrid seed can only be gained from its parent populations, as the heterozygous state loses its specific mix relation by further intercrossing.

Newer breeding techniques employ in combination of mutagenic, recombinant and hybridization DNA technologies in vitro manipulation of cell cultures in an artificial nutrient, a semisolid or suspension medium under controlled environmental conditions. They allow for example large scale breeding of life stable colonies (colony breeding); somatic hybridization between alien gametes, bypassing fertilization barriers, where whole, isolated, by dissolution of their walls stripped cells (protoplasts) of different species are fused with ones still containing a nucleus or with their nuclei removed to form a hybrid or a cybrid (cytoplasmic hybrid); embryo splitting, breaking up of embryos in the 2 - 4 cell phase, cultivation and re-implantation into two surrogate mothers; cloning, asexual reproduction of an identical, recombinant DNA molecule by mitosis out of a single somatic or germ cell.

## Gene technology

Genetic engineering as discipline of molecular genetics is a part of bio-technology. It comprises the theoretical and applied aspects of isolation, analysis, manipulation and recombination of structural and regulative genes and their introduction, expression and multiplication in other organisms apart from naturally occurring processes.

Molecular bio-technology furnishes a significant contribution to basic research in genetics. It developed methods for analysis of nucleotides and –sequences, their structures, functions, reactions and products with bio-synthetic pathways and interactions, as well as technologies for their a) isolation and identification, b) gene mapping, c) manipulation, d) synthesis, e) ligation, f) transfer, g) transformation and multiplication, f) test and production devices. Transformation following production of a passenger DNA sequence, a vector system and ligation is the last step of cloning procedures, the asexual, identical reproduction of a DNA sequence. It opened the way for gene libraries (colony banks) and commercial production.

Applications of gene technology, the 'soft' technology, concentrate on the fields of medicine, pharmacology, food production, human genetic diagnosis and therapy. They expand into reproduction technologies, forensic genetics and pest control. Patents are granted on their products and methods.

a) Methods for in vitro isolation of DNA segments are cleavage by pattern recognizing restriction enzymes together with separation of DNA fragments e.g. by blotting or polyacrylamide gel electrophoresis, separations by molecular weight with nucleic acid and protein identification.

b) Gene mapping of DNA segments on a chromosome proceeds in orientation of known genes by direct, fragmental DNA sequence determination or indirectly, e.g. by radioactive marking, cleavage and identification with a gene specific DNA probe.

c) Manipulation of a DNA segment to cause a specific change in a nucleotide or –sequence is based on the processes of DNA mutation by means of physical, chemical or bio-chemical incision, of DNA recombination by bio-chemical introduction, elimination or distortion, of DNA hybridization by cell and nucleic fusion of genetically close and distant (transgenic) materials.

d) Synthesis for construction of a specific DNA segment is achieved by bio-chemical de-novo synthesis of short oligotid sequences, followed by joining of the oligo- with polyotides, catalyzed by ligase enzymes, or by single strand synthesis through polymerization of complementary base pairs from a DNA matrix towards a complete DNA duplex, added by polymerase enzymes.

e) Ligation, joining of a passenger DNA segment often with regulative sequences into the open gap of a carrier DNA segment (replicon, vector) for stable gene expression, is achieved by covalent bonding, added by ligase enzymes, which represents via indirect integration the definite step towards recombinant and transgenic DNA.

f) Physical transfer of the vector system as an independent unit of replication into living host cells and cell nuclei is effected e.g. by concentration increase in form of a precipitate or charged complex or by in vitro laser poring, a micro-injection, physically opening the cell wall.

g) Transformation (a transposition) of a recombined vector system into the host genome aims at covalent bonding into the chromosome strands by cleavage and joining of both ends, assisted by restriction and ligase enzymes. The passenger DNA from in vitro cultivation is being multiplied in the nuclei of cell lines by repetitive transformations and cell divisions, also over the stages of ontogenesis.

h) Devices for testing and automated production demand accurate, sensitive, reliable, fast, miniaturized measurement and process control. Bio-chemical process parameters are taken up by bio-sensors, which contain two elements, an aggregate, recognizing the biological information with a molecular, cell like or microorganism bio-mass and a transducer for output of an electronic signal.

## Mutation

A mutation induces a structural change in the genotype of an organism to cause a modification of the phenotype. The mutation spectrum encompasses changes in the number of chromosomes (ploid mutation), changes in the composition of a chromosome (chromosome mutation) and changes in the structural or regulative region of a single gene (gene mutation).

Distinguished are haploid sets,  $n = 1$  single, complete sets; diploid sets,  $n = 2$  double, complete, homologous sets; polyploid sets,  $n > 2$  multiple complete, corresponding sets.

Resultant structures of a ploid mutation are cells with an aneuploid set of chromosomes, which is increased (hyperploid) or decreased (hypoploid) by a fraction of a set. Autoploid sets are species specific, - allopolyploid sets are species non-specific.

Mutational inheritable changes by mutant gametes in genetic variability constitute a basic mechanism of evolution, leading to new varieties. They arise spontaneously or induced on application of chemical agents or physical means like radiation or by means of genetic engineering. The mechanism can be a reaction between DNA and a mutagen, an error in DNA replication or recombination, an error in transcription or translation, introduction of a mutagen altered precursor.

## Hybridization

Hybridization encompasses all processes of cell fusions with and without ensuing fusion of cell nuclei, of somatic and germ cells, of genetically close and distant (transgenetic) species. In sexual reproduction of higher animals in the sex cycle of alternation of meiosis and karyogamy, individual gametes differ in composition of genetic material from each other and from the parent organisms (gametogamy) and male and female ones are distinct in size, form and mobility (heterogametes).

Gametogenesis: In all higher plants and animals, gametes, sexually differentiated copulating germ cells, arise in meiosis, in animals to form primordial germ cells in the gonads, the male (testis) and female (ovary) sex organs. They develop over several stages from spermatogonia to spermatocytes to spermatids to spermatozoa (male) or from oogonia to oocytes to ootides to ova (female), the mature germ cells. By two meiotic cell divisions (M I + M II) with recombination and random segregation of chromosome pairs, in all from one primordial germ cell mature four germ cells with a haploid set of chromosomes, where of the female three abort.

Meiosis I: The first meiotic division proceeds along 9 stages of leptotene, zygotene, pachytene, diplotene, diakinesis, prometaphase I, metaphase I, anaphase I, telophase I, interkinesis (gap phase). An intra- and interchromosomal recombination takes place from zygotene to diplotene. The homologous chromosome strands (sets A,B) pair along their lengths: 1a-1b, 2a-2b, ... 23a-23b. Held together by contact points, they form a synaptonemal complex with open, branched, four armed base chains, facilitating a crossing over (chiasma), a free, reciprocal exchange of different chromosome segments, gene combinations or single alleles by strand break, recombination and strand repair. A random assortment of chromosome pairs takes place from prometaphase I to anaphase I. The halves of the diploid set on the equatorial plane are pulled by a spindle apparatus into opposite hemispheres of the nucleus, e.g. C: 1a, 2b, 3b, ... 23a and D: 1b, 2a, 3a, ... 23b.

Meiosis II: The two nuclei with a haploid chromosome set replicate once in a short gap (G1) - synthesis (S) - gap (G2) phase, restoring the diploid set and leading to a second meiotic cell division, a mitosis, proceeding in 5 phases of prophase II, prometaphase II, metaphase II, anaphase II, teleophase II. During metaphase II and anaphase II the sister chromosomes align lengthwise on the equatorial plane to be separated as in meiosis I. The two mitotic daughter nuclei remain each with a haploid chromosome set. In all out of one primordial germ cell result after two meiotic divisions 2 genetically distinct and 2 genetically equivalent (C, C', D, D') gametes.

Manipulation of germ cells:

Mutant and recombinant DNA sequences are introduced into germ cells, zygotes and embryos in the early cell stages (surrogate genetics): into a cell group to manipulate an entire cell line; into the homoeobox to manipulate a genetic strain through subsequent stages of ontogenesis; for technical reasons, as a small amount of foreign DNA affects an entire cell type evenly, in time stable modulation, hereditarily fixed and within a short developmental time span.

## Recombination

Recombinant DNA technology comprises all physical, bio-chemical and genetic processes (recombination system), which independent of naturally occurring processes produce a new gene combination by methods of introduction, elimination or distortion of a DNA sequence in a chromosome. A small amount of manipulated or foreign DNA in the genome, mostly changing the relative amount of DNA in the host cell, is being active in gene expression, in gametes hereditarily passed on to the progeny and transgressing in nature found species (chimera).

The transfer of a passenger DNA strand (transfection) is based either on existing genetic material or on synthesized amino acid sequences. It is achieved by the in vitro steps of: recombination or de-novo synthesis or single strand synthesis of a DNA sequence with a sought for quality; construction of a vector system (replicon) to stably modulate transcription and as a carrier for the passenger DNA for integration (transposition) into the host genome; ligation, binding the passenger DNA to a vector system, - each step requiring the techniques of localization, isolation by cleavage and separation, characterization, generation, selection, verification. As carrier serve as with transposable, mutant elements often a bacterial or viral vector system, which can be integrated efficiently into the host chromosome. Main commercial application is in vivo gene amplification (of an amplicon) for production of a specific protein with sought for properties.

Gene expression: Gene action is mainly regulated via transcription and translation (modulation) rates, which respond also to external stimuli of radiation, light, heat, hormone treatment and virus infections. Both rates depend in first degree on the initiation rate as the rate limiting step, initiation being facilitated by cell specific, regulative genes of the required number at the required time in coordination with metabolic conditions like product concentrations, mix, transport and adjustments of protein synthesis rates.

In the elongation step of mRNA synthesis from a template, transcription efficiency depends on: the basic vector system, function specific enzymes like promoters, enhancers, repressors, anti-repressors, stabilizers, terminators of suitable concentration, special arrangement and transport paths, the fine structure of chromosomal base orientation in accessibility, attachment and winding - unwinding processes.

After mRNA processing and transport to the cytoplasm of the cell, the new protein is polymerized by addition from the mRNA strand, the matrix. In the elongation step translation efficiency relies on ribosomal binding sites, tRNA, GTP, ATP concentrations and on regulative, function specific enzymes. The folding process begins immediately with base sequence copying, enzyme assisted, forming out inhibitory or stimulatory structures, which with end group modifications specify the protein's transport path, function, efficiency, solubility, membrane association and anchoring.



## Population Genetics

Population genetics describes the genetic demographic structure of a reproductive community, its allelotype by allele frequencies in the common gene pool, the genetic composition being derived by count of all singular genes at a specific locus in the genome of each organism, as well as the dynamic forces (Origin of Species, 1859, Charles Darwin), which effect changes in the genetic structure to render them predictable from theory.

All closed, equally dispersed, autogame populations, reproducing by panmixia (Mendelian population), exhibit genetic variability, leading to variability of phenotypes in morphology, physiology and behaviour, which by the laws of inheritance are passed on to succeeding generations. In the evolutionary process out of genetic variability develop various forms, specialization of functions and adaptations to environmental changes. Through genetic flexibility and natural selection, a genotype survives more successfully within its own or in competition with another population or under limited resources or in a hostile environment by means of its relative fitness, the average probability of survival in one or more aspects of its phenotype like normal life span, fertility, pairing behaviour, body weight and metabolism. Through continuing genetic differentiation over geological time spans of part of a population, mostly after geographic isolation, the evolutionary process forms out new species (intraspecific evolution) and new genera (interspecific evolution).

On the genetic level, the wealth of variability, much larger within a population than between different races, is determined by all evolutionary forces: by mutation; by hybridization (with a recombination) in the process of sexual reproduction; by migration, an introduction and spreading of a gene from another population; by gene drift, a random shift of the mean of a trait distribution; by genetic correlation, their interaction and harmonization to maintain genetic cohesion; and by genetic homeostasis, the tendency to maintain and to restore a dynamic equilibrium by own regulatory mechanisms.

Quantitatively the rate of change in the frequency of an allele  $a^-$  depends mainly on: mutation and recombination rates; its mean of fitness in relation to the total fitness of its own and competing populations and in relation to its heterozygote allele  $a^+$  and alternate alleles  $b, c, \dots$ ; its relative frequency in relation to equivalent parameters; magnitude and direction of selection with elimination of alleles; its degree of dominance; the spread of genetic variability.