Magnetic Immunoassay Analyzer

XacPro-S

Operation & Maintenance Manual

(Version: 201411)

MagQu Co., Ltd.
3F, No. 12, Lane 538, ZhongZheng Road, Xindian District, New Taipei City 231, Taiwan
Website: www.magqu.com
Email Box: info@magqu.com Tel: +886-2-86671897 Fax: +886-2-86671809

Table of Contents

Safety Instructions

Please review the following safety warnings to avoid personal injuries and damages to the product and any related product.
In order to avoid potential risk, please use the product in compliance with relevant instructions.
Only qualified maintenance personnel can conduct maintenance procedure.

Prevent Fire or Personal Injury
Use Proper Power Line. Please use only the power line designated for the product and approved in the country where the product is used.

Correct Connection & Disconnection. Before lunching computer, please confirm whether the power is switching on. Switch off the power after shutting down the computer.

Ground The Product. The product is grounded through a ground conductor of the power cord. In order to avoid electric shock, the grounding conductor must be connected to the ground. Please confirm whether the product is grounded correctly before connecting the input and output terminal of the product.

Observe Power of All Terminals. Please notice power and relevant mark of the product in order to prevent any risk of fire or electric shock. Before connecting the product, please read the product manual so as to further understand relevant power information.

Disconnect Power. Please refer to concerned instructions to confirm the position to disconnect the product from power. Please do not hinder the power switch and it is accessible at any time when the product is in use.

Please do not operate before the cover is fitted on. Please do not operate the product when the cover is taken off. Be careful for refill liquid nitrogen and putting samples.

Please do not operate when doubting there is a fault. If you doubt the product is damaged, please allow qualified maintenance personnel to check it.

Prevent Circuit Exposed. Please do not touch any exposed connector and component when the current is conveyed.

Please do not operate under A moist condition.

Please do not operate in the flammable and combustible air.

Please keep the product surface clean and dry.

Keep Good Ventilation. Please refer to installation instructions of the manual for detailed information on how to install the product and provide it with good ventilation.

Warnings indicate the operation conditions that may cause injury or death.

Cautions suggest conditions or operations that may cause damage to the product or other objects.

Biohazard suggest conditions or operations that may cause environmental bio-pollution.

Other Guild lines: Indoor Use

Altitude: 2000 m

Temperature: 5 ^{o}C to 40 ^{o}C

Humidity: Maximun 80 % RH at 31 ^{o}C decreasing to 50 % RH at 40 ^{o}C

Transient overvoltage at Mains Supply: 2500 V

Pollution Degree: 2

Environmental Considerations

The section provides information relevant to the impact of the product on the environment.

Disposal of Product Discarded

Please refer to the following instructions when recycling any instrument or component.

Equipment Recycling: Nature resources of the equipment need to be recycled and reused. In the event that the equipment is not disposed correctly during discard, it may produce substances hazardous to the environment or human health. In order to avoid emission of such substances in the environment and reduce use of natural resources, recycling the product with a proper system is recommended for the purpose of ensuring most materials can be recycled and reused appropriately.

Chapter I Applications of Magnetic Immunoassay Analyzer

The magnetic immunoassay analyzer (Model: XacPro-S) launched by MagQu Co., Ltd. is used to measure the change in the ac magnetic susceptibility of a sample over time. If the sample is a mixture of a magnetic reagent and an object to be detected, it can be used to detect the concentration of bio-molecules in the object according to the change in the ac magnetic susceptibility of the mixture. XacPro-S is advantageous for bio-molecular assays in many ways, such as its operation is very simple, there is no need for users to calibrate concentration of the to-be-detected bio-molecules, it adopts CAA (Computer Automatic Analysis) with high accuracy and sensitivity and can detect low-concentration bio-molecules. XacPro-S can be applied to not only research, but also to clinical diagnosis and field trials.

To-be-detected bio-molecules mentioned above include protein [1-3], cytohormone, virus [4], nuclei acids [5], bacteria, even small molecular compounds. XacPro-S can help you to establish standard detection curves for new kinds of bio-molecules to be detected, further to measure content of the bio-molecules in the samples. It is expected that XacPro-S can be applied in the fields of *in-vitro* quantitative detection including agriculture, forest, fishing, stockbreeding, food and human body.

Chapter II Design of Magnetic Immunoassay Analyzer

Section I Principle of Magnetic Reduction Immunoassay

The magnetic immunoassay analyzer (Model: XacPro-S) utilizes the so-called immunomagnetic reduction (IMR) as its assay principle [6,7], which is described as follows.

Under external ac magnetic fields of which frequencies range from tens to millions of hertz, individual magnetic beads in a magnetic reagent will be driven by the external ac magnetic fields and swirl. The magnetic reagent produces ac magnetic signals (χ_{ac}) accordingly. Hereafter, the χ_{ac} of pure magnetic reagent is referred as to $\chi_{ac,o}$, as shown in Fig. 2.1.

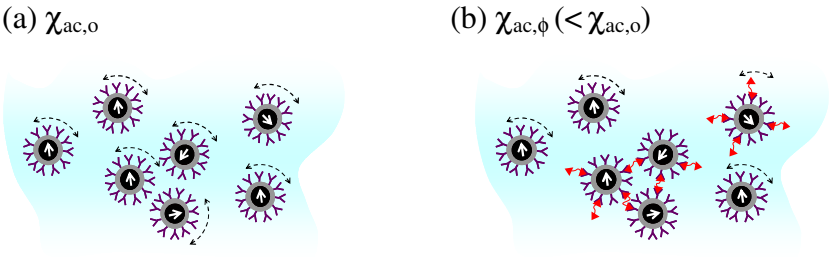


Fig. 2.1 Illustration of mechanism of immunomagnetic reduction to detect biotargets. (a) Each magnetic nanoparticle oscillates individually with the applied alternative-current magnetic field before binding with biotargets. (b) Portions of magnetic nanoparticles become larger due to the binding with biotargets. The bound magnetic nanoparticles in (b) contribute to the reduction in the alternative-current magnetic susceptibility χ_{ac} of the reagent.

When the magnetic reagent is mixed with the sample containing to-be-detected bio-molecules, bio-molecules will bind with magnetic beads via bioprobes (e.g. antibodies) on surface of the magnetic beads [8,9]. In this way, part of magnetic beads in the reagent will get enlarged, even many magnetic beads will gather together. In such case, compared with the number of swirling magnetic beads before the magnetic reagent is mixed with the sample, number of swirling magnetic beads in the reagent driven by external field is much fewer. So the ac magnetic signal (χ_{ac}) of magnetic reagent will reduce due to the binding between bio-molecules in the sample with magnetic beads; that's why we call the detection method as magnetic reduction immunoassay detection. Hereafter, the χ_{ac} of magnetic reagent mixed with a sample is denoted with $\chi_{ac,\phi}$. According to the description above, more bi-molecules the sample contains, more bindings between magnetic beads and bi-molecules will occur, and more magnetic reduction will appear. Thus

we can detect amounts of bi-molecule in the sample in reference to measurement on magnetic reduction of magnetic reagent.

To quantify the reduction in the χ_{ac} of magnetic reagent due to the binding between magnetic nanoparticles and biomolecules hereafter is defined as:

$$\text{IMR}\ (\%) = (\chi_{ac,o} - \chi_{ac,\phi})/\chi_{ac,o} \times 100\%, \tag{2.1}$$

where IMR(%) is referred as to IMR signal.
Furthermore, IMR signal was found as function of the biomolecular concentration ϕ via logistic function [1-5]

$$\text{IMR}(\%) = \frac{A - B}{1 + (\frac{\phi}{\phi_o})^{\gamma}} + B, \tag{2.2}$$

where A, B, ϕ_o, and γ are fitting parameters.

Section II Scheme of Magnetic Immunoassay Analyzer

According the mechanism of IMR, ac magnetic fields are applied to magnetic reagent. The time-evolution ac magnetic signal of magnetic reagent is detected. Thus, the magnetic immunoassay analyzer XacPro-S is equipped with sets of excitation coils, which generate ac magnetic fields to magnetize magnetic reagents [10,11]. A signal generator is used to applied ac current through the excitation coils. Once magnetic reagent is placed inside excitation coils, the reagent is magnetized. An ac magnetic signal of reagent is induced. To sense the induced ac magnetic signal of reagent, a pick-up coil is used, as schematically shown in Fig. 2.2 Then, the sensed ac magnetic signal of reagent is transferred to a

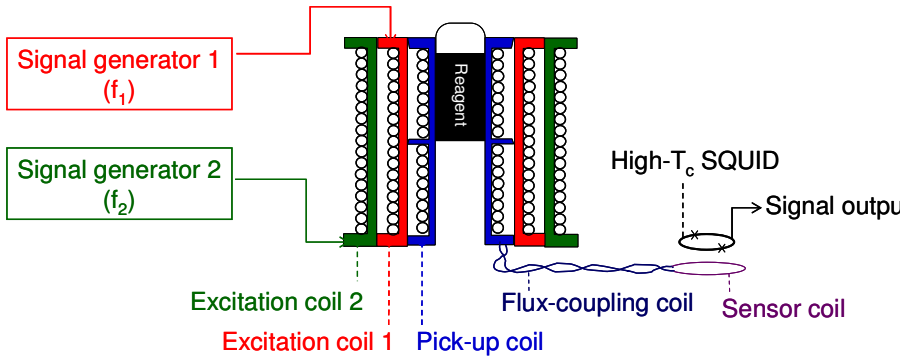


Fig. 2.2. Schematic configuration of XacPro-S for detecting ac magnetic signal of magnetic reagent.

magnetic sensor via a flux-coupling coil. One end of the flux-coupling coil is connected in serious with the pick-up coil, the other end of the flux-coupling coil is connected in serious with the sensor coil. A high-T_c superconducting quantum interference device (SQUID) magnetometer is used to detect the transferred magnetic signal at the sensor coil. Thus, the ac magnetic signal of reagent can be detected. With the time-evolution ac magnetic signal of reagent, the IMR signal can be measured. All the details of working principle of XacPro-S are available in Refs. 10 and 11

We will introduce main components consisting XacPro-S in the Chapter III.

Chapter III Hardware of Magnetic Immunoassay Analyzer

Section I Key Components

A picture to reveal the hardware of XacPro-S is as shown in Fig. 3.1.

Fig. 3.1. Magnetic immunoassay analyzer XacPro-S is consisted of three modules: sensing part, coils, and electronics.

Briefly speaking, XacPro-S is consisted of three modules:

1. Sensing part

   This part mainly contains a high-T_c SQUID magnetometer and its controller, a 5-L/10-L dewar, and electromagnetically shielded can. The high-T_c SQUID magnetometer is rf SQUID. A SQUID is a superconducting quantum interference device, serving as an extremely sensitive magnetometer. It is formed by a superconducting loop incorporating a weak link. The working mechanism of rf SQUID is described.

   The rf SQUID is formed by a superconducting loop incorporating a weak link, a so-called Josephson junction, as shown in Fig. 3.2. The

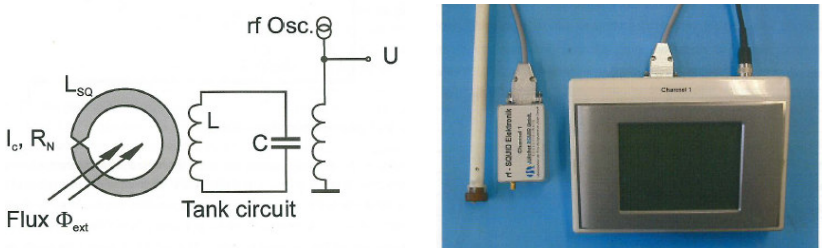


Fig. 3.2. Illustration and photo of rf SQUID magnetometer.

   laws of physics demand that the magnetic flux enclosed by a superconducting ring is quantized. The critical current of the Josephson junction, I_c its Ohmic resistance in the normalconducting

state, R_N, and the inductance of the ring, L, are the fundamental parameters governing the behavior of the SQUID. The SQUID is read out inductively by means of a tank circuit, a L_C resonance circuit operated close to its rf resonance. The main specifications of the rf SQUID magnetometer are as follows.

- Input voltage : 100/230 V 60 Hz
- AC Output voltage : 0-20 V
- AC Output frequency : 0-1 MHz
- DC Output: 5 ± 0.5 V

To achieve the Josephson effect, the SQUID must be at temperatures lower than its critical temperature T_c. For high-T_c SQUID, the SQUID is usually emerged in liquid nitrogen, which temperature is 77 K, lower than T_c. For XacPro-S, rf SQUID magnetometer is posited inside a 5-L or 10-L dewar containing liquid nitrogen.

Since the rf SQUID magnetometer is very sensitive to DC or AC magnetic signals, the ambient magnetic signals must be isolated. To do this, an electromagnetically shielded box is used, as shown in Fig. 3.3. The dewar with the rf SQUID magnetometer sits inside the

Fig. 3.3. Electromagnetically shielded box used in XacPro-S.

electromagnetically shielded box. The to-be-detected signal generated by the sample at an excitation/pick-up coil is guided to the rf SQUID magnetometer via a flux-coupling coil. The main specifications of the electromagnetically shielded box are listed below.

- Five layers consisted of either Al, Cu, carbon fiber, or μ metal.
- The shielding factor is 40-60 dB at 0.1 – 10 Hz, and is 100 dB at

1000 Hz.

- The outer diameter is 85 cm and the inner diameter is 30 cm.
- The height is 80 cm.

2. Coils

Coils include excitation coils, pick-up coils, flux-coupling coil, and sensor coil. Sample is located inside excitation coils. There are eight excitation coils. These excitation coils are located symmetrically, as shown in Fig. 3.4. Each excitation coil is equipped with a pick-up

Fig. 3.4. Photo of the assayed eight excitation coils.

coil. The size of an excitation coil is 120 ± 5 mm in diameter and 32 ± 2 mm in length. The size of a pick-up coil is 8.0 ± 1 mm in diameter and 6 ± 1 mm in length, as shown in Fig. 3.5.

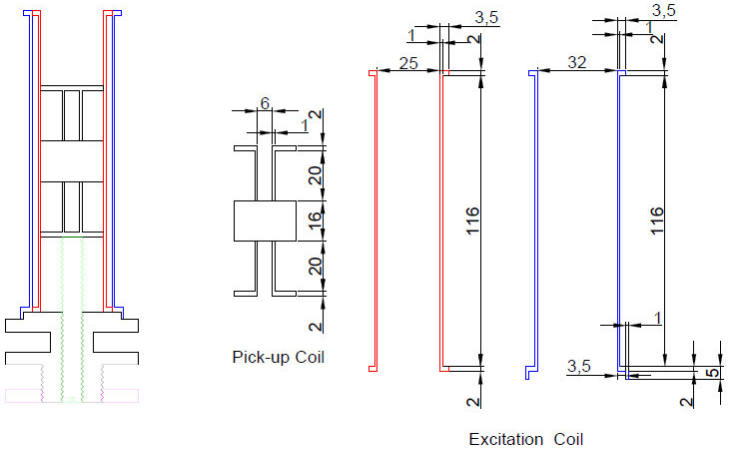


Fig. 3.5. Sizes of excitation coils and pick-up coil.

3. Electronics

Electronics are consisted of a signal generator (WF1944B, NF), switches, DAQ card (NI PCI6221/BNC2110), and a computer. For switching the driving voltage generated by the signal generator to one of the 8 sets of excitation coils, OMRON low signal relay is used. DAQ card generates +5V signal to switch on or off the relays. The signal generator, DAQ module, and relay are shown in Fig. 3.6. The detailed specifications are available on the following websites: http://www.nfcorp.co.jp/english/pro/mi/sig/f_gen/wave1/index.html

http://sine.ni.com/nips/cds/view/p/lang/zht/nid/14132

http://sine.ni.com/nips/cds/view/p/lang/zht/nid/1865

Fig. 3.6. Signal generator (upper left), relay (upper right), and DAQ module (lower left and lower right) used in XacPro-S.

Section II Important Specifications

The functional features of XacPro-S are listed below.

- Noise level < 65 μV/$Hz^{1/2}$ at operating frequency
- Signal to noise ratio > 10 for the mixture of 80-μl 0.3 emu/g magnetic fluid and 40-μl PBS solution
- Signal stability: CV < 10 %
- Amplitude of applied ac magnetic field < 20 Gauss
- Input voltage: 110/230 V_{ac}, 50/60 Hz, 500 W
- Magnetic-signal sensor: HTS SQUID Magnetometer
- Operation temperature: 25 ± 2 ^{o}C
- Operation humidity < 50 %
- Sample volume = 120 μl

Chapter IV Operation Procedure

Before installing or operating XacPro-S, please read these notifications carefully.

- Driver used with the operating software is provided by National Instruments without amendments by our company, MagQu Co., Ltd., and can be requested from the former two companies directly.
- It is required to calibrate XacPro-S with the standard solution produced by our company every year to ensure accuracy of the instrument.
- The following operational programs are the series product of Windows launched by Microsoft, which are used as OS and not applicable for Mac series and Linux System.

In this chapter, operation procedures of installation, parameter setting, measurement start up, sample preparation, and data analysis are introduced.

Section I Operating Procedure for Installation

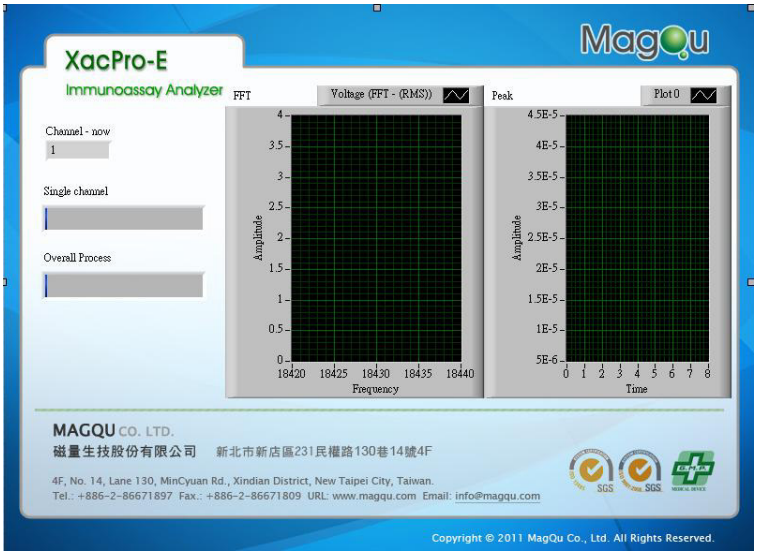
1. Installing DAQmx 8.8. (Contact to NI website)
2. Installing LVruntime engineer. (Contact to NI website)
3. Launch XacPro-S.exe

Section II Setting & Start-up Procedure of XacPro-S

1. Launch on the power, as shown.

2. Turn on the computer, and launch on the XacPro-S.exe. Setting parameters show below.

3. Push Start to measure the samples, and will end till 200 times for each channel are measured with 6 points per channel per time with saving the result.



Section III Sample Preparation

1. Take the magnetic reagent and the sample to be detected out of frig and shake them with Vortex for about 15 seconds separately.

2. Add 40 µl magnetic reagent and 80 µl sample to be detected into a detector tube commonly.

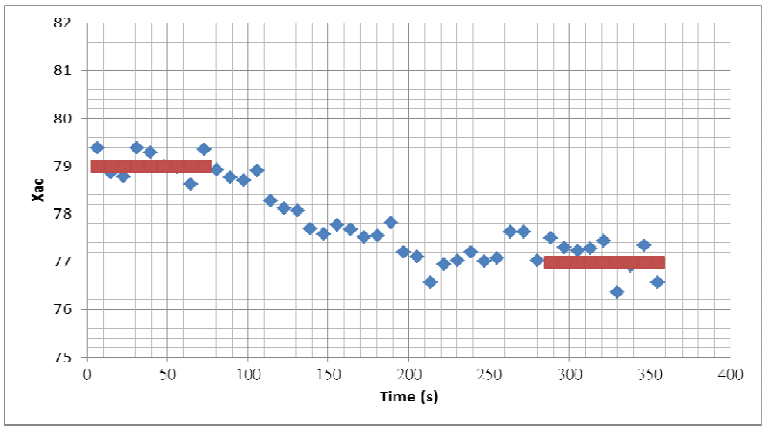
3. Shake the glass tube with Vortex for about 15 seconds to mix the magnetic reagent with the sample to be detected.

4. Place the detector tube into the sample box to measure the reaction.

Section IV Magnetic Reduction Signal Analysis

1. Open the notepad file saved with data process software and plot.

2. Calculate the mean values for relevant points before and after the reaction and adopt them in the following formula: IMR (%) = $(\chi_{ac,o} - \chi_{ac,\phi})/\chi_{ac,o}$ x 100%, in which $\chi_{ac,o}$ is the ac magnetic susceptibility signal before the reaction and $\chi_{ac,\phi}$ is the ac magnetic susceptibility signal after the reaction.



Chapter V Debugging and Maintenance

Common error information and simple troubleshooting are shown as following:

1. The furrier peak did not show while measurement.
2. The breaker shut down repeatedly.
3. XacPro-S.exe software can not launch on.

As for any situation listed or not listed in the error information mentioned above, please contact our company as soon as possible. Do not try to repair or move the equipment by your own self. The contact information is:

Tel: +886-2-86671897

Email: info@magqu.com

Chapter VI Attentions

- Please confirm whether the transformer suitable for the voltage in the situation where the analyzer is used before using it (110V or 220V).
- Please connect the analyzer with power supply to warm up for an hour before using it.
- Please store the analyzer in a location without direct sunlight at room temperature.
- Do not place the analyzer in a location with much dust please.
- Please store the analyzer in a location unlikely to shake and please do not keep it under heavy pressure during transportation.
- Please refill liquid nitrogen two times per weak.
- Please operate the analyzer with genuine consumables from our company (please contact our company if you need to order the consumables at telephone number 02-8667-1897)

Do not place the analyzer XacPro-S close to a strong magnetic field or high-power electrical products. Be careful to open or close the door.

Section I Cleaning & Maintenance

1. You only need to use a piece of soft cloth soaked with water or mild solvent to wipe and clean the analyzer.
2. Please do not use any organic solvent to clean the housing or accessories.
3. Please do not detach the analyzer discretionally; contact the distributor if you need to repair it.
4. Do not try to transport or move the analyzer; contact the distributor if you need to move it.

Section II After-sale Services & Guarantee

1. The product is provided with 1 year of free warranty term after sale.

2. As for the following cases, the services will be charged properly even in the warranty term:

   (a) Any damage or fault due to improper use or act of God such as lightning etc.

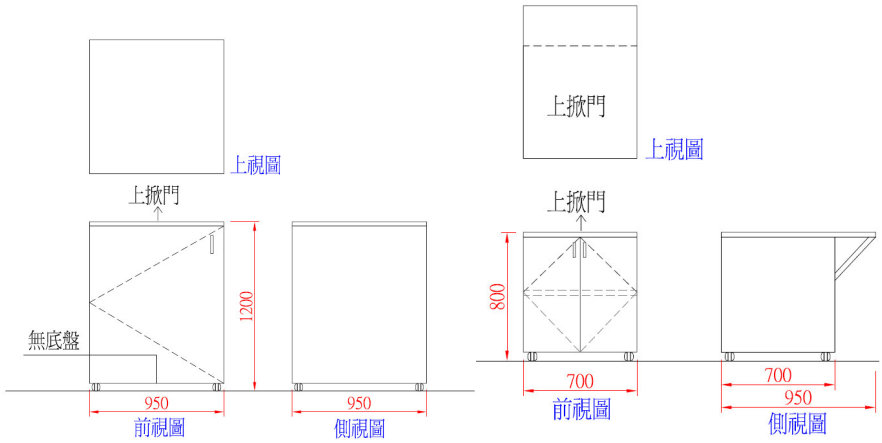
   (b) Any damage or fault due to discretional repair, modification or repair by any other third party.

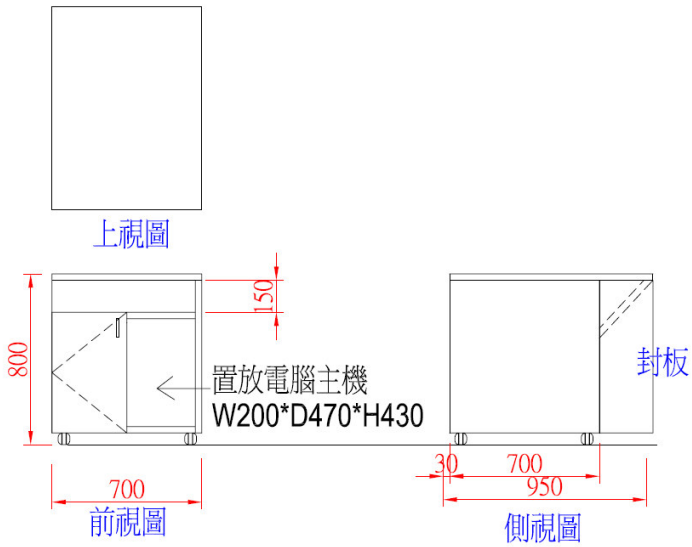
   (c) Any damage or fault due to change of installation location, transportation or falling down etc.

3. Please contact to distributors when the analyzer required repair. As the analyzer is a precision instrument, it must be transported by distributor.

Appendix A Structural Block of XacPro-S

Dimensional drawing of Magnetic Immunoassay Analyzer XacPro-S is shown as the following:





※ Net weight 150 kg

Appendix B List of Packing Inserts

XacPro-S packing list	
Accessory name	Quantity
XacPro-S working table	1
XacPro-S Shielding box	1
Dewar	1
SQUIDs with controller	1
Sample coils	8
DAQ card (PCI)	1
Computer with screen	1
Liquid nitrogen refilling tube	1
Software disc	1
Manual	1

Appendix C Warning Icon Description

This Way Up

Careful Fragile

Keep Dry

Away From Magnetic Field

MagQu Co., Ltd.
3F, No. 12, Lane 538, ZhongZheng Road, Xindian District, New Taipei City 231, Taiwan
Website: www.magqu.com
Email Box: info@magqu.com Tel: +886-2-86671897 Fax: +886-2-86671809

References

1. K.W. Huang, S. Y. Yang, C.Y. Yu, J.J. Chieh, Che-Chuan Yang, Herng-Er Horng, Chin-Yih Hong, Hong-Chang Yang, and Chau-Chung Wu, "Exploration of the relationship between the tumor burden and the concentration of vascular endothelial growth factor in liver-cancer-bearing animals using immunomagnetic reduction assay", J. Biomed. Nanotechnol. **7**, 535 (2011).

2. S.Y. Yang, J.J. Chieh, C.C. Yang, S.H. Liao, H.H. Chen, H.E. Horng, H.C. Yang, C.Y. Hong, M.J. Chiu, T.F. Chen, K.W. Huang, and C.C. Wu, "Clinic applications in assaying ultra-low-concentration bio-markers using HTS SQUID-based AC magnetosusceptometer", IEEE Trans. Appl. Supercond. **23**,1600604 (2013).

3. M.J. Chiu, Y.F. Chen, T.F. Chen, S.Y. Yang, F.P. Gloria Yang, T.W. Tseng, J.J. Chieh, J.C. Rare Chen, K.Y. Tzen, M.S. Hua, and H.E. Horng, "Plasma tau as a window to the brain-negative associations with brain volume and memory function in mild cognitive impairment and early alzheimer's disease", Human Barin Mapping, 15 Oct. (2013).

4. S.Y. Yang, J.J. Chieh, W.C. Wang, C.Y. Yu, C.B. Lan, J.H. Chen, H.E. Horng, Chin-Yih Hong, and H.C. Yang, "Ultra-highly sensitive and wash-free bio-detections for H5N1 virus via magnetoreduction assays", J. Virol. Methods **153**, 250 (2008).

5. S.Y. Yang, J.J. Chieh, W.C. Wang, C.Y. Yu, N.S. Hing, H.E. Horng, Chin-Yih Hong, H.C. Yang, C.F. Chang, and H.Y. Lin, "Magnetic nanoparticles for high-sensitivity detection on nuclei acids via superconducting-quantum-interference-device-based immunomagnetic reduction assay", J. Magn. Magn. Mater. **323**, 681 (2011).

6. Chin-Yih Hong, C.C. Wu, Y.C. Chiu, S.Y. Yang, H.E. Horng, and H.C. Yang, "Magnetic Susceptibility Reduction Method for Magnetically Labeled Immunoassay", Appl. Phys. Lett. **88**, 212512 (2006).

7. C.C. Yang, S.Y. Yang, H.H. Chen, W.L. Weng, H.E. Horng, J.J. Chieh, C.Y. Hong, and H.C. Yang, "Effect of molecule-particle binding on the reduction in the mixed-frequency ac magnetic susceptibility of magnetic bio-reagents", J. Appl. Phys.**112**, 24704 (2012).

8. Wanquan Jiang, H.C. Yang, S.Y. Yang, H.E. Horng, J.C. Hung, Y.C. Chen, and Chin-Yih Hong, "Preparation and properties of superparamagnetic nanoparticles with narrow size distribution and biocompatible", J. Magn. Magn. Mater. **283**, 210 (2004).

9. S.Y. Yang, Z.F. Jian, H.E. Horng, Chin-Yih Hong, H.C. Yang, C.C Wu, and Y.H. Lee, "Dual immobilization and magnetic manipulation of magnetic nanoparticles", J.

Magn. Magn. Mater. **320**, 2688 (2008).

10. J.J. Chieh, S.Y. Yang, Z.F. Jian, W.C. Wang, H.E. Horng, H.C. Yang, and Chin-Yih Hong, "Hyper-high-sensitivity wash-free magnetoreduction assay on bio-molecules using high-T_c superconducting quantum interference devices", J. Appl. Phys. **103**, 14703 (2008).

11. M. J. Chiu, H. E. Horng, J. J. Chieh, S. H. Liao, C. H. Chen, B. Y. Shih, C. C. Yang, C. L. Lee, T. F. Chen, S. Y. Yang, C. Y. Hong, and H. C. Yang, "Multi-channel SQUID-based ultra-high-sensitivity in-vitro detections for bio-markers of Alzheimer's disease via Immunomagnetic Reduction", IEEE Trans. Appl. Supercond. **21**, 477 (2011).


Accurate and Reliable assays make life healthy and clean