ISSN 0006-3509, Biophysics, 2012, Vol. 57, No. 2, pp. 237–243. © Pleiades Publishing, Inc., 2012.
Original Russian Text © V.N. Binhi, 2012, published in Biofizika, 2012, Vol. 57, No. 2, pp. 338–345.

COMPLEX SYSTEMS BIOPHYSICS

Two Types of Magnetic Biological Effects: Individual and Batch Effects

V. N. Binhi

Prokhorov Physical Institute, Russian Academy of Sciences, Moscow, 119991 Russia

E-mail: binhi@kapella.gpi.ru

Received April 27, 2010; in final form, February 2, 2011

Abstract—Frequency distributions of the values of magnetic effects have been calculated from the results of ~120 thousand single trials during psychophysical testing of 40 people under normal conditions and exposure in a hundredfold weakened geomagnetic field. Two types of such distribution were shown to be attributed to (a) the individual reactions to the change of magnetic field and (b) the batch magnetic effect on the set of individual reactions. The methodological consequences significant for detecting magnetic biological phenomena and studying their nature are discussed.

Keywords: geomagnetic field, magnetic biological effect, magnetoreception.

DOI: 10.1134/S0006350912020066

INTRODUCTION

The present work concludes the five-year series of studies on the action of altered constant magnetic field (MF) on the human organism. It has turned out that a 100-fold reduction of the natural MF around a human has a slight but statistically significant effect (on average, ~2%, $p < 0.01$) on the accuracy and speed of performing psychological tests. At that the individual reactions in separate tests could reach 20–40%. The aim of the work was to unite the data of heterogeneous tests into one set of commonly determined magnetic effects and to consider the features of statistical distributions on this set.

Normal living conditions imply the presence of a usual geomagnetic field (GMF) of some 50 μT. A significant decline in the local MF is not indifferent for the organisms. The physical mechanisms of the biological action of low-intensity MF have not yet been established. Most often discussed (see [1, 2]) are those based on (a) possible presence of magnetic nanoparticles in tissues, (b) metabolic involvement of reactions with participation of spin-correlated free-radical pairs, (c) long-lived rotational states of dipole protein molecules, (d) metastable states of liquid water.

A physical mechanism indispensably includes interaction of MF with the magnetic moment of the supposed target. This moment is a macroscopic one in magnetic nanoparticles, or a molecular moment determined by orbital motion or spins of electrons and protons. In any case a significant decrease of the MF entails qualitative changes in the dynamics of targets. For a part of magnetic nanoparticles found in tissues of many organisms, this is a change in the form of the rotational potential from a two-well to a single-well one [3]. For molecular moments, this is cancellation of Zeeman splitting into magnetic sublevels and formation of one degenerate state. Therefore, exposure in a weakened MF is convenient in that it should be expected to raise the probability of observing nonthermal effects of MF, notorious for specifically reduced reproducibility. Whatsoever the dynamics of primary targets of MF, it must undergo qualitative changes in a substantially weakened MF—in "magnetic vacuum."

The given work sums up the results of personal testing under magnetic deprivation. The persons having given informed consent to take part in the experiment were examined for cognitive performance in several psychological tests. Each of the 40 examinees passed the testing twice: in the weakened MF and, for comparison, in normal GMF under the same conditions. The measured quantities, further called parameters, were (a) the time of executing the task and (b) the number of mistakes in the following tests: (1) a simple motor reaction, (2) recognition of correspondence between the meaning of color-denoting words and their color, (3) short-term color memory, and (4) recognition of rotated/flipped letters. Tests 2 and 4 were modifications of known tests [4] in psychophysiology of vision. Thus in total, there were eight measured parameters.

In weakened MF, the number of mistakes and the execution time increased by ~2%. The reaction of young women to MF weakening was especially significant. Apart of age and gender, the magnitude of mag-

Editor's Note: I certify that this text exactly reproduces all factual statements and largely conveys the phrasing and style of the original Russian publication. *A.G.*

netic effects also correlated with factors of health and proneness to allergic reactions. Correlation with temperature and pressure was insignificant. The experimental protocol, statistical methods and the results have been described in [5, 6]. The use of methods of dispersion, discriminant and factor analysis [7, 8] has allowed determining the sample statistics and establishing the existence of a magnetic effect in each test. Of interest are also the integral characteristics of individual and "batch" magnetic sensitivity determined on the bulk of the data obtained. Joining the results of measurements into a unified aggregate is hampered by the heterogeneity of the measured physical quantities and the dissimilar size of the samples.

In the present study the indicated difficulty has been overcome by generalization of the data processing algorithm. The character of sample statistical distributions describing the magnetic effects has been analyzed. The distinctions of these distributions point to the existence of two types of magnetic effect—individual and batch.

METHOD

Relative magnitude of effect. A magnetic biological effect (MBE) is called a regular change in some quantity characterizing the state of the organism upon a change of the magnetic conditions of its residence. If there are datasets of measurements in a usual and an altered MF, then, applying e.g. dispersion analysis, one can calculate the probability that the hypothesis of nonrandom difference in datasets is correct. But what is the numerical magnitude of the effect?

The effect magnitude is often determined as the difference in mean values for sample distributions in «control» and in «experiment». In such determination the effect magnitude has a physical dimension, which is not always convenient: it is impossible to collate the effects obtained by measuring different quantities. Such a problem arises in magnetobiology as well. In consequence of the specifically reduced reproducibility of MBE, the experiment is sometimes conducted by measuring several biological quantities having in the general case different dimensions. Therewith the specifics of biological measurements gives rise to differences in dataset volume. For example, under the action of MF different effects have been obtained in measurements of different parameters—response time and mistake number. What is the magnitude of magnetic effects on the average?

It is clear that the correct way to calculate the mean values consists in uniting the control sets into a unified control set, the experimental ones into a unified experimental set, and then calculating the statistics of the effect. Yet uniting the sets is not always possible, at least because of the dissimilar physical dimension. In this case one should first compose relative dimensionless magnitudes, relative to the mean in the control, and then unite the sets. But even then there may arise a difficulty if the control measurements yield on average a (nearly) zero value. Such does happen, and the relative effect as a result becomes great or even infinite, which points to the ineffectiveness of the standard determination of relative effect in this situation. For this reason in our previous works we used simultaneously two types of determination of the relative effect, for continuous and for discrete quantities, which presented a methodological shortcoming.

There arises, consequently, a necessity of constructing a relative index that would serve as a characteristic of the magnitude of effect at zero mean control values as well and would thereby provide the possibility of uniting the datasets.

Let us consider the construction of such an index on the example of a control **c** and "experimental" **x** sets of sizes n and m respectively. Here and further the boldface denotes measurement sets. Let the measurements record the errors in trials: 0 – correct answer and 1 – wrong answer. Repeat that the usual determination of the relative mean magnitude of effect in the form

$$X = (x - c)/c, \tag{1}$$

where x and c denote the sample mean of the corresponding random quantity, is impossible, because in some trial series there appear sets **c** containing only zeros (no errors).

Let us circumvent this difficulty by introducing indices of fallacy and faultlessness instead of the number of errors. It is reasonable to define faultlessness, e.g. in control, as the ratio $(n - k)/n$, where n is the number of trials and k is the number of errors. Accordingly, faultlessness in "experiment" is $(m - j)/m$, where m is the number of trials and j is the number of errors. Then the relative faultlessness, against the value in control, is $(m - j)n/[(n - k)m]$, and the relative fallacy is the inverse quantity $(n - k)m/[(m - j)n]$. Now, even if there are no errors in the control, the relative fallacy remains a finite quantity.

Admissible is a generalization for the case of continuous positively defined random quantities, such as measurements of time and distance, if the **c** and **x** sets are preliminarily normalized to their common maximal element. All elements of the sets now fall into the interval [0,1]. The relative magnitude of the effect then is determined by relationship

$$X = \frac{m\sum_{i}^{n}(1 - c_i)}{n\sum_{i}^{m}(1 - x_i)} = \frac{1 - c}{1 - x}, \tag{2}$$

where x_i and c_i denote elements of the sets. Expression (2) of course converts to $(n - k)m/[(m - j)n]$ for a random discrete quantity with a set of values 0 and 1. Def-

inition (2), as distinct from (1), is applicable to practically any sets of measurements.

Determination of magnetic effect. As will be clear from the following, because of the existence of an individual magnetic effect it is expedient to conduct control and "experimental" measurements for one and the same examinee or organism when possible. Here there is another difficulty, connected with that the control and «experimental» measurements cannot be conducted simultaneously. But the magnitudes of the measured parameters are subject to systematic and random changes with time. Therefore the calculated values of the magnitude of effect contain contributions both from the magnetic influence and from natural time trends. To reduce the contribution of systematic changes, caused e.g. by physiological rhythms or habit acquisition in the course of testing, use is made of so-called mock or sham exposure, or placebo control. The gist consists in that a part of experiments are conducted in the absence of exposure, in our case in the absence of GMF suppression, of which the examinees are intentionally not informed. Inasmuch as in our works the automated collection and processing of measurements excluded subjectivism, such conditions on the whole corresponded to the so-called double blind control. In order not to introduce indices for values pertaining to these two types of experiment, let us further accept the following designations of the sets. For real GMF suppression, **c** – control and **x** – experiment; for sham suppression, **s** – control and **y** – experiment.

Thus, the mean relative effects in experiments with real and sham exposure are respectively

$$X = \frac{1-c}{1-x} \quad \text{and} \quad Y = \frac{1-s}{1-y}. \tag{3}$$

The mean relative magnetic effect can be specified with one of two equivalent definitions: $M = (X - Y)/X$ and $M = (X - Y)/Y$. At small observed magnetic effects in the 0.01–0.1 range, the difference has the second order of smallness and can be disregarded. However it is the former definition that is preferable. Substituting X and Y from (3), we get

$$M = 1 - \frac{(1-s)(1-x)}{(1-y)(1-c)}. \tag{4}$$

The fact that this expression is a linear function of x permits considering (4) as the mean over elements of the set of magnetic effects

$$\mathbf{M} = 1 - \frac{(1-s)(1-\mathbf{x})}{(1-y)(1-c)}.$$

Here addition of the constant to the set and multiplication by the constant means application of these operations to every element of the **x** set. Further, sets **M** obtained upon examinee with ordinal number n passing the test numbered m are denoted as $\mathbf{M}_{nm}$, and the means over these sets as M_{nm}. As already said, the means over several statistical sets, the moments of distributions or the distributions themselves should be more correctly constructed by uniting the sets. Sets $\mathbf{M}_{nm}$ may be united inasmuch as they are composed of dimensionless elements grouping about zero in the absence of effect. Let us designate the union of sets $\mathbf{M}_{nm}$ in one of the indices, e.g. m, in the form $\mathbf{M}_n = \mathbf{M}_{n(m)}$, i.e. by parenthesizing the correspond index. In the given case, set $\mathbf{M}_n$ is the set uniting the sets of magnetic effects demonstrated by examinee n in measurements of all eight test parameters.

It is essential that the magnetic effects demonstrated by different examinees are statistically stable. The corresponding distributions yield differing mean values, not only in the magnitude but also in the sign of the effect. In other words, the magnetic effects are individual. Therefore, union of sets in index n, although possible, has no practical sense. The individual magnetic effects of different sign, which by themselves may be statistically significant, upon uniting are mutually compensated and in the unified set are not seen but are reflected therein only as an increased standard deviation. Another approach provides more important information.

Of interest are: (i) the general *shape* of individual distributions of the magnitudes of magnetic effects, i.e., the common in individual distributions that is not their mean values, and (ii) the shape of distribution of the *individual mean* magnetic effects. Let us denote a distribution built on elements of some set, e.g. **z**, as $\mathbf{R}(u, \mathbf{z})$, where u is the distribution variable, the magnitude of magnetic effect. In these designations the objects of computation are distributions (i) $\mathbf{R}_n = \mathbf{R}(u, \mathbf{A}_n)$, $\mathbf{A}_n = \mathbf{M}_n - M_n$ being centered sets, i.e. the shapes of individual distributions; and (ii) $\mathbf{R}(u, \mathbf{B})$, the distribution of individual means. Here M_n is the mean over elements of set $\mathbf{M}_n$, and **B** is the set formed by such means.

For constructing distributions, use is made of a density estimate for a distribution function with the kernel in the form of a normal distribution $\mathbf{N}(u, \mu, \sigma_0)$ with mean μ and standard deviation σ_0. For example, the density estimate for a distribution of elements of set **z** sized n has the following form:

$$R(u, \mathbf{z}) = \frac{1}{n}\sum_{i=1}^{n} N(u, z_i, \sigma_0),$$

where z_i is an element of set **z**. The density estimate, as can be easily seen, is normalized by the unit area under the curve, which is convenient for comparing distributions. A density estimate is a continuous analog of a histogram. The extent of detail of the estimate is specified by kernel parameter σ_0. Throughout the following, use is made of an adaptive σ_0 value making 1/5 of standard deviation σ of the set elements, which corresponds roughly to five bars in the histogram in the main part of the distribution, in the $(-\sigma, \sigma)$ interval

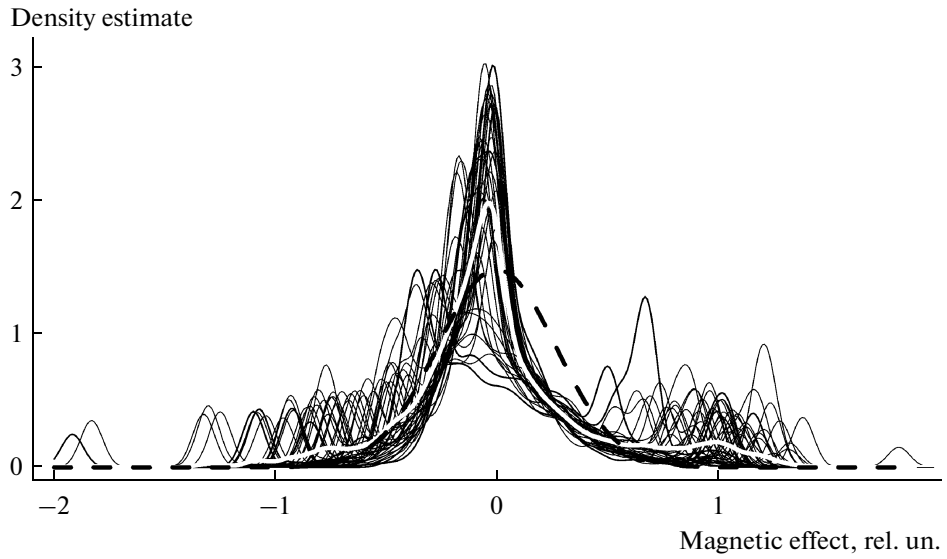

Fig. 1. The individual distributions of magnetic effects for centered sets $\mathbf{A}_n \equiv \mathbf{M}_n - M_n$ (black curves), total distribution $\mathbf{R}(u, A_{(n)})$, i.e. averaged form of individual distributions (white curve), and the approximating Gaussian (dashed). The total distribution built on a set of 39738 trials, which were normalized using another 79026 trials.

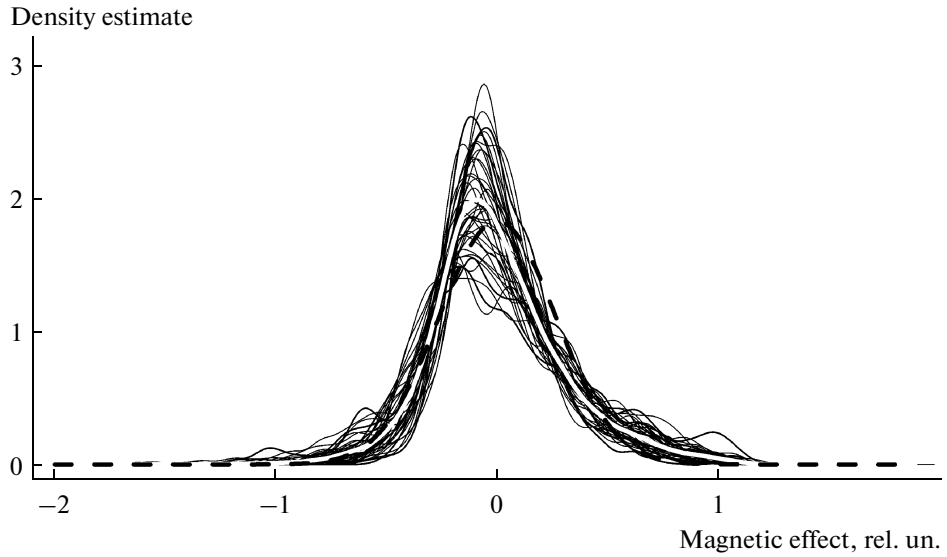

Fig. 2. The individual distributions of magnetic effects for centered sets built on measurements of only parameters with nearly continuous spectrum (response time and color memory). The total distribution built on a set of 26522 trials, which were normalized using 52604 trials.

for Gaussian sets. The density estimate as compared with a histogram is more vivid and has other advantages.

RESULTS

The described algorithm of calculating the magnetic effects and plotting distribution densities from the earlier obtained 1280 sets **c**, **x**, **s** and **y** (about 120 thousand element) has been implemented as a program. Figure 1 shows the shapes of individual distributions of magnetic effects and the general averaged shape of these distributions $\mathbf{R}(u, \mathbf{A}_{(n)})$.

The "wings" of distribution arise because of the discrete character of the spectrum of parameter values in the measurements of error number. This is evident from Fig. 2, which presents the same curves as Fig. 1 with the exception that the sets of testing error measurements consisting of zeros and unities are left out of account. Initially the "wings" were associated with the possible presence of a distinguished group of especially

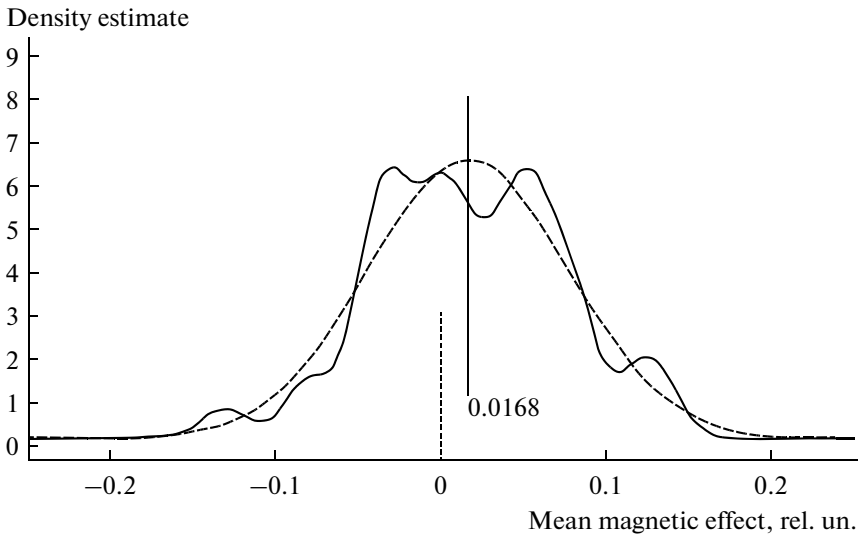

Fig. 3. The distribution on a set of 40 values of mean magnetic effects M_n and the approximating Gaussian with standard deviation 0.061.

sensitive people demonstrating large MBE, yet this hypothesis finds no confirmation.

The asymmetry of the total distribution is conditioned by the contribution of the results of measuring the color memory. Here measured is the distance between vectors the components of which are normally distributed. Then the distance has a Rayleigh distribution, which adds to the Gaussian overall distribution of response time measurements.

The approximating Gaussians in Fig. 1 and Fig. 2 are close, have standard deviation 0.27 in the former case and 0.26 in the latter. Apparently, a value 0.25–0.30 is characteristic of the expected scatter in repeated measurements of individual magnetic effects.

It should be emphasized that the total distribution was constructed on the basis of uniting sets of individual effects with the deduction of their means, inasmuch as the mean magnetic effects were not random and presented as an individual characteristic of the examinees. In this way it has proved possible to reveal the *common shape* of individual distributions. Whereas if one unites the sets without subtracting their means, one will obtain a global set of magnetic effects $\mathbf{M}_{(n)}$ with a mean value 0.017 ± 0.002.

Let us now consider the distribution of the individual mean magnetic effects themselves, M_n, presented in Fig. 3. As evident, this distribution possesses a substantially smaller dispersion than the individual magnetic effects: the standard deviation of the approximating Gaussian equals 0.061. The distribution possesses a mean value of 0.0168. Note the stability of this result. If the distribution is plotted only by the sets of response time measurements, then the mean effect equals 0.0164. While if the results are disregarded for six examinees having shown the maximal effects, then the mean magnetic effect about 0.0149 also retains statistical significance $p < 0.01$ [9]. In this way, the global mean MBE is formed by the entire mass of mean magnetic effects and all examinees. It is neither a consequence of especial effectiveness of any test nor a consequence of the presence of especially sensitive examinees.

DISCUSSION

Evident from Figs. 1–2 is that measurement of individual magnetic effects gives quite a large scatter about the mean value—a scatter corresponding to a standard deviation σ on the order of 0.25–0.30. How large must be the mean value to prove statistically significant at such distribution density? It is clear that this depends on the number of measurements from which the mean is determined. The number of necessary measurements can be approximately estimated proceeding from that the sample mean μ must be larger than the standard error of the mean $\sigma/\sqrt{n}$. Hence, for registering a 10% mean magnetic effect one needs about 10 measurements; for a 1% effect, about 1000 measurements. In the given work the global mean magnetic effect was determined on a sample of size about 40000, which practically guarantees the reliability of the second digit in the estimate of the global magnetic effect of 1.7%.

What is known about the reproducibility of MBE? It is that this reproducibility is insufficient by strict scientific measure. Analysis of the shapes of distribution of magnetic effects shows that one of the causes of insufficient reproducibility, at least with respect to the biological effectiveness of magnetic vacuum, consists in the differences between the individual and the batch magnetic effects. Specifically, the small reproducibility is connected with that the scatter of individual

effects is significantly greater than the mean magnitude of the batch effect. In the given work, 16 times greater. The mean magnitude of a batch MBE may be close to zero, and accumulation of more and more new data would then lead to a conclusion that on average there is no magnetic effect. Therewith an opponent of magnetobiology implicitly takes that concrete realizations of measurements are noisy with extraneous factors, being realizations of a random quantity with zero mean. This is not so: the batch magnetic effect is formed by averaging of individual effects, each of which is in a substantial measure nonrandom and even by itself may be a statistically significant effect. A near-zero batch effect does not signify the absence of magnetic effects in general.

Despite their similarity, the individual and the batch magnetic effects are different effects, at least on the strength of the dissimilar nature of their dispersions. The scatter in these effects is conditioned by factors of different origin. Analogously, for example, the time of individual sensomotor reaction contains a random component formed by many factors of brain activity and nerve pulse conduction, while the variability of this trait in the population is determined by phenotypic dispersion.

At the same time, the distinction between individual and batch magnetic effects is quite conditional. This is connected with the conditional character of the definition of an individual or whole biological system. The border is not strictly defined, and can be drawn in different ways. For example, a cell culture presents an individual organism or a batch depending on the conditions of observation.

Because of the nonspecificity of MBEs they exist and may exhibit statistical stability on different levels of organization of biological systems. The border is conditional: the individual magnetic effect of examinee M_n may be regarded as a batch one for M_{nm} effects registered in different cognitive tests. Another example: a batch effect of several tens of examinees presents as individual if this group is taken to belong to some distinguished population—age, urban, geographic, etc. among a multitude of such populations. In other words, any observed magnetic effect presents simultaneously as individual and batch one relative to elements of different level of systems organization.

A separate organism possesses a unique reaction to a change of MF. For this reason the notion of a mean MBE value may be as useless as a notion of a mean dactyloscopic pattern. In the latter case, averaging boils down to the absence of any pattern altogether. Likewise the mean magnetic effect is small but this does not mean that the individual magnetic effects are small. In the given work among the 40 examinees, 16 showed a mean magnetic effect exceeding 5% in absolute value, eight exceeding 8%, and in four examinees the magnetic effect was greater than 10%.

The common that is present in unique magnetic reactions is the batch magnetic effect. The particular that is contained therein is the individual magnetic effect. In the measurements of the reaction of the organism to MF, there are contributions of both effects. To separate these contributions, it is necessary to include into the experiment many organisms and subject each of them to multiple trials. The fact that this is far from being always practically feasible manifests itself as the reduced reproducibility of magnetobiological phenomena.

Throughout the above the magnetic effect meant the effect of a 100-fold weakening of the local MF observed in the parameters of psychophysical testing of 40 examinees. On a whole, the action of MF on organisms does not possess expressed specificity. Such action has been observed in all physiological systems of the organisms and at all levels of their organization beginning with processes in single cells. On the strength of this nonspecificity there are grounds for believing that the regularities discussed in the present work have a more fundamental significance and remain valid in respect of biological reception of changes in the level of constant MF in general, or in respect of magnetic biological phenomena on the whole.

CONCLUSION

1. There exist two different types of distribution of magnetic effects. The distribution of single measurements of the reaction of a whole organism to MF determines the individual mean magnetic effect, which possesses statistical stability and may, at a sufficient magnitude, possess statistical significance. The distribution of individual magnetic effects forms the mean batch magnetic effect.

2. On the strength of the existence of individual stable reactions to MF and their broad scatter as compared with the mean batch effect, in the measurements of magnetic effects the most probable are the least significant results.

3. The mean value does not present an informative characteristic of the batch magnetic effect. Such is the shape of the stable batch distribution of individual mean magnetic effects.

4. It is methodologically important in magnetobiological studies to take into account the difference between the individual and the batch magnetic effects and to choose beforehand the investigation strategy guaranteeing attainment of statistical stability of the results.

5. For studying the primary mechanisms of magnetoreception, expedient is preliminary selection of individual organisms possessing elevated sensitivity to MF variations.

ACKNOWLEDGMENTS

The author thanks his colleagues V.A. Milyaev and R.M. Sarimov for participation in organizing and conducting the experiments and the group of examinees who kindly agreed to be tested.

REFERENCES

1. V. N. Binhi and A. B. Rubin, Biomed. Tekhnol. Radioelektron. **2–4**, 63 (2007).
2. M. N. Zhadin, Bioelectromagnetics **22**, 27 (2001).
3. V. N. Binhi and D. S. Chernavskii, Europhys. Lett. **70**, 850 (2005).
4. R. N. Shepard and L. A. Cooper, *Mental Images and Their Transformation* (MIT Press, Cambridge, 1982).
5. R. M. Sarimov and V. N. Binhi, Biomed. Radioelektron. **1**, 20 (2009).
6. R. M. Sarimov, V. N. Binhi, and V. A. Milyaev, Biofizika **53**, 856 (2008).
7. G. Sheffe, *Dispersion Analysis* (Nauka, Moscow, 1980) [in Russian].
8. D.-O. Kim, et al., *Factor, Discriminant and Cluster Analysis* (Finansy i Statistika, Moscow, 1989) [in Russian].
9. V. N. Binhi and R. M. Sarimov, Electromagn. Biol. Med. **28**, 310 (2009).