*Commentary*

# The blazing life of N V Timofeeff-Ressovsky

## 1. From undergraduate student in the USSR to the Head of the Department in Germany

Nikolai Vladimirovich Timofeeff-Ressovsky (NV for short) was born in Moscow on September 7, 1900, studied in school in Kiev and then at Moscow University. Later, he joined the Institute of Experimental Biology. As he recalled later, his teachers were Nikolai K Koltsoff, the founder of experimental biology in Russia, corresponding member of the then USSR Academy of Sciences, and Sergei S Chetverikov, the founder of evolutionary and population genetics in Russia, whose ideas, together with those of Vladimir Vernadsky and Vladimir Sukachev, Nikolai Timofeeff-Ressovsky popularized all his life.

In 1925 Oskar Vogt, the director of the Kaiser Wilhelm Institute for Brain Research invited NV to organize a department of experimental genetics. The corresponding recommendations to Vogt were given by N K Koltsoff and by People's Commissar of Health N A Semashko. At that time NV was 25 and did not possess even an undergraduate degree. After a few years he became the Head of the Department of Genetics and Biophysics, Kaiser Wilhelm Institute for Brain Research (Berlin-Buch) which he headed for twenty years as a leading researcher in the field of population and radiation genetics.

In these years NV became a participant of the Niels Bohr seminar on physics in Copenhagen and cooperated with leading biologists, physicists and mathematicians of the world. Also he organised his own discussion group in Berlin-Buch.

## 2. From micro-evolution to the dimension of the gene

NV and his wife Elena (Helen) Alexandrovna (along with the Russian-American geneticist Theodosius Dobzhansky) were among the first to study micro-evolution, pleiotropy, as well as penetrance and expressivity. These studies (initiated in Russia in the early 1920s, Timofeeff-Ressovsky 1925) revealed that several genes can influence the same characteristics, such as fecundity, and the combined action of two mutant genes cannot necessarily be predicted by their action when only one is present (Timofeeff-Ressovsky and Timofeeff-Ressovsky 1926). Thus, geneticists came to the understanding that genetic variability of populations should not be viewed as a consequence of independent and non-interacting entities (as proposed by Ernst Mayr) but as an integrated cohesive whole. NV established that much of the genetic diversity in a wild population is hidden in the form of recessive mutations. He and his wife performed inbreeding experiments in natural populations of *Drosophila* and produced individuals in which both genes resulted in recessive mutant traits. Their paper published in 1927 was the first proof of the existence of significant amounts of hidden genetic polymorphism (Timofeeff-Ressovsky and Timofeeff-Ressovsky 1927).

Much later in the USSR, NV summarized his ideas on the problems of evolution in his monographs written with his pupils (Timofeeff-Ressovsky *et al* 1969, 1973).

In general, NV significantly influenced genetic and evolutionary research, not only through his own classical works but also by transmitting Russian ideas about the mechanisms of evolution (S S Chetverikov, the founder of Russian population genetics, developed an innovative synthesis of Mendelian genetics and classical Darwinism) and about the template principle in biology (N K Koltsoff developed the concept of "genonema" – a giant molecule serving as the carrier of genetical information and as the template for its own reproduction). The achievements and history of the "Moscow School of the Evolutionary

Genetics" is described in Bobkoff (1985).

After the discovery by H J Muller of the mutagenic effect of ionizing radiation (this discovery was presented in the V International Genetical Congress in Berlin in 1927), the discipline of radiogenetics was born. A detailed study of the quantitative regularities of the mutagenic effects of radiation initiated a new era in biology. The general hope was that the bombardment of living cells by ionizing particles would lead to the understanding of the structure of a gene as the bombardment of the atom by X rays revealed the structure of the atom in the classical experiments of E Rutherford. This hope brought the physicists and biologists closer.

In 1933 Max Delbrück joined the discussion group led by NV which included the nuclear physicist Karl G Zimmer, with whom NV was then collaborating with in the study of the genetic effects of ionizing radiations (Timofeeff-Ressovsky 1934). One of the primary foci of interest of the group was the then still utterly mysterious physical nature of the gene, especially as it had to be grasped from the interpretation of radiogenetic data. The experiments and discussions resulted in the publication in 1935 of a classical paper by NV, K G Zimmer and M Delbrück entitled *On the Nature of Gene Mutation and Gene Structure* (Timofeeff-Ressovsky *et al* 1935).

### 3. The hit concept and the target theory

This paper (Timofeeff-Ressovsky *et al* 1935) is interesting in two aspects. First of all, the "hit concept" and the "target theory" were formulated in it for the first time, and now serve as the basis for cell radiobiology and radiation genetics. Secondly, the results of experimental estimation of gene sizes are first pre-

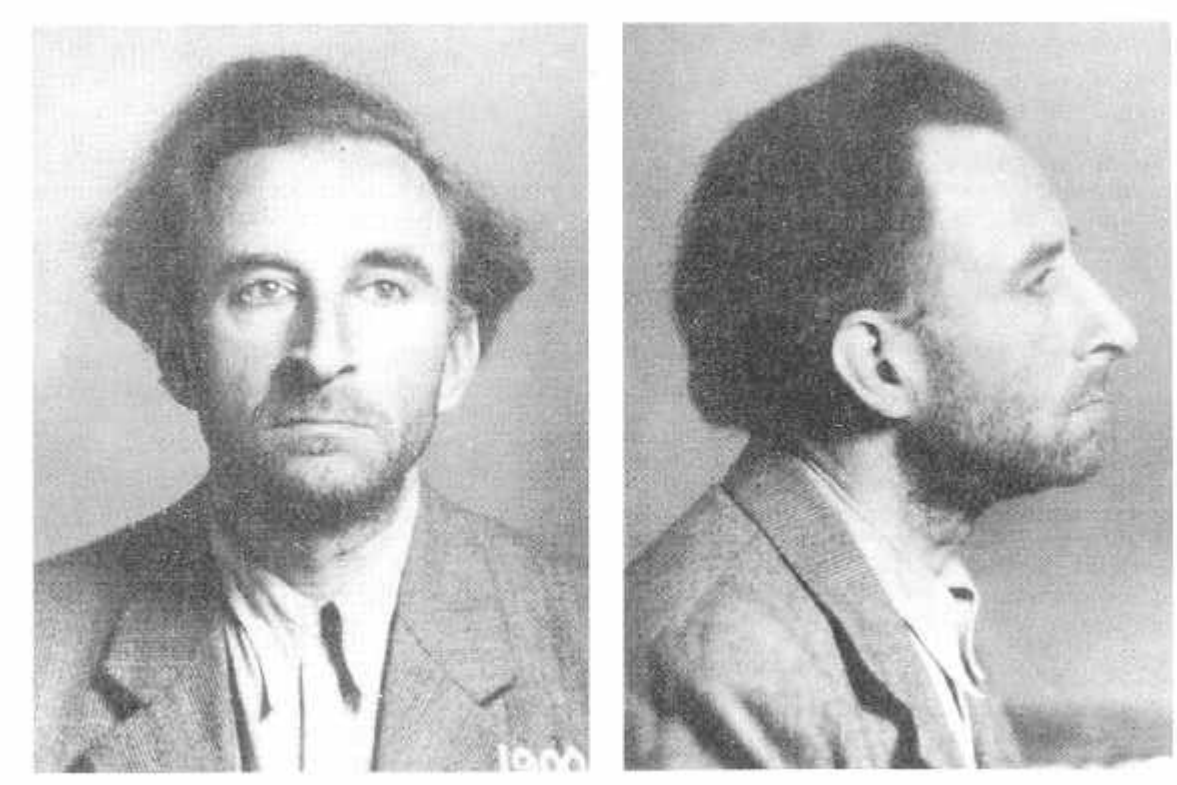

**Figure 1.** The prisoner Timofeeff-Ressovsky N V arrested on September 13, 1945. Sentenced to 10 years of imprisonment in corrective labour camps on July 4, 1946. In 1951 "conditionally released from prison because of great successes in scientific research work". Given amnesty in 1955. Recognised as innocent and rehabilitated in June 1992. Photograph from the Archive of the People's Commissariate of State Security, October 1945 (Goncharov and Nekhotin 2000).

sented here as well as the estimation of the number of genes in chromosomes and the dependence of the frequency of gene mutations on the radiation dose.

The principal discovery of NV was his observation of a linear relation between the total radiation dose and the number of mutations. Whether the dose was administered in a single shot, or in several fractions or continuously at a low level over an extended period appeared irrelevant. The intensity of dose did not affect the number of mutations produced. NV also found no minimum dose below which mutations were not generated. These properties suggested that X rays produce mutations like particles hitting targets (Timofeeff-Ressovsky 1934). The idea of hitting was formulated as the act of interaction of the quantum (or particle) with a target. The target is a region (or structure of a cell) in which the hitting in it of an ionizing particle could produce a mutation. With the usage of these principles and with mathematical modelling of the curves of "dose-effect", the size of a gene (or the size of a minimal target which ionization inactivated in a gene) was estimated. It was found to be a volume consisting of approximately 1000 atoms (Timofeeff-Ressovsky *et al* 1935; Timofeeff-Ressovsky and Delbrück 1936). Thomas H Morgan in 1910 demonstrated that genes are located at fixed positions on the chromosome. NV made this description more precise: the gene has the dimension of a large organic molecule (as was foreseen by his teacher N Koltsoff). All these results were employed by Erwin Schrödinger as the basis for his book "*What is Life? Physical Aspects of the Living Cell*" (1945), which dramatically influenced further the development of molecular genetics.

In the "German" period of his life, among those who regarded themselves as pupils of NV were Sh Auerbach, A Buzzati-Traverzo, K Zimmer, F Halveek and M Delbrück. The older colleagues of NV such as N Bohr, V Vernadsky, T Dobzhansky, G Meller and T Morgan greatly influenced his scientific outlooks.

## 4. From Hitler s Germany to Stalin s Russia

NV was a Russian patriot deeply dedicated to his Motherland, but the most productive period of his life he spent in Germany before and during the Nazi era. After the Nazis seized power in 1933 they expanded support for genetic research but also required obeisance to the new regime. During the same period the communist regime in the USSR enhanced the political purges and terror. A lot of innocent people were arrested, tortured, imprisoned and executed. The younger brother of NV (Valdimir) was executed, another brother (Dmitri) was imprisoned. Many of his wife's relatives were arrested.

Under the influence of the agronomist Trofim D Lysenko, the study of Mendelian genetics was outlawed in favour of the Lamarckian belief that evolution occurs primarily through the inheritance of acquired traits induced by the changes of environments. N K Koltsoff had been dismissed as director of his Institute. S S Chetverikov had been arrested and exiled. N I Vavilov was arrested in 1940 and in 1943 died from starvation in prison.

During this period communist officials through the Soviet Embassy in Berlin suggested that NV should return home. Thinking that NV would obey the order to return, N K Koltsoff (at great personal risk) reportedly warned him: "Of all the methods of suicide you have chosen this is the most agonizing and difficult. And this not only for yourself, but also for your family." NV refused to return to Russia. On June 22, 1941 Nazi Germany attacked the USSR, the war started. The chances of homecoming vanished. When the Nazi authorities proposed German citizenship to NV, he answered: "I was born Russian and see no need to change this fact."

During World War II he continued his research. Overall, the political pressure on scientists was remarkably slight. Scientists did not have to become Nazi party members to obtain grants for biological research. The Institute granted his department virtual autonomy in everything except material requests. NV had never been involved in weapons development. Using his administrative position and formal and nonformal influence, NV helped many people to avoid repression and death. He was one of a handful of scientists in Germany who protected the persecuted, including people of Jewish descent, Russian refugees and prisoners of war.

His older son Dmitri (nicknamed Phoma, born in 1923) joined an anti-Nazi underground group providing support to prisoners of war. Phoma, who knew French, sheltered two French pilots from arrest. In 1943 the anti-fascist group was betrayed and Phoma was arrested by the Gestapo. The attempts to save him, made by W Heisenberg and C Weizsaecker (friends of NV) were not successful. Phoma was sent to the concentration camp Mauthausen. The circumstances of his death are unknown. According to one version he par-

ticipated in the rebellion of war prisoners.

At the end of the war NV had the opportunity to evacuate to Göttingen and after the war, to work in the Carnegie Institute at Cold Spring Harbor, USA. But he decided to wait for the arrival of the Soviet Army. After it arrived NV was arrested for he had "betrayed the Motherland by going over to the side of the enemy" and was sentenced to 10 years of imprisonment. At one point he was incarcerated in the same prison as Alexander Solzhenitsyn, who described in the "*Gulag Archipelago*" (Part II, Chapter 4) the scientific seminars which NV continued to organise there. The future Nobel Prize winner in literature emphasised that it was for the first time he saw and felt the invincible power of the human spirit which deeply influenced and inspired his life. After a few months NV was transferred to a corrective labour camp in North Khazahkstan. For two years he was an ordinary prisoner, and his friends and family were unable to learn where he was or even whether he was alive.

In 1947 when the USSR became deeply involved in nuclear research, a special secret prison research facility (Object 0211) was set up in the Ural near Sverdlovsk (now Ekaterinburg) where scientists studied the biological effects of radiation. In 1947 his wife was permitted (if she so wished) to join her husband. In 1948 she, with their younger son Andrei, went to Object 0211. NV as the Head of the Biophysics Department of Object 0211 directed study on some problems of radiation biogeocenology (now this field is called radiation ecology) – the analysis of the distribution, accumulation and migration of radioactive isotopes in experimental and natural systems. Some results of this research were published later (Timofeeff-Ressovsky 1962).

## 5. From radioecology to global ecological problems

In 1955, after the death of Stalin (1953) NV was released. He moved to the Ural's Branch of the Academy of Sciences, USSR (in Sverdlovsk) where he organized the Laboratory of Biophysics and a special experimental station near Lake Miass for radioecological research on radiation and population genetics. He reinitiated his scientific seminars, which developed into annual unofficial workshops on genetics where dozens of young scientists received their first experience in genetics, which (because of the Lysenkoism) was an officially banned field of science.

In 1964 NV moved to Obninsk when he organized the Department of Genetics and Radiobiology at the Institute of Medical Radiology. During this period NV continued his research and writing in population genetics, radiation biology and evolution (Timofeeff-Ressovsky *et al* 1981) in spite of his poor vision, which was the direct consequence of his near death starvation due to pellagra in the corrective labour camp.

The ideas of Timofeeff-Ressovsky, Zimmer and Delbrück were used in the work of Lea (1946), Timofeeff-Ressovsky and Zimmer (1947) and Timofeeff-Ressovsky *et al* (1968). They laid the foundation for the modern theory of the biological effect of ionizing radiation know as the "Probability Model of Radiation Injury of Cells" (Kapul'tsevich 1978) which most accurately described the cell's reactions to radiation.

The genetic concept of the biological effect of ionizing radiation is closely connected in radiobiology with the name of NV. In particular, the phenomenon of post-radiation cell recovery as well as the interphase cell destruction of differentiating tissue already in a "pre-molecular period" were interpreted in terms of the hit principle and the target theory, and so far, i.e. almost half a century after the discovery of these phenomena, this interpretation has remained effective.

In radioecology, or as NV preferred to call it, radiation biogeocenology, this meant that first of all, an enormous amount of research carried out by his wife E A Timofeeva-Ressovskaya and himself concerning the determination of the coefficients of different radionuclides accumulated by water and different representatives of biota (Timofeeff-Ressovsky 1962; Ivanov 1991). This research enabled them to take a new view of the migration of elements in the biosphere and the role of living matter in this process. The other side of this problem is the use of various representatives of the biosphere to purify terrestrial and aquatic areas from radionuclides. At present, this problem lies beyond radioecology and is developing as chemo-ecology and radio chemoecology. Results of the work were applied as countermeasures in the nuclear wastes explosion accident in South Ural and after the Chernobyl disaster. The development of this field is the result of research on the combined action of low capacity radiation doses and

various physical and chemical factors on biota and man.

In 1970 NV retired from his administrative position in Obninsk, but continued to write and work as a consultant at the Institute of Medical Biological Problems (Moscow) which was engaged in space genetics, at the Institute of Developmental Biology (Moscow), and at Moscow State University.

Although he was an eminent geneticist and evolutionist with high international reputation, NV did not receive any academic degrees during his life in Germany. In fact, he was never interested in formal academic degrees. Later, in the USSR to receive an academic degree was impossible because of

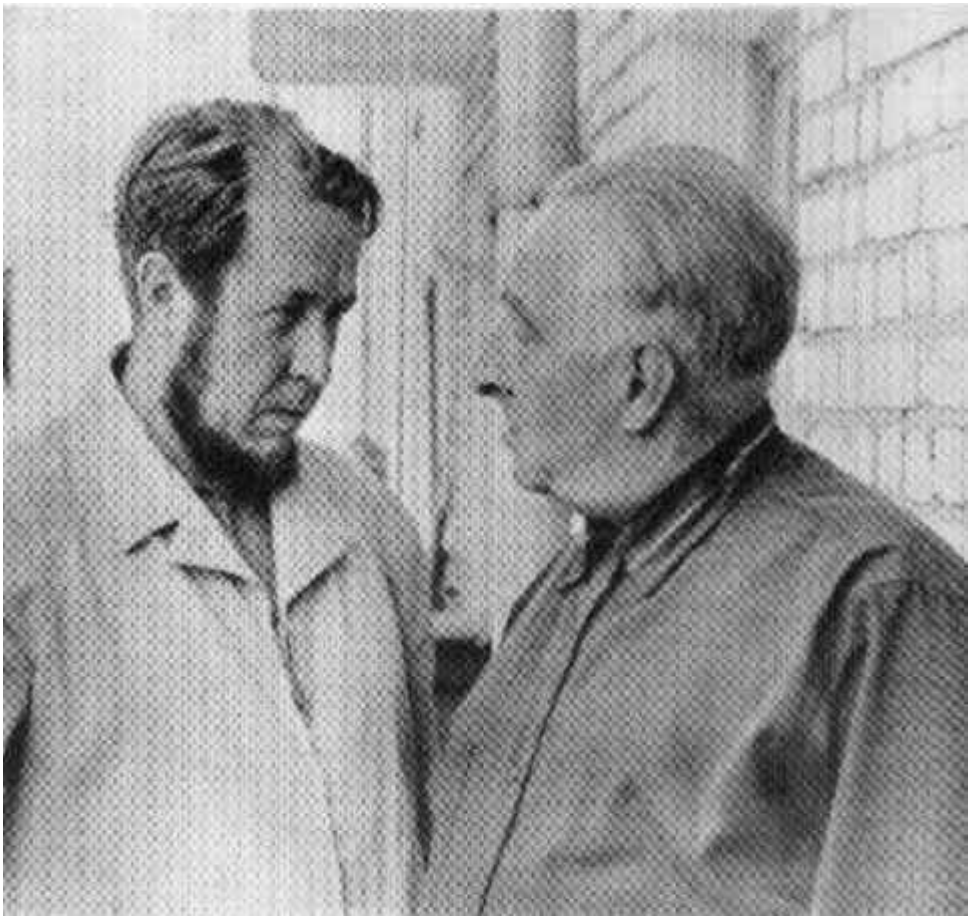

**Figure 2.** Timofeeff-Ressovsky and Alexandr Solzhenitsyn. At the Lubyanka, Solzhenitsyn and Timofeeff-Ressovsky were co-prisoners. Twice a day, water would be poured from a bucket without a spout into the prisoners' teapot, usually spilling on the floor. This is what Solzhenitsyn (1973) remembers: "There was nothing at the Lubyanka, . . ., which so offended him (Timofeeff-Ressovsky) as this spilling on the floor. He considered it striking evidence of the lack of professional pride on the part of the jailers, and of all of us in our chosen work. He multiplied the 27 years of the Lubyanka's existence as a prison by 730 times (twice for each day of the year), and then by 111 cells – and he would seethe for a long time because it was easier to spill boiling water on the floor 2,188,000 times and then come and wipe it up with a rag the same number of times than to make pails with spouts." (photograph by Zh. Medvedev.)

Lysenkoism. After the fall of Lysenko he was awarded the degree of "Doctor of Biological Sciences" and only in 1966 he was invested with the title of "Professor".

Nikolai Vladimirovitch died on March 28, 1981, in Obninsk.

Medals named after NV have been awarded to Russian and foreign scientists such as A Arkrog (Denmark), N Luchnik (Russia), I Chigematsu (Japan), D Regula (Germany) and others.

Special mention must be made of his article which was dictated by him in the last year of his life (Timofeeff-Ressovsky 1980) and where he formulated the unsolved problem (which long tormented him) of the mechanisms of progressive evolution and outlined a way for further elaboration of this problem.

Being an optimist, NV paid enormous attention to the problem of the biosphere and mankind. He was sure that given a reasonable attitude to it, the productiveness of our planet can be increased dozen-fold (e.g. by increasing the efficiency of the photosynthetic processes), which would allow the feeding of many more people, in comparison with the present population of the planet, thus increasing the stability of the biosphere on the whole. The above mentioned ideas, as well as pilot research on the consequences of anthropogenic contamination conducted by his students and followers, elaboration of methods of eco-restoration and reappraisal of the relationship between nature and *Homo sapiens*, as one of nature's components, appeared to be in concord with the Declaration on the Environment and Development at the UN Conference in Rio de Janeiro (June 3–14, 1992) and with the activity of a recently (1998) organized International Union of Eco-ethics.

Mankind is now facing a need to preserve biodiversity, the problem of organizing a universal system of ecological monitoring and the rehabilitation of a growing number of polluted areas on land and in water. These global problems can be solved on the basis of the ideas of NV.

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