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High temperature superconducting magnetic system for neuron activity researches

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The paper describes a high-temperature superconducting magnetic system (HTS SMS) to equip an experimental stand intended for neuron activity researches under constant and low-frequency magnetic fields up to 1 T. The design of the magnetic system together with its electromagnetic and cryogenic parameters is briefly discussed. The test results of the preliminary experiments conducted in liquid nitrogen at 77 K for two interchangeable magnets are given. The first magnet was manufactured in the form of a double pancake coil wound with 4 mm high HTS tape. The second magnet was made of pure copper wire with no frame and was impregnated with a thermally conducting epoxy resin. The advantages of the HTS pancake coil were demonstrated in comparison with the cryo-resistive solenoid. Low energy consumption of the HTS magnetic system will allow conducting continuous non-invasive monitoring of biological objects in a magnetic field.

Keywords: superconductivity, high-temperature superconductor, REBCO tape, cryogen magnetic system, magnetic field, neuron activity.

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Introduction

Technical superconductivity already today is efficiently used in medicine and biology. Magnetic resonance tomographs (MRT), nuclear magnetic resonance (NMR) spectrometers and accelerators for proton therapy of oncological diseases, made of low-temperature superconductors (LTSC), have become indispensable tools for doctors and biologists [1,2]. Thereat, superconducting technologies are being constantly developed. The progress in industrial production of second-generation high-temperature superconducting tapes (HTS-2) [3] has resulted in a fundamentally new possibility to engineer cost-effective superconducting magnetic systems (SMS) for generation of high magnetic fields with the minimum costs of cryogenic facilities.

Persistent scientific search for new applications of superconducting technologies in gene engineering and other medical-biological research is underway. Superconductors are indispensable in the creation of new-generation high-field tomographs for monitoring of human brain activity in the course of information processing. As an example, we can mention the works for the creation of an MRT-magnet with the magnetic field density of 11.7 T [4], as well as MRT unit projects with a magnetic field of 20 T [5]. Another promising area is the development of a method for drug delivery to a specific area of the organism. In this technology, positively charged magnetic nanoparticles, precoated with a negatively charged biologically active agent, are injected into living tissue and are delivered to the focus of a disease by means of a local source of external magnetic field. Such research is being conducted in ophthalmology, for the treatment of malignant tumors and in genetic experiments [6,7]. For instance, paper [8] describes the development of HTS-2 of an SMS that generates a magnetic field with the gradient of 20−70 T/m for studying the gene transport processes. Projects have also been suggested to substitute permanent magnets in the form of Halbach arrays in biological experiments by HTS-2 windings [9]. Superconducting quantum interference devices (SQIDs) in magnetic encephalography (MEG) record infinitesimal (approximately 10^{-15} T) electromagnetic signals of the brain, while HTS-2 tapes are used for magnetic shielding [10]. This paper deals with another sphere of SMS application in biological studies, namely the creation of devices for studying the neuron activity under the magnetic field action.

Clarification of brain activity mechanisms is a most interesting fundamental task of medical physics. When solved, it will help open efficient methods for treatment of a number of diseases, as well as develop fundamentally new computing devices and control systems that simulate brain activity.

The optogenetic method is one of the techniques to study neural activity. In this method, special light-sensitive channels (opsins) are injected into nerve cell membranes, and neurons are activated or deactivated under exposure to light of a certain wavelength. The evident shortcoming of this method is its invasiveness — a part of the skull must be removed and optical fibers must be implanted in the brain.

An alternative can be a magnetogenetic technology for non-invasive simulation of certain cognitive functions of the brain (e.g., particular memory traces). In this method, the magnetic field induces selective activation of a separate population of neural networks in the brain marked by magnetically sensitive proteins. The evident advantage of the magnetic field used as an activator is the greater (as compared to light) depth of penetration in living tissues. The maximum measured depth of magnetic field penetration into brain structures is 9 cm.

Most magnetogenetic experiments [11–14] are conducted in two stages. Neurons are first exposed to a magnetic field, and then behavior of the subject of research is observed. From the biological viewpoint, it is more interesting to continuously monitor the behavior of neurons in a constant or variable magnetic field.

It is considered that a neural response will be most likely received under three types of magnetic action: when the subject of research for a long time stays in a constant magnetic field with a density of up to 1 T with continuous state monitoring, under the action of a variable field with a frequency of up to 100 Hz and amplitude of up to 0.5 T, as well as under the action of a variable field with a frequency of up to 500 kHz and amplitude of up to 50 mT.

Selection of a magnetic field source for magnetogenetic experiments is an optimization problem that depends on peculiarities of specific trials. The cost of magnetic system manufacture and operation costs are also no less important. The most affordable magnetic field sources are permanent magnets based on rare earth elements with needle concentrators of magnetic flux, which are most frequently used in neuron research. However, their capabilities are restricted to generation of a permanent magnetic field with a density of less than 0.5 T on a specimen. Resistive non-cooled electromagnets consume too much power.

Cryomagnetic systems can solve the problem. Copper windings cooled by liquid nitrogen are simple and can be used in short experimental sessions to generate variable magnetic fields with an intensity of up to 0.5 T. HTS-2 SMS, despite the relatively complex technology of winding manufacture and the high conductor cost, are universal sources of magnetic field. At a temperature of $65-77$ K, they, combined with magnetic flux concentrators, can generate both a constant and a variable magnetic field with the amplitude of 1 T and higher for a long time, power consumption being low [15].

Since 2019 we have been working on the creation of a cryomagnetic system for the specialized experimental stand at the Laboratory for Memory Mechanisms and Technologies of the Neurosciences Department at the NBICS-Center of „Kurchatov Institute“ NRC for neuron expression study *in vitro* in a constant and low-frequency (up to 100 Hz) magnetic field [16–18]. The need for placement of a cryostat with SMS on the already existing stand based on the Nikon Eclipse TI research microscope, initially intended for optogenetic research, imposes several limitations on the cryomagnetic system design. Moreover, at the moment it is not quite clear which operating mode of the magnet will be most widely used. Therefore, within the framework of R&D we have made and tested two interchangeable magnets designed for operation at $T = 65-77$ K: a cryoresistive magnet of high-purity copper and a superconducting one of HTS-2 tapes.

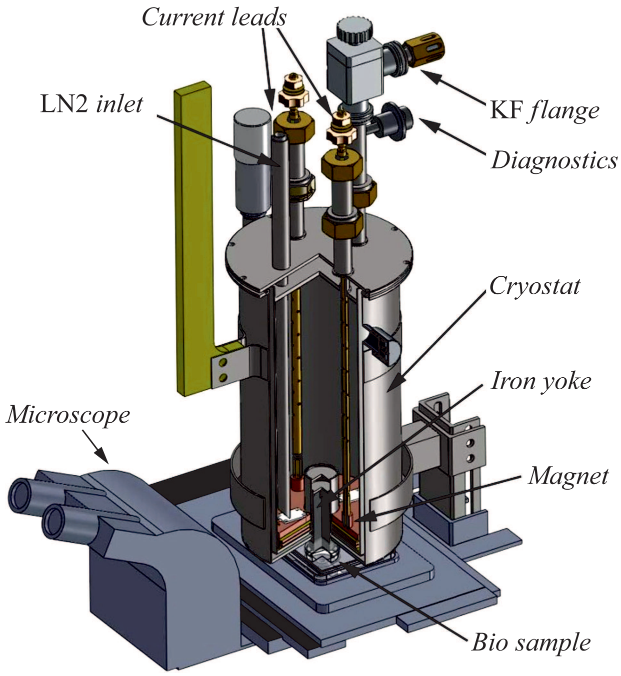

Figure 1. Three-dimensional sketch of the high-temperature superconducting magnetic system for neural research assembled with a microscope.

The next sections give the design features of the cryomagnetic system, its electrical and cryogenic parameters, the magnet manufacture technology, as well as the results of their testing in liquid nitrogen.

1. Cryomagnetic system

The sketches of the cryomagnetic system for neural research and the photo of the made cryostat are shown in Fig. 1 and 2. The magnet is placed in a cryostat with liquid nitrogen. A container of $D = 36$ mm with a biological subject of research is located 30 mm below the magnet's lower end. The magnetic flux is concentrated on the specimen using a cylindrical core made of permendur 49K2F with the diameter of 30 mm, placed in a blind „warm“ hole of the cryostat. The core's lower end is pressed to the specimen container cover. Diagnostics of the cryomagnetic system includes three temperature sensors and two Hall sensors for magnetic field measurement.

Evaporating nitrogen passes through the brass current leads with a developed cooled surface. In extended biological experiments, the cryostat filling hole may serve as a terminal for cryogenic feeder connection (LN2 feeder) —

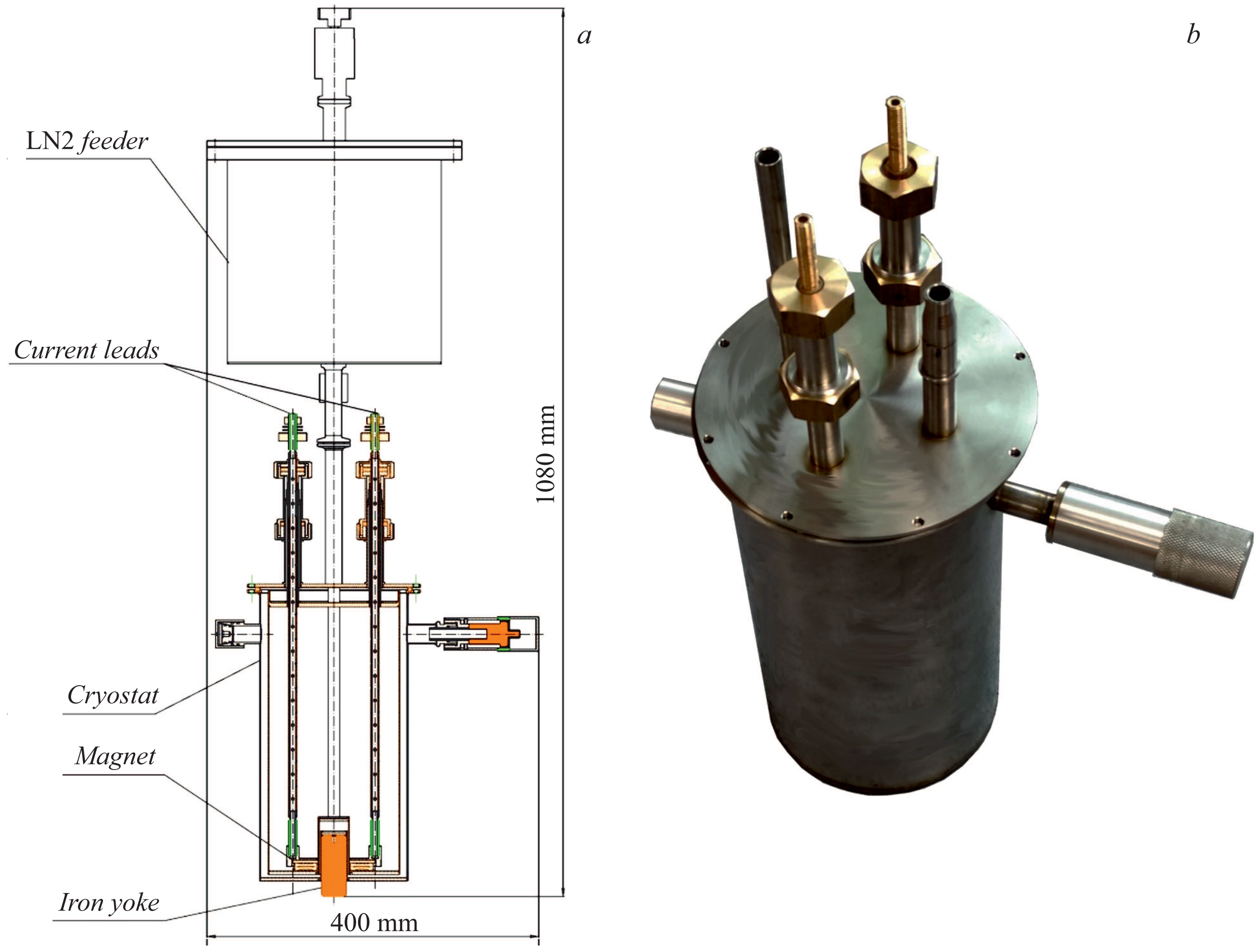

Figure 2. Overall dimensions of the high-temperature superconducting magnetic system (a) and its cryostat assembly (b).

Fig. 2, *a*. The latter is a Dewar vessel with coolant and branch pipes for its supply by gravity to the main cryostat. The cryostat design provides for operation in sub cooled nitrogen with pumping-out at $T = 65\,\mathrm{K}$ in order to increase the operating current of the HTS-2 magnet and the generated magnitude of magnetic density. We have already tried this method earlier [19]. At present, all the cryostat parts have been made and are being assembled (Fig. 2, *b*).

2. Magnets

The interchangeable magnets of a copper wire and a HTS-2 tape are shown in Fig. 3 and 4. Their main operational characteristics are compared in the table. A frameless copper magnet, made in the form of a multi-layer solenoid, was impregnated with three-component cryogenic epoxy adhesive during winding. Heat transfer from the internal turns of the cryoresistive winding was improved by using powdered aluminum oxide (Al_2O_3), thermal conductivity of which at a temperature of $77-40\,\mathrm{K}$ is $2-6$ times higher than that of copper [20]. 2 weight fractions of adhesive corresponded to 1 weight fraction of additive.

The superconductive magnet wound of a 4 mm HTS-2 tape manufactured by SuperOx in varnish polyimide insulation, has the form of an oppositely directed double pancake coil with an internal junction. The pancake coil sections are isolated from each other by a polyimide gasket. The internal junction of the HTS-2 pancake coil (Fig. 4, *b*) was made using an auxiliary former the diameter

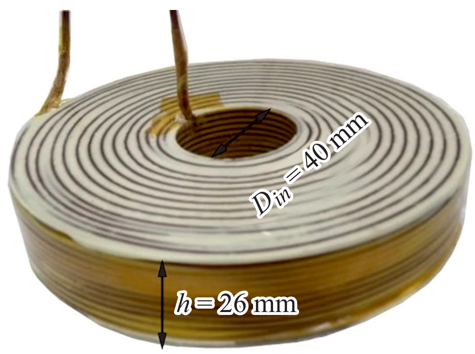

Figure 3. Resistive magnet after winding.

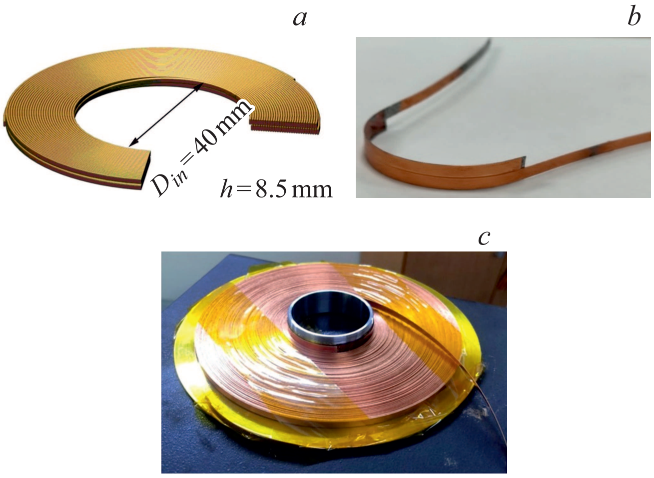

Figure 4. Model of a double HTS-2 pancake coil sized (*a*); junction of HTS-2 tapes on the internal turn of pancake coil (*b*), double HTS-2 pancake coil on a steel framework during winding (*c*).

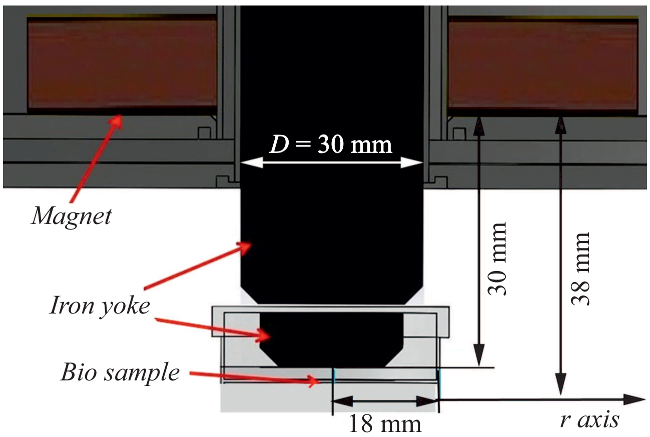

Figure 5. Layout of the magnetic system for calculation of distribution of magnetic field density on a biological specimen.

of which matched the internal diameter of the pancake coil framework. Resistance of the HTS junction, preliminarily measured in liquid nitrogen, was equal to 116 nΩ at 77 K.

Distribution of magnetic field density in the biological specimen location area for both magnets with cores was calculated in the Finite Element Method Magnetics (FEMM) package [21]. The program allows for modelling of axisymmetrical electromagnetic fields by the finite element method and can be used to solve electromagnetic two-dimensional problems. The magnetic system geometry used in the calculation is shown in Fig. 5. The design winding current density is specified in the table.

The calculation results for the superconducting and resistive magnet assemblies with a magnetic flux concentrator made of permendur 49K2F are shown in Fig. 6. It is seen that both magnet assemblies with a warm core can generate a magnetic field with the density of ~ 0.5 T at the liquid nitrogen temperature of ($T = 77$ K). When operating with pumped-out sub cooled liquid nitrogen ($T = 65-70$ K), the HTS-2 magnet with a core will yield a field above 1 T.

The table and the calculated curves in Fig. 6 show well the advantages of the HTS-2 magnet as compared to the copper one. The main disadvantage of the resistive magnet is the high power consumption. With the current of (150–200) A and $T = 77$ K, it will be 1.35–2.40 kW, corresponding to the liquid nitrogen flow rate of 30–54 l/h. Due to this, a cryoresistive solenoid can be used in short-term biological experiments with a constant field, as well as for generation of a variable magnetic field with a frequency of up to 100 Hz.

Thanks to the almost twice higher field/current coefficient, the HTS-2 magnet places the core in the magnetic saturation zone. On the one hand, it provides the maximum magnetic density value on the specimen $B_{max} = 1.2$ T (when the magnet operates in sub cooled nitrogen), on the other hand — it causes greater dissimilarity of magnetic field density on the specimen (Fig. 6, *b*).

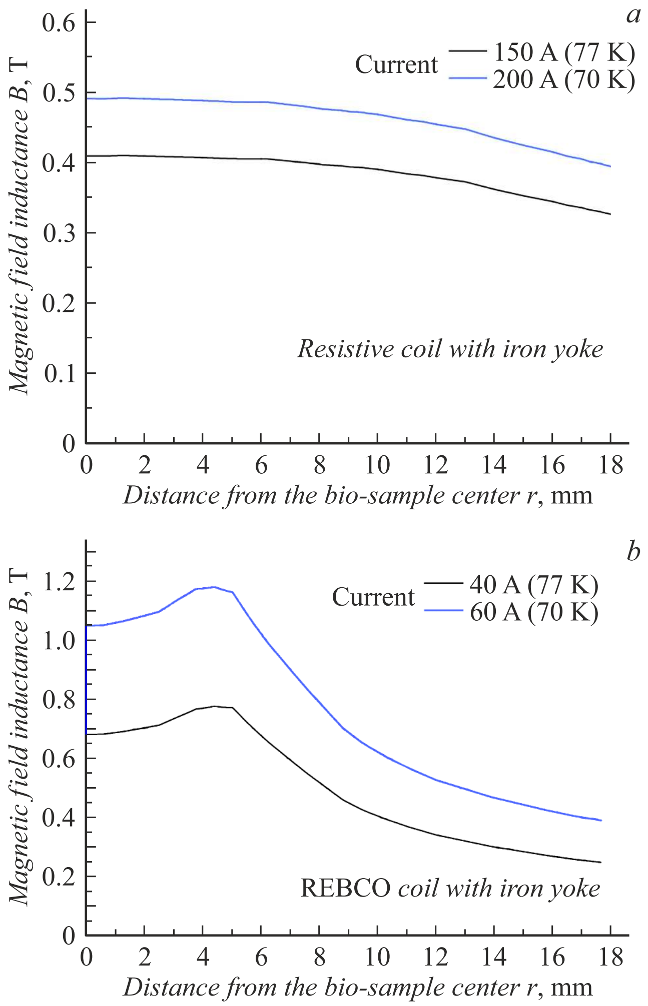

Figure 6. Calculated distribution of magnetic field density on a biological specimen: resistive magnet with core (*a*), HTS-2 magnet with core (*b*).

Characteristics of cryomagnets

Magnet type	Superconducting	Resistive
Conductor	HTS-2 tape 4×0.1 mm, SuperOx, Ic_min $(77\,K) = 110$ A	Round wire made of M0 copper, $D = 2.1$ mm
Insulation type	Kapton varnish with coating thickness of $10\,\mu$m	Varnish ML-92 with coating thickness of $50\,\mu$m
Magnet resistance, Ω	$116 \cdot 10^{-9}$ (77 K) — junction	0.06 (77 K) 0.052 (70 K) 0.047 (65 K)
Winding shape	Double oppositely directed pancake coil Dry winding without impregnation	Multi-layer solenoid, embedded with epoxy resin ED-20 with added Al_2O_3 in 2:1 weight ratio
Framework material	12X18H10T	No framework
Internal diameter, mm	40	40
Outer diameter, mm	135	140
Height, mm	8.5	26
Number of turns	236 per each pancake coil section, total 472 turns	299
Winding density, 1/cm^2	117	23
Operating current at 77 K, A	40	150
Operating current density at 77 K, A/mm^2	47	35
Conductor length, m	130	93
Experimental field/current coefficient, mT/A	7.2	4.13
Inductance, mH	18	4
Heat release in the winding with constant operating current, W	< 1 (65–77 K)	1350 (77 K) 1170 (70 K) 1060 (65 K)

The cryoresistive solenoid does not saturate the core, so that the relationship between the magnetic field and current in the solenoid remains linear, while the field on the specimen is more homogeneous. However, the maximum value of magnetic field density in this case does not exceed $B_{\max} = 0.5\,\mathrm{T}$ (Fig. $6, a$).

The optimal parameters of magnetic fields (frequency, amplitude, homogeneity) for magnetogenetic studies are not yet known. All such studies are search-oriented, therefore at present we cannot predict how the increased dissimilarity of the external magnetic field in the case of a HTS-2 magnet affects biological specimens. Probably, our two interchangeable cryomagnets with a different magnetic field homogeneity will make it possible to conduct comparative studies of this type after magnetic system installation on a microscope.

3. Magnet testing

Preliminary tests of two magnets were carried out alternately in an open nitrogen bath without a permendur core. Current was injected by a Lambda GEN10-500 programmable current source. Current injection rate was 0.2 A/s. A protective diode was connected in parallel to the tested magnet for source protection during current output.

Signals from the current measurement shunt, Hall sensor and solenoid voltages were recorded by a NI CompactDAQ multi-channel measurement system. The Hall sensors were located in the magnets geometric center. The process and results of testing of the frameless resistive solenoid are shown in Fig. 7. Current was injected in two stages: the first injection — up to 40 A, then output up to zero,

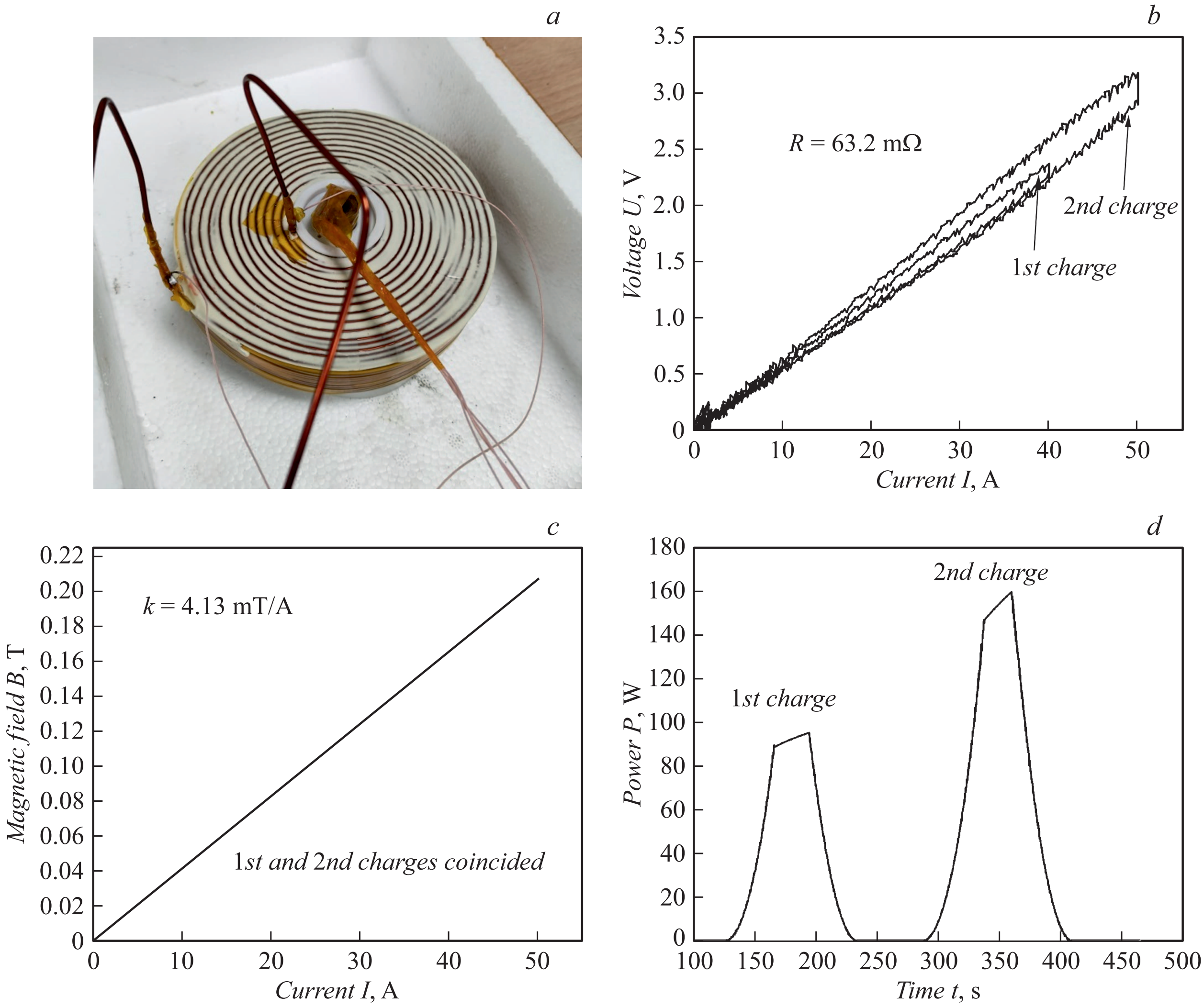

Figure 7. Resistive solenoid during testing (*a*); volt-ampere characteristic of the resistive solenoid (two inputs) (*b*); plot of magnetic density in the resistive magnet center vs. current (*c*); plot of power released in the resistive magnet vs. time (*d*).

and then the second injection up to 50 A. The measured field/current coefficient (4.13 mT/A) matches the design value (4.39 mT/A), obtained by the finite element method, the error being 5.8%.

Fig. 7, *b, d* shows heating of the resistive winding during current passage. In other words, magnet heat release under a load exceeded the heat removal capabilities of liquid nitrogen, even despite the presence of a heat-conducting additive in the epoxy adhesive used to impregnate the magnet turns. The conducted experiments make it possible to conclude that a resistive cryomagnet can be operated in short test sessions.

The test results for the HTS-2 magnet are given in Fig. 8. Current was injected in steps to compensate the reactive voltage component during superconductive magnet testing. The critical current of the HTS-2 pancake coil, determined according to the criterion of $0.1\,\mu$V/cm, was equal to ~ 42 A at the temperature of 77 K, which corresponds to the magnetic field density in the magnet center of $B = 0.3$ T and agrees well with the calculated load curve for the HTS-2 magnet (Fig. 8, *c*). The experimental field/current coefficient was equal to 7.20 mT/A, which matches the design value of 7.53 mT/A obtained by the finite element method, within 4.0% error. Heat generation in the HTS-2 magnet is due only to the presence of a junction and does not exceed 1 W.

Conclusion

The study of neuron behavior in a magnetic field may help improve the understanding of thinking and memory formation mechanisms, find new methods for treating a number of diseases, as well as create algorithms for new-generation computers.

Application of superconducting magnetic systems opens up new opportunities for biological research. Installation of a research biological stand based on the Nikon Eclipse TI microscope at the laboratory of the biomedical Center

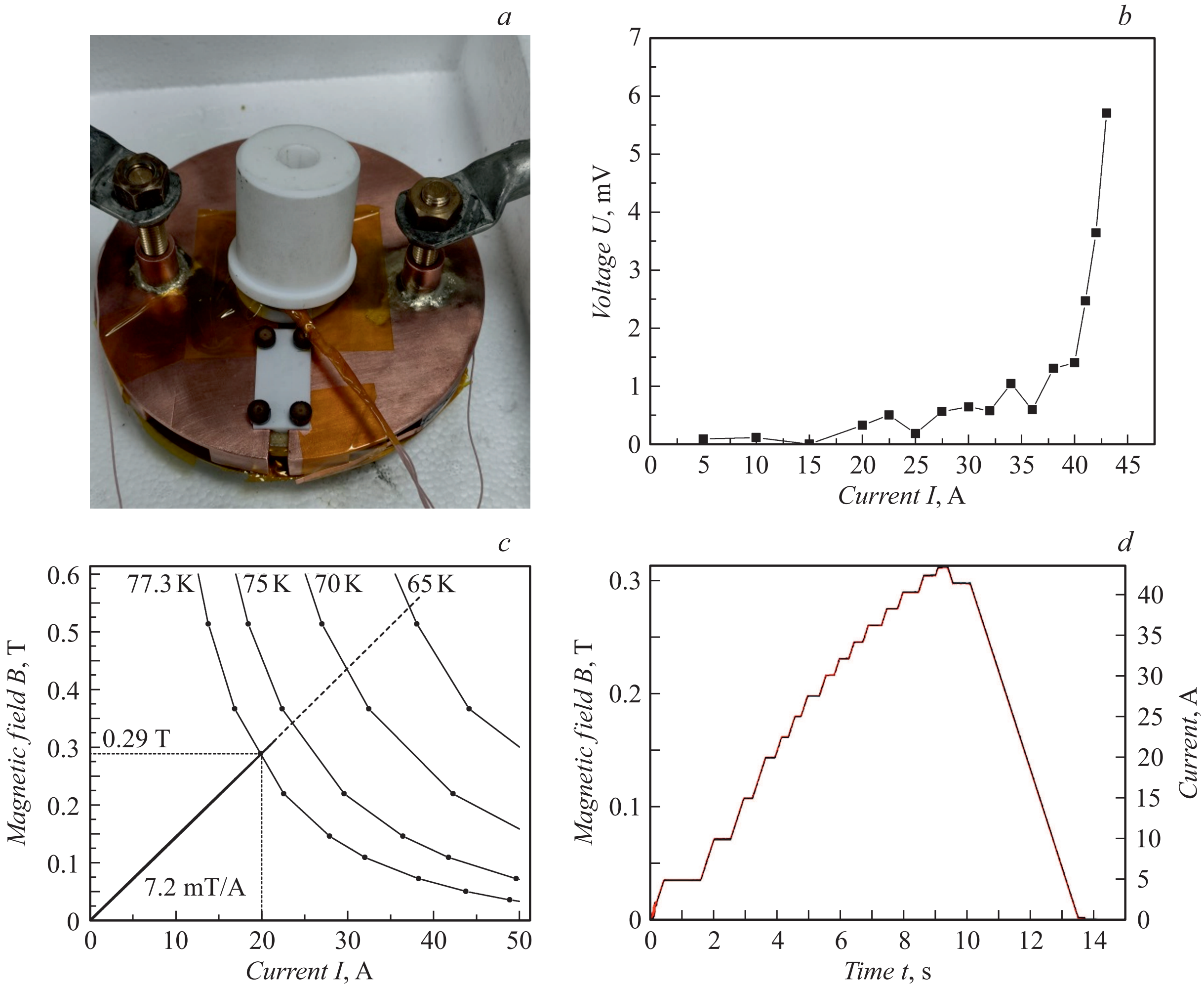

Figure 8. HTS-2 magnet during testing (*a*); volt-ampere characteristic of HTS-2 magnet (*b*); load curve of HTS-2 magnet without a core (*c*); plot of current magnitude and magnetic density in the center of the HTS-2 magnet without a core vs. time (*d*).

of „Kurchatov Institute" NRC with a superconducting magnetic system will allow for long-term continues *in vitro* monitoring of biological objects in a magnetic field with a density of up to 1 T.

The results of preliminary comparative tests in liquid nitrogen have demonstrated an evident advantage of the HTS-2 magnet as compared to the direct-current cryoresistive one. Out next actions include planning of testing of the made alternating-current cryomagnets with frequencies of up to 100 Hz in the operating cryostat of the stand assembled with a permendur core, as well as final installation of the SMS on the stand for neuron behavior study in a magnetic field in combination with a microscope. Further development of this topic suggests the creation of a trial HTS-2 cryomagnetic system for placement of animals in a magnetic field and study of cognitive processes and memory functions *in vivo*. Success will make it possible to create a fundamentally new non-invasive technology for specific magnetogenetic stimulation of cognitive networks in the brain, which can be used for treatment of diseases of the central nervous system, screening of pharmaceutical drugs, biological prosthesis control etc.

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Conflict of interest

The authors declare that they have no conflict of interest.

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