Elegant NMR®
User Manual

Elegant Mathematics LLC

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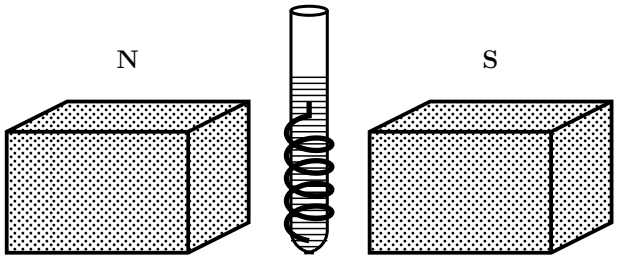
1 Purpose and Scope



All chemical elements are composed of one or more isotopes. Every isotope is either a zero-spin isotope or a non-zero-spin isotope. Nuclear magnetic resonance (NMR) is a physical phenomenon in which non-zero-spin isotopes absorb and re-emit electromagnetic radiation (energy) when placed in an external magnetic field.

NMR occurs at a specific resonance frequency; this frequency has a linear relationship with the strength of the permanent magnetic field and the magnetic properties of isotopes in the target field. Resonance occurs when the absorbed alternate magnetic field is transmitted orthogonally in the direction of the permanent magnetic field.

NMR spectrometers and magnetic resonance imaging (MRI) devices generally comprise one or more magnets that produce a strong magnetic field within a test region. These magnets are usually superconducting magnets, thus NMR applications are restricted to laboratory environments. Currently, anisotropic permanent magnets, i.e. having all parts magnetized in one direction, can achieve magnetic fields of only 1.5 T in strength compared to the 23 T of superconductor magnets.

$$\text{SNR} \sim B^2$$

The NMR signal response (i.e. SNR — signal to noise ratio) grows quadratically with regard to the magnetic field strength used in the experiment, which highly constrains the sensitivity and informativity of spectra produced by NMR spectrometers and/or MRI devices that have permanent magnets. NMR devices with permanent magnets are often referred to as low-field NMR spectrometers.

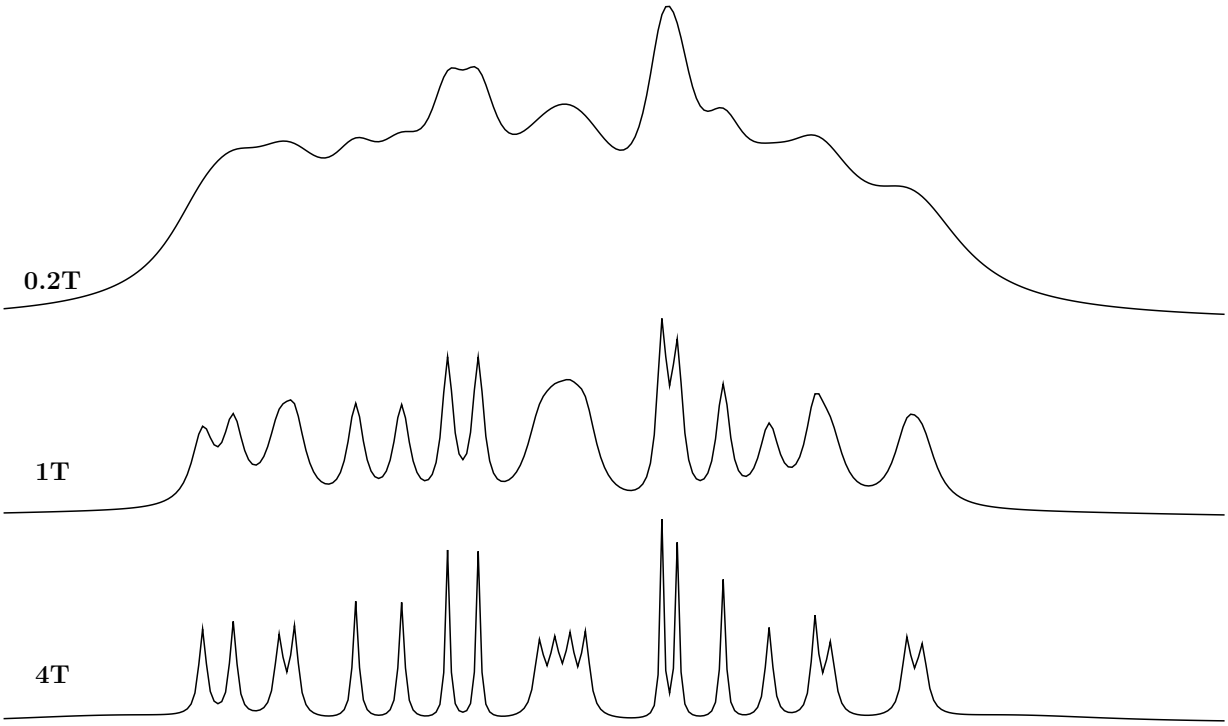
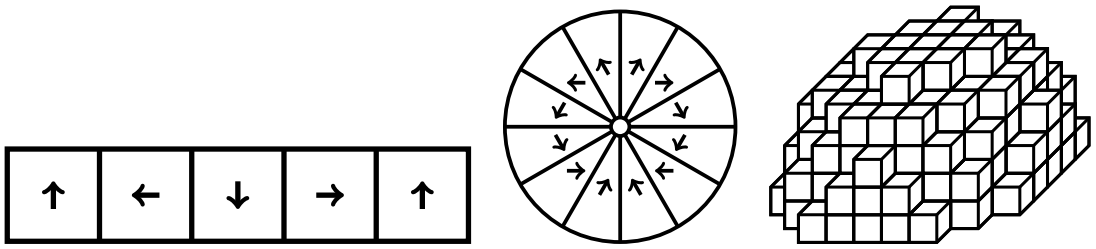


Figure 1: One dimensional 1H NMR Spectra of 1,2-dichlorobenzene (o-dcb) under ideal conditions on 0.2T, 1T and 4T. All spectra are scaled to [-7.6, -6.8]ppm chemical shift range.

When permanent magnets are combined with several other parts having appropriate magnetization, it is possible to build a focused magnetic field of greater strength than the maximal field achievable with the permanent magnet alone. One well-known combination is the Halbach structure, introduced by Klaus Halbach in 1980, which makes a 5 T magnetic field possible with permanent magnets. This structure is often used in NMR spectrometers; however, it requires joining an enormous number of magnetized pieces. Doing so may be commercially ineffective, or unreasonably sophisticated when using magnets of small size.

The second problem characteristic of the Halbach structure is the high instability of the generated magnetic field in terms of both time and temperature if the same material is used throughout. Patent US8148988 describes a Halbach system that compensates for this drawback through using several permanent magnets of different materials, albeit it only obtains almost half of the maximally achievable magnetic field strength.

Halbach structures may be roughly classified as follows: 1D - linear, 2D - cylindrical, and 3D - spherical. The maximal achievable magnetic field strength for 1D structures – is $2B$, for 2D – is $B\log(R_O/R_i)$, and for 3D is $(4/3)B\log(R_O/R_i)$, where B is the maximum achievable magnetic field for an anisotropic structure and R_O and R_i are the outer and inner radiuses of cylinders and/or spheres. This shows that 3D structures deliver the highest possible magnetic field: they are superior to 2D by a factor of 4/3, which increases sensitivity by almost a factor of 2!



1D	2D	3D
$2B$	$B \log\left(\frac{R_o}{R_i}\right)$	$\frac{4}{3}B \log\left(\frac{R_o}{R_i}\right)$

B=1.43T(NdFeB), $R_o = 10mm$, $R_i = 2.0mm$, ∼100 g

2.8T	2.3T	3.0T
4.0	2.6	4.0 (SNR)

B=1.43T(NdFeB), $R_o = 40mm$, $R_i = 1.5mm$, ∼2.5 kg

2.8T	4.7T	6.3T
4.0	11	19 (SNR)

At the same time, 3D structures require joining an enormous number of magnetized pieces, compared to 2D and 1D structures. They may be almost impossible to build in the case of small-sized, portable magnets, or they may not achieve the desired magnetic field because the process of gluing and joining reduces magnetic field strength.

In addition, one of the biggest disadvantages of low-field NMR spectrometers is the high fluctuation of their magnetic fields. If the magnets are small (of a size appropriate to a portable device), the intensity and direction of the external magnetic field may be adversely affected. Even turning a 1.5 T NMR spectrometer to an angle about six degrees perpendicular to the Earth's magnetic force lines will ruin any measurements, and the device will have to be recalibrated. Even a slight movement of the table on which a spectrometer is placed may significantly disturb the spectra generated. Another related difficulty is that currently available spectrometers usually require high temperature stability (of the order of 0.01^{O}C), which is incompatible with chemical production equipment and in-situ measurements in chemical reactions.

Due to the low signal-to-noise ratio, one-dimensional NMR spectra for low field NMR have very broad peaks (see Figure 1), resulting in prohibited usage of low field NMR spectrometers in advanced scientific or industrial applications.

There are two well-known and widely-used primary approaches that improve the sensitivity of NMR measurements: multi-nuclear and multi-dimensional spectra acquisition and dynamic nuclear polarization (DNP).

The acquisition of multi-nuclear spectra usually requires one receiver coil for each type of nucleus and/or calibration of each spectrum to internal standards; this requirement makes it impractical to fit currently available NMR spectrometers into smaller, portable devices.

The DNP method polarizes the spins of electrons in molecules. The normally random spins of the many electrons situated around the nuclei being investigated blur the nuclei's response. DNP forces all electron spins to point in the same direction, enhancing the NMR response from non-zero-spin isotopes. This well-known, widely-established method was first developed by Overhauser and Carver in 1953, but at that time, it had limited applicability for high-frequency, high-field NMR spectroscopy due to the lack of microwave (or gigahertz) signal generators. The requisite generators, called gyrotrons, are available today as turn-key instruments, and this has rendered DNP a valuable and indispensable method, especially in determining the structures of various molecules by high-resolution NMR spectroscopy. However, gyrotrons remain cost-prohibitive because they require expensive components, i.e. high-voltage generators, independent permanent magnetic field generators, and deep vacuum devices such as turbomolecular pumps.

Recent research [1] demonstrates a drastic improvement of NMR spectra sensitivity through the help of dynamic nuclear polarization (DNP). 1D NMR spectra has up to 500 times improved sensitivity, whereas multidimensional spectra improve NMR sensitivity up to 250,000 times that of NMR without DNP [2]. It is normally observed either by solid state NMR or by NMR of fluids with (<1T) [3].

Considering the fact that DNP improves sensitivity of heteronuclear spectra about 250,000 times, a 0.5T DNP NMR machine will produce similar sensitivity to a heteronuclear multidimensional NMR spectra at 12T (500MHz), a NMR spectrometer that operates on superconductor magnets!

The main disadvantage of multidimensional spectra is that spectra collection is a lengthy process. The method for obtaining sparse NMR spectra is already known, was discovered 20 years ago, and has been in use since then [4]. However, until recently, sparse data acquisition could only be performed by an experienced NMR operator, as the dynamic selection of sparse data acquisition points along with numerical processing on the fly has not yet been built into any one modern NMR spectrometer.

Currently, chemical analysis, particularly portable and benchtop analysis, is usually associated with chromatography devices. Chromatography is a laboratory technique for the separation of a mixture. The mixture is dissolved in a fluid called the mobile phase, which carries it through a structure holding another material called the stationary phase. The various constituents of the mixture have different partition coefficients and thus travel at different speeds, causing them to separate. Separated components are then flowed past a detector that is usually based on either conductivity or optical (UV, IR) absorption measurements. In some very rare cases, NMR may be used as detector or in parallel with a standard optical detector, but this is very restricted in application due to high equipment costs.

[1]: doi: 10.1073/pnas.1315778111
[2]: doi: 10.5194/mr-2-117-2021, 10.1016/j.jmr.2016.01.015, 10.1039/C7CC00635G
[3]: doi: 10.1016/j.pnmrs.2011.10.002
[4]: doi: 10.1002/nla.297, 10.1038/nmeth900

Chromatography has better sensitivity than NMR, but is less informative as the response of a chromatograph comprises only a retention time; no additional information about chemical composition is available. If the substance(s) in the mixture are unknown and need to be characterized, one must perform many different measurements, most likely with different chromatography columns and mobile phases, to conclusively identify the components.

In contrast, if NMR analysis is performed on one unknown substance, then a multidimensional NMR spectrum usually is sufficient to get all the information necessary for its identification, including not only its atomic composition but also the real spatial distribution of atoms in the molecule.

The straightforward combination of chromatography for separation with currently available NMR spectrometers for characterization is hindered by the inherent flaws of both methods: separation on a chromatographic column usually takes long periods of time (hours), and there is almost no control over how components separate; furthermore, the separated components are then flowed over the detector, remaining situated in the detector for only a few seconds (or even milliseconds). The vast majority of the time, the detector is filled with a known substance — the mobile phase. NMR detection itself requires a long time, usually hours, so that said straightforward combination of chromatography for separation with currently available NMR spectrometers requires slowing down the flow speed by several orders. These measurements occur on a timescale of several days or even weeks that is unrealistic in regards to commercial applications.

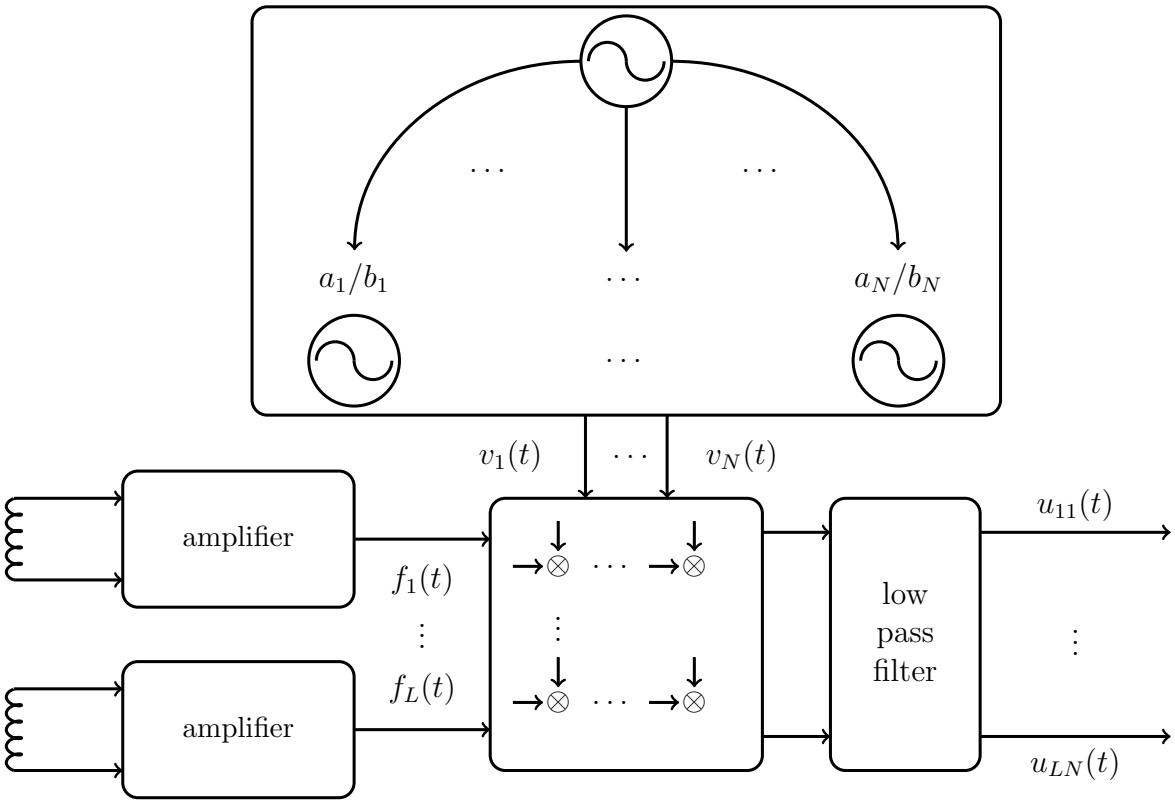
Taken together, prospective inventors of a portable/benchtop NMR spectrometer for industrial environments must overcome the following problems:

- construct a signal acquisition scheme that is stable despite fluctuations of the permanent magnetic field and/or of the signal generator;
- use NMR to detect all (or most) visible, non-zero-spin isotopes that are present in the investigated area to perform heteronuclear multidimensional spectra aquisition, with automated sparse non-uniform sampling and with automatic spectra recognition;
- construct a new device as a DNP polarizer that does not require high voltage generators, expensive deep vacuum devices such as turbomolecular pumps with size constrains, that that preferably use the same permanent magnetic field as the NMR transmitters;
- construct compact magnets with Halbach or Halbach-like structures that have better magnetic field strengths and are resistant to large temperature range;
- find an appropriate solution for using chromatography in conjunction with NMR to leverage the advantages of both methods.

2 Features

To address the aforementioned difficulties in the development of portable/benchtop NMR spectrometer, the Elegant Mathematics Team invented and developed the following technologies:

2.1 Correlated Oscillator Method

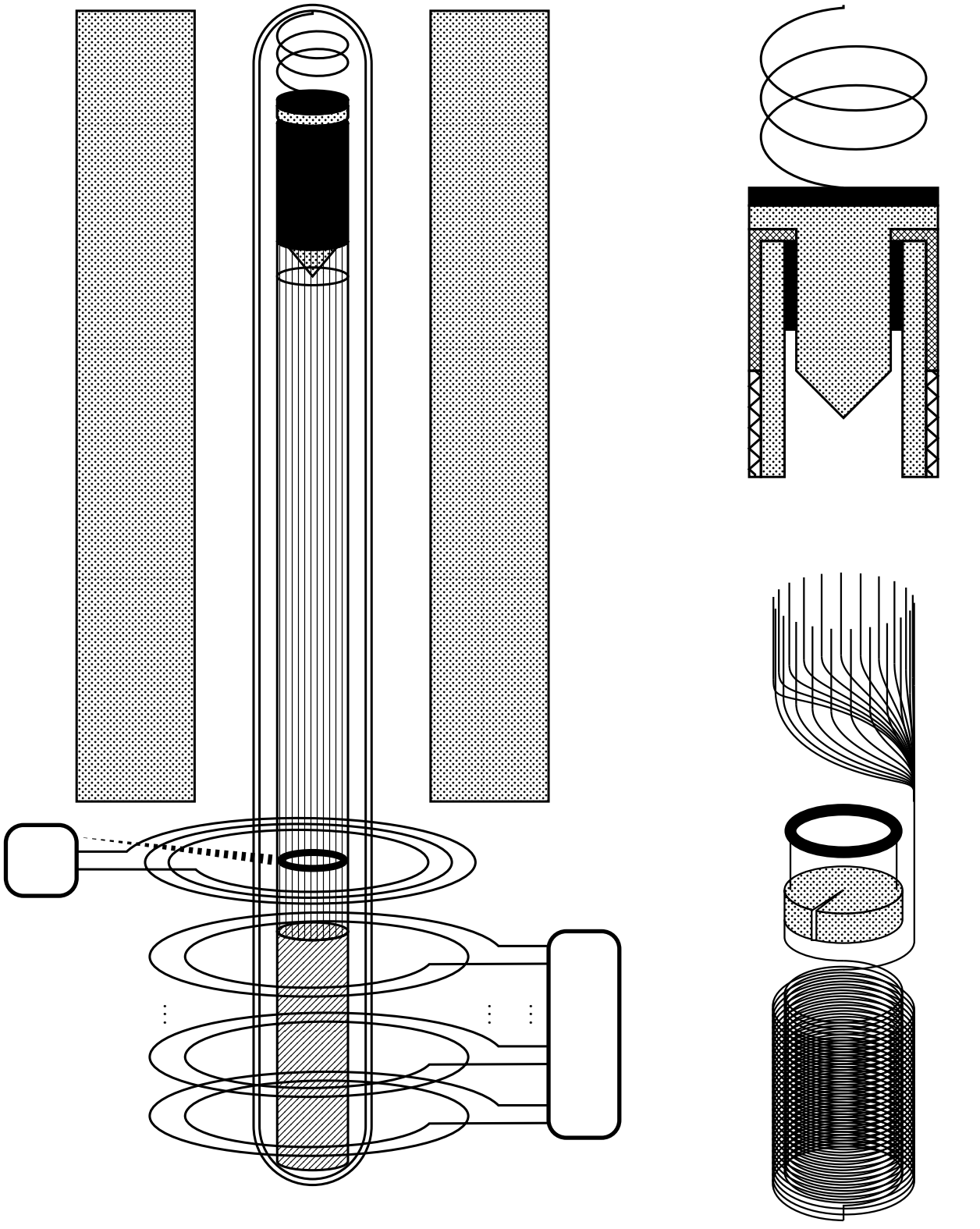


Some important considerations should be taken into account:

- affordable unstable oscillators do have local stability and are stable for a short period of time (several microseconds and less); however, they may be unstable over longer periods (several milliseconds and more);
- in normal laboratory or industrial conditions, a magnetic field does not fluctuate with high deltas, which only occur in an exceptional cases like close proximity to electromotors, electromagnets, high current switchers, etc; said magnetic field can be stable for a short period of time (several microseconds and less), but it may be unstable over longer periods (several milliseconds and more).

Patent pending technology that is incorporated in our Elegant NMR® system.

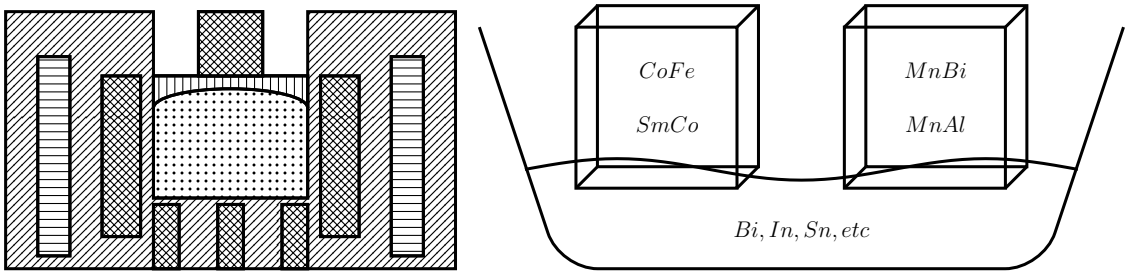
2.2 Affordable Dual Band Microwave Transmitter for DNP NMR



In the Elegant NMR® measuring system, there is no need to use expensive ultra-high vacuum turbomolecular pumps to perform DNP NMR.

The Elegant NMR® allows any measurement to be carried out with a conventional laboratory vacuum pump, which is reflected in the patented technology in US 10773092 B2.

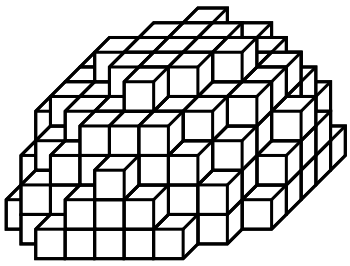
2.3 Focused Magnets with New Magnetic Material



Nowadays, there are many magnetic materials available for magnet construction by either sintered or casted processes. Elegant NMR® uses patented technology (US 10646722 B2) with affordable components like Co, Fe, Mn, Bi, that

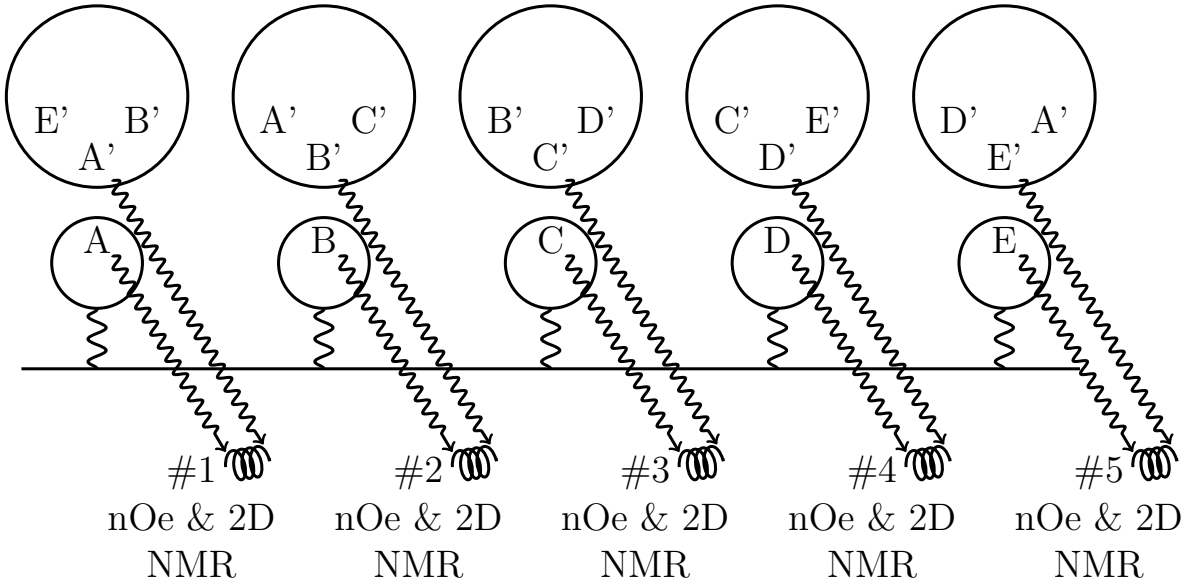
- can be sintered at low pressure (1000 bar),
- can be casted at low temperature (500°C and below),

and is perfectly suitable for a Halbach-like sintering/casting process (we achieved 4T on ca. 100mm diameter and 1.6T on 24mm diameter).



Hence, crystalline structure of Co-Fe and Mn-Bi alloys (ca. 1-2 μm linear dimensions of said crystals) build a spherical Halbach structure additionally providing high homogeneity of achieved magnetic field.

2.4 HPLC Like Method of NMR Detection



A system that demonstrates a method and an apparatus for chemical analysis which consists of an area filled with different markers, so-called stationary phases. Each marker contains one or several active parts, abbreviated as A, B, C, D, E, that each possess good affinity to different organic groups (A, B, C, D, E) presented in an investigated mixture. These markers cause different substances in the investigated mixture to rotate differently upon interaction and build the corresponding intermolecular iteration (A-A, B-B, C-C, D-D, E-E). For each region with a corresponding marker, we perform a different multidimensional NMR experiment, so that the magnetization transfer from each particular organic or element group in said marker mainly progresses to particular components or parts in the unknown mixture, and this transfer is measured over multidimensional NMR responses. Doing such an experiment does not require physical separation of the mixture; the NMR spectra separate in different regions and allow the detection of all components in the unknown mixture.

This approach is particularly important because separation is no longer required for the detection of components in a mixture, only changes of orientation in mixture components compared to the markers. This leads to drastic simplification of experiment design, with choice of marker types becoming the key consideration. It is well known that the difference of Gibbs energy of two substances interacting with the stationary phase (ΔU_1 and ΔU_2) refers to the separation coefficient α_{1-2} of these substances by the formula

$$\alpha_{1-2} = e^{\frac{\Delta U_1 - \Delta U_2}{RT}}.$$

If the Gibbs energy of interaction of one component ΔU with the stationary phase is around 10 kJ/mol or greater, that component interacts so strongly with the stationary phase that it may chemically bind to molecules of the stationary phase, leading to degradation of the separation column. Conversely, if a difference in Gibbs energy ($\Delta(\Delta U)$) between two components is below 1 kJ/mol, separation columns with large numbers of theoretical plates are

needed to separate them. This usually requires larger separation columns, higher pressure (20000 psi and above), and a very sophisticated experimental setup.

The Elegant NMR method allows scenarios where the Gibbs energy of investigated substances interacting with markers (ΔU) and the difference in said Gibbs energies for different substances ($\Delta(\Delta U)$) may be as low as several J/mol, thus a wide variety of markers can be used and overall device construction is drastically simplified.

Further information is available in the patent application US 16695200.

2.5 Huge Molecule Database

The ability of the Elegant NMR measuring system to automatically interpret heteronuclear DNP NMR spectra on an adaptive grid completely disrupts the status quo in which 7- and 8-dimensional DNP NMR spectra, having sparsity values less than 0.1i%, are very difficult not only to interpret, but even to visualize.

In the Elegant NMR® system, such spectra are identified with reference to a huge database containing about 1.7 billion spatial molecular structures.

This database is integrated into the computer server and Elmathron devices, thereby enabling analysis and results even in remote locations (i.e. portable applications) which may lack access to the Internet.

The Elegant NMR® measuring system automatically identifies components of an unknown mixture without need for reference spectra of pure substances, including the discovery of novel chemical structures.

It does this by applying tensor decomposition methods to NMR spectra, which can analyze multicomponent mixtures without any preliminary separation. Such methods make it possible to analyze multicomponent mixtures without their preliminary separation.

The tensor decomposition method, sometimes referred as multidimensional decomposition or three- or multi-way decomposition, is a well established method that was first used a dozen years ago in chemometrics [5] for fluorescence spectra and psychometric data interpretation. It was first used in NMR almost 20 years ago. However, only recent tunes and implementation [6] allow this technology to achieve good quality results.

[5]: doi: 10.1002/sapm19287139, 10.1007/BF02289464, 10.1007/BF02310791, 10.1016/0024-3795(83)80041-x, and Harshman, R. A. Foundations of the PARAFAC procedure (1970). UCLA Working Papers in Phonetics, 16, 1-84.

[6]: US 10,773,092 B2 and in particular supplementary materials for this patented technology

3 Technical Characteristics

Suppose we have an unknown mixture of N components such that each component has $M_1, \ldots, M_N$ non-zero spin isotopes and corresponding molar concentrations of these components differs a maximum of 100 times. Up to now the Elegant NMR® system usually resolves mixtures with less than 300 significant NMR responses, i.e. $R = \sum_{i=1}^{N} M_i < 300$.

If R is large or the molar concentrations of the components of the components differ by more than 100 times, then the device either may require a very long amount of time to measure, or fail to produce good prediction results.

It is important to note that if a substance has multiple isotopes with zero spin, mixture prediction may no longer work for small molecules. For example, it is impossible to detect pure CO_2 using $^{12}C^{16}O_2$, since it has only isotopes with zero spin.

The strict upper limit of the number of NMR responses per component in a mixture is 256, so substances in a studied mixture with 256 isotopes with nonzero spin cannot be properly identified. It is highly recommended to carefully check the results for smaller substances with 60+ non-zero spin isotopes, as the recognition of the spectra of these substances may be hindered by responses from other components.

The tensor decomposition method for spectra interpretation decomposition without access to pure spectra can automatically recognize spectra of an unknown mixture. The tensor decomposition method is included in the Elegant NMR system. This method is ideal for mixtures containing a small number of unknown components, usually less than 10 components. In the Elegant NMR® system there is no theoretical or practical upper limit for the total amount of components that have been established or applied. However, mixtures containing significantly more components can be difficult for automatic spectra interpretations.

Elegant NMR® users are strongly encouraged to provide any known information about substances in the investigated mixture on the advanced parameters screen.

By entering this information ahead of time, some known substances in your measured mixture will be identified in our database and their signals will be removed from the heavy numerical tensor approximation algorithm. In return, this gives a better sensitivity of spectral matching, the ability to work with a wide range of molar concentrations (up to concentrations of mmol/L), and many components (up to 100 different components in a mixture).

The unknown mixture is drawn into the measuring device through a standard 1/16” HPLC connector with an internal syringe and directed to the measuring unit.

Measurements are performed fully automatically according to the parameters entered by the user via the web interface. Sparse points in non-uniform sampling are selected by the device automatically based on previous information about the measured substance and additional advanced parameters entered by the user through the web interface.

The measurements are combined into sets, with each set running from 10 to 200 seconds. During this set, up to 20,000 one-dimensional DNP-NMR measurements can be collected.

The granularity of the fluid volume is about 1 nl. This is the smallest possible amount of fluid that can be measured. For greater accuracy and complex mixtures, it is recommended to apply at least 100 nL of liquid and at least 10 L of gas.

The maximum possible flow rate is about 0.5 μL/s. However, at this rate, measurements are not possible and are used only to supply the mixture to the device. The maximum average rate for real measurements is 1 μL/m.

The liquid is supplied to the measuring device through a capillary. It is very important to have liquid without any particles. Thus, it is recommended to use inlet filters.

The liquid must have a low viscosity, otherwise the inner syringe and the measuring zone may be irreversibly destroyed. Liquids with more than 90 mPa·s at room temperature are not allowed for measurements.

Fluid flows in the inlet capillary from the inlet to the measurement area. Increasing capillary size can drastically increase the time between the liquid being sucked into the inlet capillary and real measurements. You can work around this problem by using a very small-bore capillary. However, please note that high viscosity liquids cannot be sucked out with a syringe.

To optimize the feeding of samples to the Elmathron measuring device, including sample viscosity and the chosen analysis method, a built-in software calculator can be used to pre-check all the inlet parameters.

The appropriateness of the inlet settings can be checked through the Device Inspection section, found within the Inlet screens in the web interface of ELegant NMR® system.

It is also possible to predict inlet tract parameters, inlet problems, clean the inlet tract and internal measurement area, and perform a baseline check in the device inspection section.

It is important to provide an acceptable vacuum of approximately 0.1-0.3 Pa for proper DNP transmitter operation. A vacuum of 0.05 Pa can slightly improve the quality and speed of measurements. Operation above 1 Pa dilutes DNP signals significantly, so it is not recommended to use pressures above 1 Pa. The system automatically stops collecting data if the pressure exceeds 10 Pa. The Elegant NMR® system is equipped with a vacuum sensor that warns you if the vacuum is unacceptable or if there is a leakage in the vacuum line.

Usually, due to DNP, the mixture is so strongly excited that by the end of the measurement the temperature of the mixture high enough that it usually evaporates. Some substances can be destroyed or have their properties irreversibly changed. Instead, the Elegant NMR® system removes the overheated mixture residues via the vacuum line so that the instrument operates with a destructive analysis method. Hence, the vacuum is used both for the DNP sensor and for extracting the measured substance from the measuring area.

It is important that the vacuum pump can draw 1 μL/min of liquid in vapor state into the vacuum line, which roughly corresponds to a flow of 650 L/m at 0.1 Pa or 200 L/m at 0.3 Pa. A lower flow rate of up to 10 L/m is also allowed, but the instrument may automatically slow down the measurement.

The Elmathron can carry out continuous measurement and analysis of large quantities of samples without operator intervention by means of an autosampler, which is equipped with computer vision capability.

The Elegant NMR® system has multi-user support so that multiple devices can be controlled with different access levels (e.g. in classrooms) limited by time, date, name, and device, and full control can be accessed from any computer or mobile phone using a regular browser.

It allows the spectra of multicomponent mixtures of substances to be interpreted as tables and graphs of substance concentrations and the three-dimensional forms of those substances to be presented.

Built-in DFT ab initio and molecular mechanics methods additionally allow the software to recognize even the spectra of unknown substances not already in the molecular database.

Using integrated correlation methods, the Elegant NMR® measuring system can automatically interpret experiment results and their correspondence to classes of narcotic and prohibited substances.

The system also supports correlation analysis for pulmonary disease detection via determining the presence of various low-molecular-weight marker-detectors in air exhaled by a patient, which can be used to detect various types of diseases.

If similar substances are present during different measurements, you can choose to perform a correlation analysis between those experiments.

The Elegant NMR® measuring system can analyze rapidly-changing mixtures in a continuous manner. For example, it can monitor chemical synthesis products in real time.

Hence, this easy-to-use NMR technology is available for:

- medical and pharmaceutical industry: an easy-to-use and affordable method for the detection small size molecules and their mixtures in metabolites;
- universities and research institutions: for real-time monitoring of chemical synthesis,
- chemical and oil/gas industries: for real-time, monitoring of droplet size, chemical processes, and quality control,
- beverage and food industries: for real-time quality control,
- industrial automation: for real-time quality control.

Suitable for nearly all chemical reactions, the Elegant NMR® provides real-time monitoring of key information, allowing advanced understanding and control of reactions.

4 General Information

4.1 Advantages of the Elegant NMR® System

In developing the Elegant NMR measuring system, Elegant Mathematics LLC was motivated by the goal of creating a new generation of analytical equipment that is compact and convenient to use, does not require additional training of specialized personnel, and is inexpensive and accessible to every chemist.

The Elegant NMR® embodies this goal, as none of the following expensive components are needed for chemical analysis with this system:

- Huge permanent magnets with cooling agents - Elegant NMR® uses small permanent magnets with focusing in the measurement area, according to the patented technology in US 10646722B2.
- A specially equipped room to house the device - small in size, the Elegant NMR® measuring system is not sensitive to external fluctuations of magnetic fields, according to the patented technology in US 10773092B2.
- A large volume of analyte - for one measurement, the Elegant NMR® system only needs at minimum 1 nL of liquid or 1 mL of gas to obtain high measurement accuracy using DNP NMR, according to the patented technology in US 10773092B2.
- A high vacuum turbomolecular pump for DNP - the Elegant NMR® system uses a laboratory pump.
- Highly-trained specialists for interpretation of multidimensional NMR spectra - the Elegant NMR® Software with integrated artificial intelligence will do the full interpretation of the experimental results for you!

The Elmathron® measuring device, part of the Elegant NMR system, detects substances and mixtures through constructing sparse multidimensional heteronuclear DNP NMR spectra (HSQC-HMBC-NOESY) with non-uniform sampling (NUS). Such spectra make it possible to detect not only the spatial structures of molecules, but also to determine multiple components in a mixture.

Fully populated, these spectra usually have very high dimensionality, being 7- and 8-dimensional. Recording a complete 8-dimensional structure with good resolution requires a lot of time, so our equipment implements non-uniform sparse sampling (Sparse-NUS) with adaptive mesh generation.

As it is almost impossible to not just visually interpret but even display an 8-dimensional spectrum on an uneven sparse grid with 0.01% filling, our equipment implements the automatic interpretation of such spectra with reference to a ready-made set of molecular structures and their concentrations.

In addition to reporting analysis results in the form of molecular structures and their concentrations, the Elegant NMR® system features a *Drug Detection* option for the statistical calculation of whether found substances belong to classes of narcotic and prohibited substances,

and a *Disease Detection* option for correlating found substances with marker-detectors of lung diseases.

In the medical context, an inexpensive express *Disease Detection* analysis with the Elegant NMR® system can be performed on air exhaled by a patient to determine the presence of various low-molecular-weight markers, which can in turn be associated with various types of diseases, including COVID-19. The cost of one such analysis does not exceed 10 cents.

For universities and scientific institutions, the Elegant NMR system will be useful for real-time analysis of chemical synthesis products.

4.2 Patents and Trademarks

All of the innovative technologies used for the production of the *Elegant NMR®* measuring system were patented by Elegant Mathematics LLC in 2020: US 10646722B2, US 10773092B2, US 10773093B2.

There are several patent applications pending.

Elegant Mathematics LLC also owns the issued trademarks *Elegant NMR®* and *Elmathron®*.

4.3 Configuration

Basic *Elegant NMR®* system configuration:

- *Elmathron® Device*: Measuring device in which unknown mixtures of substances are directly assayed using DNP NMR.
- *Computation Server*: Unit in which the storage and computer processing of measurement data takes place.
- *Autosampler*: Provides for the automated supply of samples to the Elmathron® device (included in the basic version upon customer request).
- *Elegant NMR® Software*: User interface for the control, monitoring, and interpretation of measurements.
- *Vacuum Pump*: Creates a vacuum in the measuring device (included in the basic version upon customer request).

The *Elmathron®* device is equipped with Wi-Fi and 1 GBit/s Ethernet for reliable communication with the web interface and computation server.

Computational algorithms for searching and processing spectra and molecular structures are installed on a specialized high-performance Linux server (data processing unit) with GPU/CUDA support and having minimal vulnerability to trojans and viruses.

The initial measurement data is first preprocessed in the *Elmathron®* measuring device and then stored in its internal memory, which makes it possible to perform analysis even when the processing server is either not turned on or not available.

As soon as the *Elmathron*® device connects to the server, preprocessed data is automatically transferred from its internal memory to the server and deleted from said internal memory.

In the basic configuration of the system, the internal memory of the *Elmathron*® device is designed to support a week of autonomous work without a server connection.

By prior arrangement before the purchase of an *Elegant NMR*® system, the basic *Elmathron*® device can be expanded with additional memory in order to increase its capacity for autonomous work.

The *Elegant NMR*® system uses a vacuum ranging from 0.1 to 1 Pa to create a DNP beam via *Elmathron*® technology. This vacuum can be achieved with a standard pump and does not require a turbomolecular pump.

You can also assemble, at your request, any configuration encompassing several *Elmathron*® measuring devices, autosamplers, and computation servers.

For more information, you can contact us directly using the contact information on our website: https://www.elegant-nmr.com/

4.4 Elegant NMR® System Specifications

- Size: 50x30x15 cm.
- Weight: 18 kg.
- Injection fitting: 1/16-inch stainless steel.
- Power supply: 100-240 VAC.
- *Elmathron*® technology according to US10773092B2.
- Casted focused permanent magnets according to US10646722B2.
- Supercomputing system with 150 processors inside the *Elmathron*® device.
- User interface: web interface on Android, Windows, Mac, or Linux.
- *Elegant NMR*® Software: license-free smart analysis design with CUDA/GPU-accelerated AI algorithms.

4.5 Elegant NMR® Software

The *Elegant NMR*® Software does not require an additional license and can be installed both on the server of the *Elegant NMR*® system and on a customer-provided server.

The user interface software does not require additional app installation on a mobile device.

The *Elegant NMR*® Software is based on the knowledge-intensive algorithms of Elegant Mathematics LLC, and features the following capabilities:

- Control and monitoring of the operation of the *Elegant NMR*® measuring system for performing DNP NMR measurements.

- Recognition and processing of multidimensional DNP NMR spectra.
- Molecular mechanics simulation.
- Density functional theory and *ab initio* simulation with DNP NMR spectrum prediction.
- Storage and display of measurement results.
- Searching of a large molecular database for molecules, their spatial structures, and their quantum-mechanical properties.

4.6 Service Offers

Elegant Mathematics service includes free *Elegant NMR®* Software updates for eight years after purchase.

You can find new software updates for all devices of the *Elegant NMR®* system, which we will periodically offer for sake of improving the measurement process, in the *Status of All Devices and Server* screen. 

You may order a vacuum pump from us together with the system, use one already present in your laboratory, or buy one separately from a third-party company of your choice.

4.7 Warranty Period

The warranty period for the basic version of the *Elegant NMR®* system is two years, subject to purchase from the manufacturer's warehouse and mandatory intermediate inspection after one year of operation.

The warranty period can be extended to as much as five years by passing annual inspections of the measuring system.

The warranty period starts from the moment the customer receives the *Elegant NMR®* system.

The vacuum pump supplied with the *Elegant NMR®* measuring system is not covered by the Elegant Mathematics LLC warranty.

4.8 Copyright & Disclaimer

Disclaimer When analyzing with the *Elegant NMR®* system, the results of your experiments are saved in the database of experiments in special formats developed by Elegant Mathematics LLC. These formats are then used by the *Search Results* program which is included in the *Elegant NMR®* Software v1.11 to perform a quick and efficient search for the experimental results of interest.

Elegant Mathematics LLC does not guarantee that any attempt by you to perform any action on the data of the results of experiments carried out by the *Elegant NMR®* system using any third-party search programs or using any other third-party programs, for example, to process and store experimental data and others will be successful. Your use of such third-party programs may lead to either the complete absence of any results, or to unpredictable results, for the accuracy and reliability of which Elegant Mathematics LLC is not responsible, nor is it responsible for any damage incurred by you in connection with the use of such results.

The information used by the *Search for Molecules in the HugeMDB* programm which is included in the *Elegant NMR®* Software v1.11 is partially based on data from the PubChem database.

You can go to the molecule search program *Search for Molecules in the HugeMDB* by clicking the button 

Elegant Mathematics LLC does not participate in the creation of the PubChem database and does not guarantee its accuracy and relevance. Elegant Mathematics LLC is not responsible for any errors, omissions or other deficiencies in the content (any information) contained both in the PubChem database and in the *Search for Molecules in the HugeMDB* program. Also, Elegant Mathematics LLC cannot be held liable for any damage incurred by users of this program in connection with the use of the aforementioned content or in connection with any other actions of users with the aforementioned content.

For complete information about our company and our products, please use the contact information in the *Contacts* section of the corporate website: https://www.elegant-nmr.com/

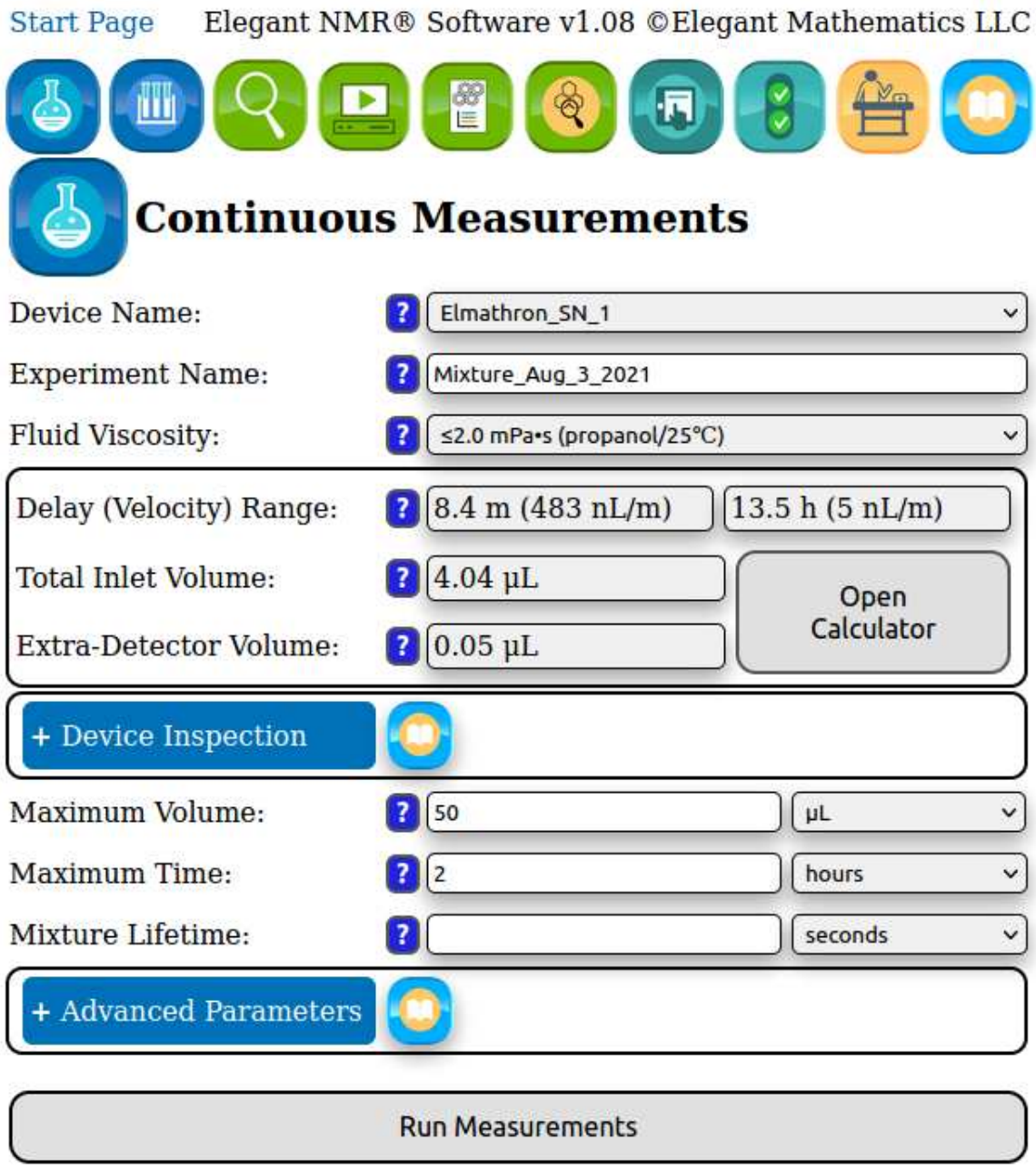
5 Getting started

To start working you need:

- the Elmathron® measuring device;
- capillary and accesories included in the standard version;
- vacuum pump capable to generate vacuum of 0.1-0.3 Pa;
- computational server;
- any computer or mobile telephone with internet/ethernet access and browser support.

You must turn on Elmathron, connect a vacuum, start up the device, connect a capillary to the inlet and place the inlet capillary in the liquid to be measured.

6 Continuous Measurements



The current information window contains useful recommendations and examples of how to correctly enter parameters in the *Continuous Measurements* screen in order to quickly analyze a mixture of unknown substances using the Elmathron device in continuous measurement mode. Prompts are available regarding how to fill each input field and select experiment options. You can easily open these prompts by clicking the associated question symbol. To hide a prompt, click again either on the question symbol or anywhere in the prompt field.

Please read and follow the prompts carefully to make your chemical analysis as accurate as possible!

Attention! If after logging in you do not see the Elmathron device or autosampler you need, or data in the experiment database corresponding to any Elmathron device, then the username under which you logged in is not allowed to operate or use data from this device.

To obtain the rights, a superuser must correct the user account's access rights as listed in the *User Properties→Device Rights* field in *Settings* screen Measurements with the Elegant NMR system should always be carried out at standard atmospheric pressure. The permissible inlet pressure is in the range of 80 to 120 kPa.

Pressure values outside that range will cause irreversible breakdown of the analytical system!

The Elegant NMR system allows you to analyze only those liquids that are volatile at temperatures above 200^{o}C. Non-volatile components can permanently settle on the walls of the measuring path and irreversibly spoil it.

The Elegant NMR measuring system is not intended for analysis of liquids having a viscosity of more than 90 mPa·s.

Before starting any analysis, we recommend you carefully check all inlet connections leading to the Elmathron measuring device.

Depending on the configuration of your Elegant NMR measuring system - namely, with or without an autosampler - you must first specify in the *Settings* screen which Elmathron measuring devices are connected to the autosampler at the time the analysis is started.

The listing of Elmathron devices by type of connection is automatically transferred to the *Continuous Measurements* screen and *Measurements with Autosampler* screen Next, you can enter measurement parameters in each of the input fields in the *Continuous Measurements* screen Follow the recommendations in the prompts to get maximally accurate and fast results!

If any parameter in the *Continuous Measurements* screen was entered inaccurately (for example, you accidentally wrote letters instead of numbers in the *Maximum Time* field), then the field with erroneous input will be highlighted in red and you will not be able to initiate the experiment until it is corrected.

Device Name:
In this list, the Elmathron measuring devices to be used for continuous measurements can be selected by name.

Attention! This list shows only those Elmathron devices that are not connected to autosamplers, according to the *Settings* screen

Experiment Name:
In this field, you can assign a unique name for the experiment, which will be saved in the database for identification of the corresponding measurement results.

You can also leave this field blank. You should assign each experiment a unique name. This will allow you to easily look up the results, even after some time has passed.

Fluid Viscosity:
Here you select from a list the approximate viscosity of the substance being investigated in your experiment.

This should reflect the maximum viscosity for your sample. All viscosity values in the list are indicated at a temperature of 25^{o}C.

If you select a viscosity that is significantly lower than the actual viscosity of the measured substance, the analysis can malfunction and irreversible damage can be inflicted on the internal parts of the Elmathron device.

The Elegant NMR system is not intended for the analysis of liquid having a viscosity of more than 90 mPa·s.

You may check fluid viscosity at the following external resource:
http://murov.info/orgsolvents.htm

Maximum Volume:
Here, you enter the maximum allowable volume of the substance being measured and select the volume units.

You should first use the calculator to generate the calculated fields and then enter the maximum allowable volume.

You can determine the minimum volume of the investigated substance required for analysis based on the calculated *Total Inlet Volume* of the inlet tract; that is, the maximum volume of substance must be significantly greater than the calculated total volume of the inlet tract.

You can also leave this field blank. If you have a sufficient volume of the substance, you can leave the *Maximum Volume* field blank. If you do indicate a maximum volume, measurements by the Elmathron device will cease as soon as that quantity of substance has been analyzed.

Maximum Time:
In this field, you can enter the maximum permitted analysis time and select the units of time measurement.

You should first use the calculator to generate the calculated fields analyze the calculated data in the calculator field and then enter the maximum permitted analysis time.

You can determine an appropriate minimum time based on the calculated *Delay (Velocity) Range* of the substance in the inlet tract.

Specifically, the maximum time value should be significantly greater than the estimated residence time of the investigated substance in the inlet tract.

If the maximum time is less than the minimum period the substance is in the input tract, then the analysis is meaningless.

If you have abundant time for analysis, you can leave this field blank. In the event that you simultaneously specify both a maximum time and a maximum volume, the Elmathron measuring device will try to operate at a velocity with which both the maximum time and the maximum volume can be achieved simultaneously. It will also take into account the calculated *Delay (Velocity) Range*.

Mixture Lifetime:
If the chemical composition of the mixture of substances being measured can change while passing through the inlet tract (for example, if you are investigating rapid chemical reactions), you should fill out the *Mixture Lifetime* field.

The residence time of the substance in the inlet tract can be estimated from the calculated field *Delay (Velocity) Range*.

If the *Mixture Lifetime* you specify is very small compared to the minimum transit time of the substance through the inlet tract as informed by the *Delay (Velocity) Range* values, then the Elmathron measuring device will not be able to follow your request exactly, but will strive to pass the substance along the inlet tract at the maximum possible speed.

You can leave this field blank if your test substance does not change its chemical composition over time. The advanced parameters allow you to indicate what you already know about the substances being analyzed so as to optimize the analysis time.

For example, you may know in advance the type of solvent in the mixture, or may be able to make an assumption about which class of substance is being analyzed. Providing any such available information will significantly speed up the analysis and reduce the volume of sample required.

For information on how to correctly enter advanced parameters, go to the *Advanced Parameters Help* screen

Before starting an analysis, first review all of the entered parameters and double-check that you are authorized to carry out measurements.

If you see a button *Unlock Measurements* with a lock symbol, it means that you have not yet passed authorization and cannot perform measurements.

To enter your credentials, you can either go to the *Settings* screen or simply click on the button with the lock symbol 

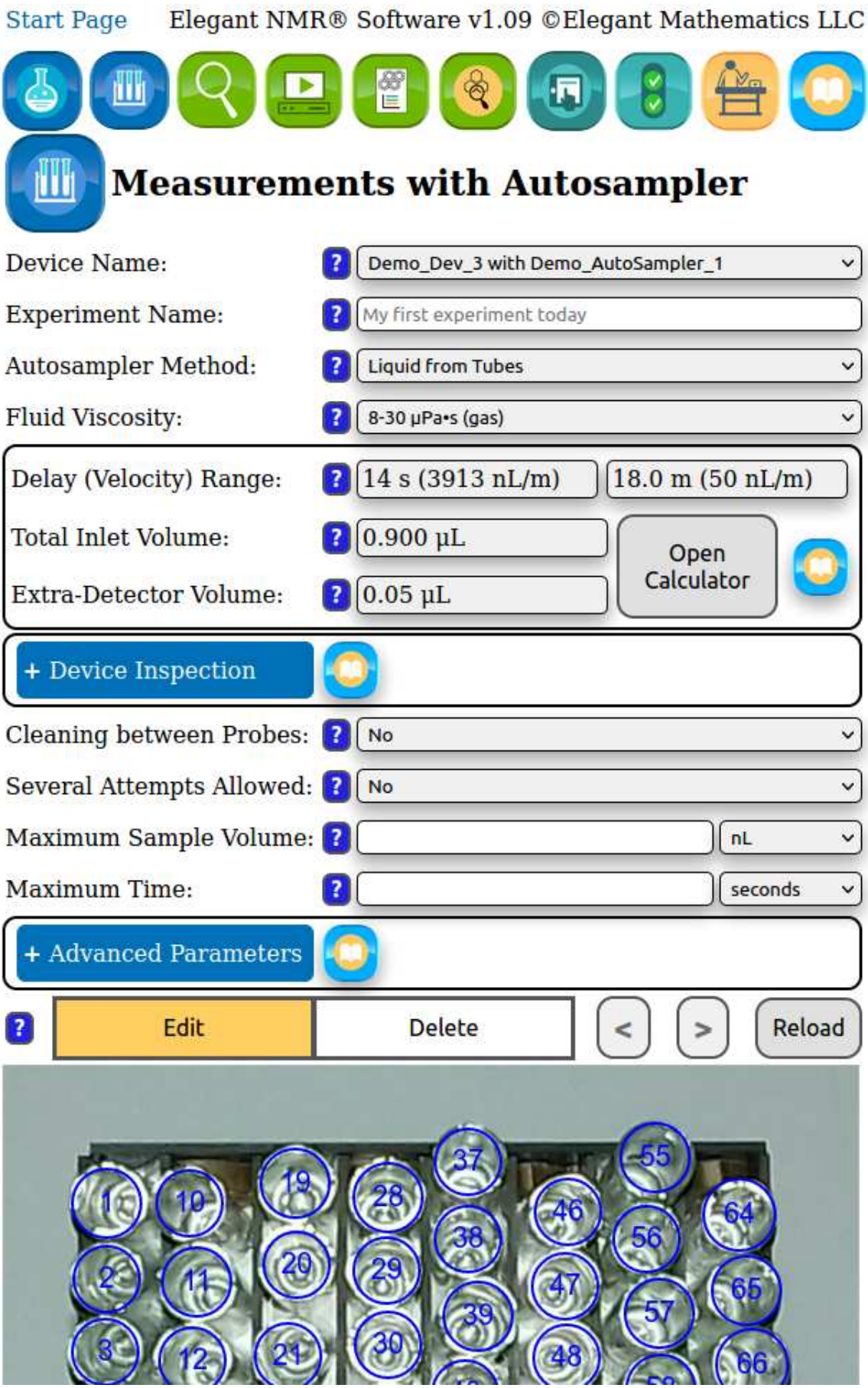
After successfully confirming your authorization, the **Unlock Measurements** button with the lock symbol will be substituted by either the **Run Measurements** button, or the **Stop Measurements** button.

To start the measurements, click on the **Run Measurements** button.

To stop the measurements at any time, click on the **Stop Measurements** button.

Measurement data will automatically be transferred to the computation server of the Elegant NMR system. You can view the analysis results at any time, and also return to the saved settings and repeat the analysis procedure.

7 Measurements with Autosampler



The current information window contains useful recommendations and examples of how to correctly enter parameters in the *Continuous Measurements* screen in order to quickly analyze a mixture of unknown substances using the Elmathron device with autosampler. Prompts are available regarding how to fill each input field and select experiment options. You can easily open these prompts by clicking the associated question symbol. To hide a prompt, click again either on the question symbol or anywhere in the prompt field.

Please read and follow the prompts carefully to make your chemical analysis as accurate as possible!

Attention! If after logging in you do not see the Elmathron device or autosampler you need, or data in the experiment database corresponding to any Elmathron device, then the username under which you logged in is not allowed to operate or use data from this device.

To obtain the rights, a superuser must correct the user account's access rights as listed in the *User Properties→Device Rights* field in *Settings* screen Measurements with the Elegant NMR system should always be carried out at standard atmospheric pressure. The permissible inlet pressure is in the range of 80 to 120 kPa.

Pressure values outside that range will cause irreversible breakdown of the analytical system!

The Elegant NMR system allows you to analyze only those liquids that are volatile at temperatures above 200^{o}C. Non-volatile components can permanently settle on the walls of the measuring path and irreversibly spoil it.

The Elegant NMR measuring system is not intended for analysis of liquids having a viscosity of more than 90 mPa·s.

Before starting any analysis, we recommend you carefully check all inlet connections leading to the Elmathron measuring device.

Depending on the configuration of your Elegant NMR measuring system - namely, with or without an autosampler - you must first specify in the *Settings* screen which Elmathron measuring devices are connected to the autosampler at the time the analysis is started.

The listing of Elmathron devices by type of connection is automatically transferred to the *Continuous Measurements* screen and *Measurements with Autosampler* screen Before starting measurement of an unknown substance using an autosampler, you should place a rack with test tubes in an autosampler connected to an Elmathron measuring device, and then press the **Measurements with Autosampler** button in the general menu (i.e. the autosampler symbol) to go to the *Measurements with Autosampler* screen Next, you can enter measurement parameters in each of the input fields in the *Measurements with Autosampler* screen Follow the recommendations in the prompts to get maximally accurate and fast results!

If any parameter in the *Measurements with Autosampler* screen was entered inaccurately (for example, you accidentally wrote letters instead of numbers in the *Maximum Time* field), then the field with erroneous input will be highlighted in red and you will not be able to initiate the experiment until it is corrected.

Device Name:
In this list, the Elmathron measuring devices to be used for measurements with an autosampler can be selected by name.

Attention! This list shows only those Elmathron devices that are connected to autosamplers, according to the *Settings* screen  When you select an Elmathron device with a connected autosampler from the *Device Name* list, you will see in the *Measurements with Autosampler* screen  an image and the computer vision-based recognition results of all samples in the associated autosampler at the present moment.

Experiment Name:
In this field, you can assign a unique name for the experiment, which will be saved in the database for identification of the corresponding measurement results.

You can also leave this field blank.

Autosampler Method:
It is possible for the autosampler to carry out different sampling methods.

If you are analyzing a set of substances in test tubes or in the microwell plates or positions of a liquid autosampler, then you should choose the sampling method *Liquid from Tubes*.

If you are analyzing a set of substances in closed vials with rubber caps, you should select the *Liquid from Closed Vials* method. In this case, a thin needle will be used to pierce the vial lid and extract the sample for analysis.

If you analyze a gas phase in vials, then you need to select the *Gas from Vials* method.

For non-volatile liquids and solids, you can use either the glow discharge sampling method or the *MALDI* method.

If you are analyzing a set of solid state substances in microtest plates or dies, then you need to choose *2D Glow Discharge Emission* or *2D MALDI on Prescribed Positions* methods.

In the case where you are analyzing a 3D object want to study the chemical composition at each point of the object's surface, you will need to select either the *3D Surface Glow Discharge Emission* or *3D Surface MALDI* method.

By default, the *Liquid from Tubes* option is used.

Fluid Viscosity:

Here you select from a list the approximate viscosity of the substance being investigated in your experiment.

This should reflect the maximum viscosity for your sample. All viscosity values in the list are indicated at a temperature of 25^{o}C.

If you select a viscosity that is significantly lower than the actual viscosity of the measured substance, the analysis can malfunction and irreversible damage can be inflicted on the internal parts of the Elmathron device.

The Elegant NMR system is not intended for the analysis of liquid having a viscosity of more than 90 mPa·s.

You may check fluid viscosity at the following external resource:
http://murov.info/orgsolvents.htm

Cleaning between Probes:
An important part of analysis with an autosampler is the cleaning of the inlet parts between samples.

If analyte concentrations do not vary much between samples, and the accuracy of the analysis is not so important, then you can choose not to clean the inlet parts between samples.

That said, for greater analysis accuracy, we recommend you select one of the cleaning options.

When using the *Gas Cleaning* option, a connector must supply cleaning gas, and when using the *Liquid Cleaning* option, you should have a sample named *LC* that contains the cleaning solvent.

Several Attempts Allowed:
The Elegant NMR system can carry out an initial analysis for each sample, and if necessary refine the result by analyzing the same sample multiple times.

To allow the system to do this with the autosampler, please select the *Adaptive* option.

By default, multiple injection attempts are not made with an autosampler, indicated by the *No* option.

Maximum Sample Volume:
Here, you enter the maximum allowable volume of the substance in a sample being measured and select the volume units.

You should first analyze the calculated data in the calculator field and then enter the maximum allowable volume.

You can determine the minimum sample volume of the investigated substance required for analysis based on the calculated *Extra-Detector Volume*; that is, the maximum sample volume of substance must be significantly greater than the calculated extra-detector volume of the inlet tract.

You can also leave this field blank. The smallest possible sample volume for one analysis in the Elmathron device is about 100 nL for liquid and about 5 L for gas. To ensure accurate analysis, we recommend that you utilize 2-3 orders of magnitude more of the investigated substance.

If you have a sufficient volume of each sample, you can leave the *Maximum Volume* field blank.

Maximum Time:
In this field, you can enter the maximum permitted analysis time and select the units of time measurement.

You should first use the calculator to generate the calculated fields analyze the calculated data in the calculator field and then enter the maximum permitted analysis time.

You can determine an appropriate minimum time based on the calculated *Delay (Velocity) Range* of the substance in the inlet tract.

Specifically, the maximum time value should be significantly greater than the estimated residence time of the investigated substance in the inlet tract.

If the maximum time is less than the minimum period the substance is in the input tract, then the analysis is meaningless.

If you have abundant time for analysis, you can leave this field blank. In the event that you simultaneously specify both a maximum time and a maximum volume, the Elmathron measuring device will try to operate at a velocity with which both the maximum time and the maximum volume can be achieved simultaneously. It will also take into account the calculated *Delay (Velocity) Range*.

Action Buttons:
The software shows a picture of the current sample load inside the autosampler and the computer vision-based system recognition of sample locations, which are displayed as an overlay on the image - blue circles containing the respective sample names.

To change a sample's location or name, use the special options for the visualization field.

There are two such options, which are selected with the *Edit-Delete* slider.

The *Edit* option is intended for carrying out the following actions:

- Change the location of a sample with the mouse:

  - If you press and hold at the edge of a marker circle, then only that edge will move; the opposite edge will remain in place, thereby letting you change the diameter of the circle.
  - If you click in the central part of a marker circle, you can move the whole circle without changing its diameter.
- Load the full name of a marker in the Name field by clicking on its circle, and, if necessary, rename the sample by editing that field.
- Add a new marker to the visualization field by clicking on an empty space that is sufficiently separated from any other marked samples.

When a marker is selected, its full name is displayed in the *Name* field and it is highlighted in red.

The *Delete* option is intended for the deletion of a marker, which is done by clicking on it with the mouse.

In the event of an accidental input error, you can revert a previous action or restore a canceled action using the buttons < (Undo) and > (Redo). The advanced parameters allow you to indicate what you already know about the substances being analyzed so as to optimize the analysis time.

For example, you may know in advance the type of solvent in the mixture, or may be able to make an assumption about which class of substance is being analyzed. Providing any such available information will significantly speed up the analysis and reduce the volume of sample required.

For information on how to correctly enter advanced parameters, go to the *Advanced Parameters Help* screen

Before starting an analysis, first review all of the entered parameters and double-check that you are authorized to carry out measurements.

If you see a button *Unlock Measurements* with a lock symbol, it means that you have not yet passed authorization and cannot perform measurements.

To enter your credentials, you can either go to the *Settings* screen or simply click on the button with the lock symbol 

After successfully confirming your authorization, the **Unlock Measurements** button with the lock symbol will be substituted by either the **Run Measurements** button, or the **Stop Measurements** button.

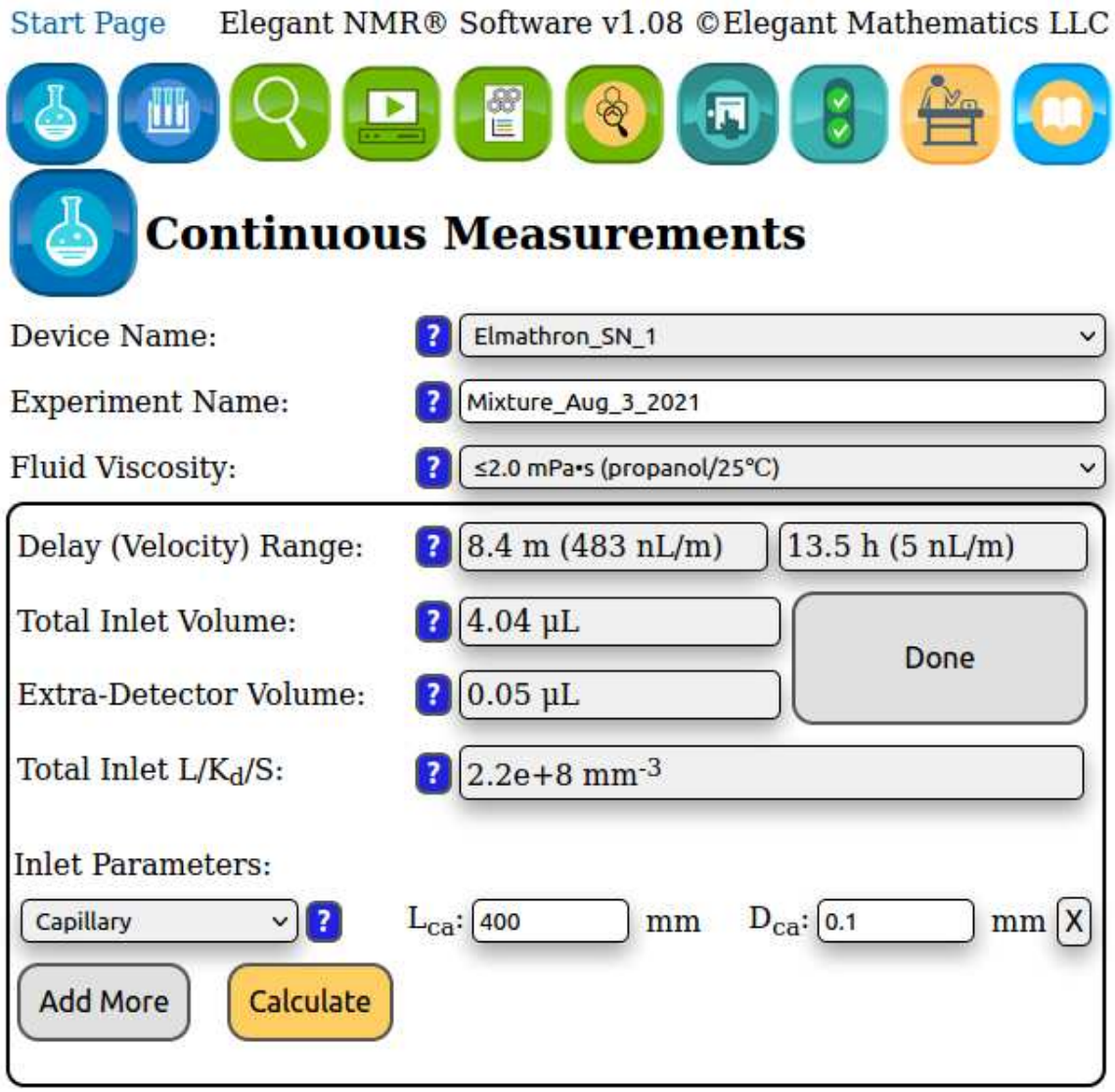
To start the measurements, click on the **Run Measurements** button.

To stop the measurements at any time, click on the **Stop Measurements** button.

Measurement data will automatically be transferred to the computation server of the Elegant NMR system. You can view the analysis results at any time, and also return to the saved settings and repeat the analysis procedure.

8 Options

8.1 Inlet Calculator



To optimize the runtime and the volume of the investigated substance, we suggest you calculate important parameters of the inlet tract, such as:

- the duration of analyte delay in the inlet tract: *Delay (Velocity) Range*;
- the total volume of the inlet tract: *Total Inlet Volume* ;

- the *Extra-Detector Volume*, which characterizes the level of mixing between two adjacent zones with different substances in the inlet tract.

Calculating these parameters will allow you to correctly determine which values should be entered to ensure optimal performance of your experiment.

To open a working field with a calculator, please click the **Open Calculator** button.

After you have entered all inlet parameters for your input tract, the corresponding inlet tract parameters can be calculated by clicking on the **Calculate** button.

Please note that the calculation results depend on the values selected in the *Fluid Viscosity* list!

Delay (Velocity) Range:
Analyte delay times and flow velocities of the substance passing through the inlet tract are calculated as ranges by the software based on the parameters you entered for the inlet tract (for example, capillary and filter sizes).

The calculated flow velocity corresponding to a delay time is indicated in parentheses.

Since these calculated characteristics depend on the viscosity of the test substance, you must first select its viscosity and then decide which connection elements of the inlet tract you will use.

Please note that if the minimum and maximum values are close to each other in value, the accuracy of the analysis may be poor.

If dash symbols rather than numerical values appear in both input fields, analysis is not possible for the settings you have selected.

In this case, you need to choose a different type of inlet connection or refrain from analyzing highly viscous substances using the selected inlet tract.

Total Inlet Volume:
This value represents the calculated total volume of the inlet tract, which is determined by the software based on the entered inlet tract parameters (for example, capillary and filter sizes).

With this value, you can determine how much of the investigated substance you need for analysis; that is, the volume you enter for the investigated substance in the *Maximum Volume* field should be significantly greater than the calculated total volume of the inlet tract.

Extra-Detector Volume:
This value characterizes the degree of mixing that occurs between two adjacent zones harboring different substances in the inlet tract.

It is calculated by the software based on the entered inlet tract parameters (for example, capillary and filter sizes).

With this value, you can determine how much of each sample is needed for analysis; that is, the sample volume should be significantly higher than this calculated value.

This volume should be significantly higher than the calculated value of the volume, which characterizes the amount of mixing of two adjacent zones with different substances.

Total Inlet L/K_d/S:
The total **L/K_d/S** of the inlet and internal tracts is used in the Darcy equation.

The value of the fluid resistance is linearly dependent on this coefficient, the flow rate, and the viscosity of the fluid in flow.

This value is determined based on the connection parameters described below and is used to calculate the *Delay (Velocity) Range*.

The larger this value, slower the fluid must be pumped through the inlet.

Capillary Lenght and Diameter:
Please enter capillary parameters in the corresponding input fields: length L_{ca} and inner diameter D_{ca} both in millimeters.

These parameters can also be imported from the Elegant NMR system's experiment database if a similar experiment has already been carried out.

By changing the value in the *Fluid Viscosity* field and clicking on the **Calculate** button, you can determine whether the combination of inlet tract parameters and substance viscosity is suitable.

Union Dead Volume Lenght and Diameter:
Please enter the parameters of the union in the corresponding input fields: length L_{un} and inner diameter D_{un} in millimeters.

These parameters are required for calculating the dead volume inside the union. If you think that the dead volume of the union tends to zero, specify **0** in both fields.

These parameters can also be imported from the Elegant NMR system's experiment database if a similar experiment has already been carried out.

By changing the value in the *Fluid Viscosity* field and clicking on the **Calculate** button, you can determine whether the combination of inlet tract parameters and substance viscosity is suitable.

Connector Dead Volume Lenght and Diameter:

Please enter the connector parameters in the corresponding input fields: length L_{co} and inner diameter D_{co} in millimeters.

These parameters are required for calculating the dead volume inside the connector.

If you think that the dead volume of the connector tends to zero, specify **0** in both positions.

These parameters can also be imported from the Elegant NMR system's experiment database if a similar experiment has already been carried out.

By changing the value in the *Fluid Viscosity* field and clicking on the **Calculate** button, you can determine whether the combination of inlet tract parameters and substance viscosity is suitable.

Standard Filter:
Here you can select the filter being used in the inlet tract; each number corresponds to a standard in-line HPLC filter from well-known manufacturers.

These parameters can also be imported from the Elegant NMR system's experiment database if a similar experiment has already been carried out.

By changing the value in the *Fluid Viscosity* field and clicking on the **Calculate** button, you can determine whether the combination of inlet tract parameters and substance viscosity is suitable.

Filter Parameters:
If you did not find your inlet tract filter in the list offered under *Standard Filter*, you can specify its parameters here: $\mathbf{L/K}_d\mathbf{/S}$ the ratio of the thickness **L** of the filter, in millimeters, to the product of the permeability coefficient $\mathbf{K}_d$ and the cross-sectional area **S** of the flow, in square millimeters; and the approximate volume $\mathbf{V}_{mix}$ of the filter, in microliters.

If $\mathbf{K}_d$ is unknown, you can roughly estimate it with the formula:

$K_d = \epsilon\ d^2\ /\ 64$, where

d is the average pore diameter of the filter, in millimeters, and

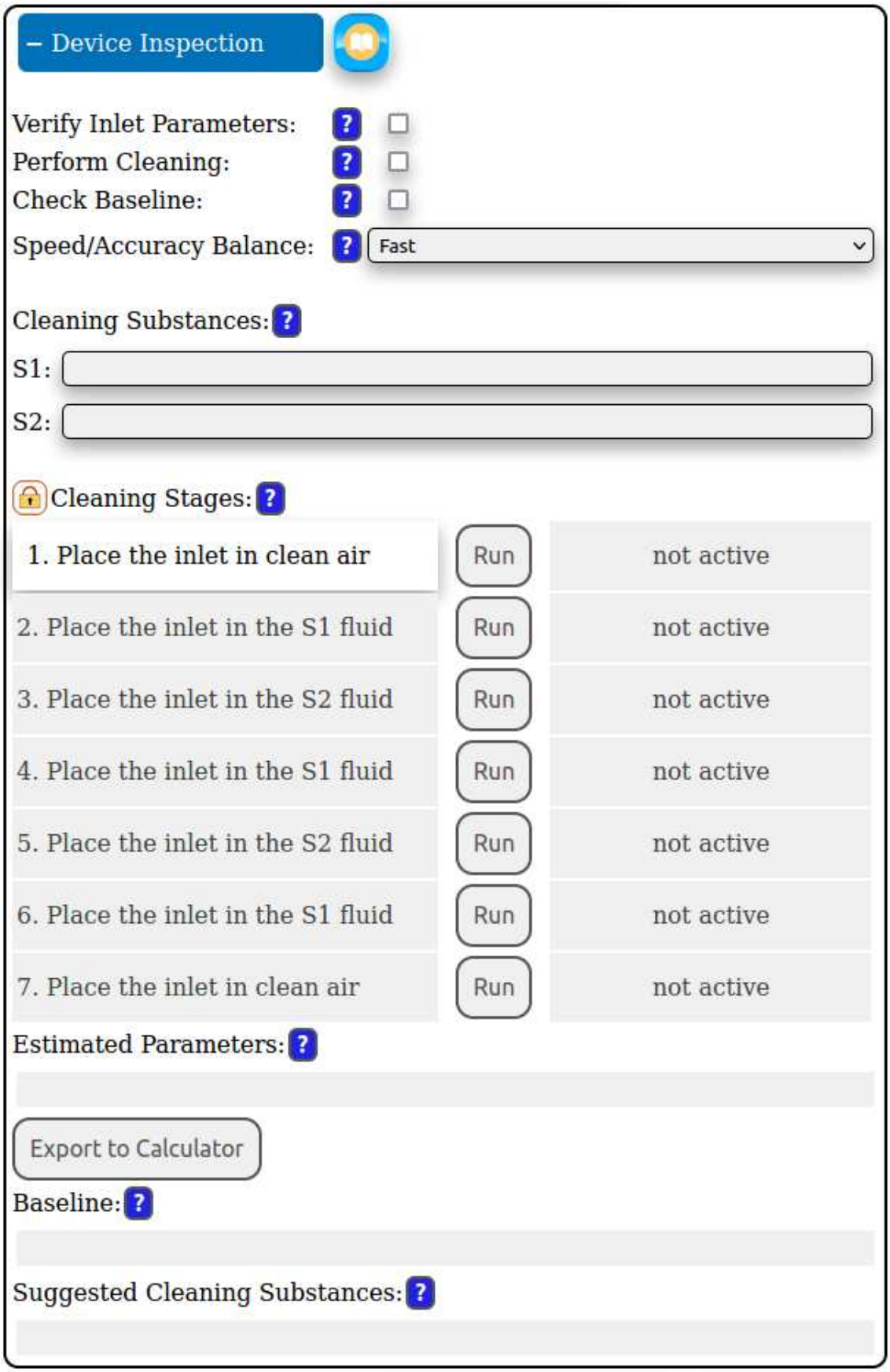
ϵ is the filter porosity, i.e. the proportion of pore volume in the total volume.

If calculating the $\mathbf{L/K}_d\mathbf{/S}$ value in millimeters is difficult, please calculate it first in meters and then divide by $\mathbf{10}^9$.

These parameters can also be imported from the Elegant NMR system's experiment database if a similar experiment has already been carried out.

By changing the value in the *Fluid Viscosity* field and clicking on the **Calculate** button, you can determine whether the combination of inlet tract parameters and substance viscosity is suitable. After calculating approximations of the parameters required to optimize your experiment, you can proceed with filling in the remaining input fields in preparation for performing substance analysis.

8.2 Device Inspection at Continuous Measurements



The current information window contains useful recommendations on how to properly use the *Device Inspection* section to perform a preliminary check and ensure good accuracy of analyses using the Elegant NMR measuring system.

Attention! Do not conduct inspection at a temperature significantly different from room temperature (15-30^{o}C) ! Prompts are available regarding how to fill each input field and select experiment options. You can easily open these prompts by clicking the associated question symbol. To hide a prompt, click again either on the question symbol or anywhere in the prompt field.

Please read and follow the prompts carefully to make your chemical analysis as accurate as possible!

Verify Inlet Parameters:
Select this check box to confirm the reliability of the inlet tract for your measurement system.

For example, if the fitting in a union is not tightened securely, undesirable additional volume can be created within the union, in which case mixing of different analyte samples will occur.

We recommend that you perform this inspection if you are unsure of the performance and reliability of the inlet assembly, or if you notice any inconsistencies in measurement results.

During the inspection process, the Elmathron measuring device needs to take several samples of known substances. After each sample has been taken, the Elmathron will ask you to swap out for the next substance into which the inlet tract will be placed.

You will need to follow all such instructions and click each corresponding **Run** button to progress through all stages of the inspection.

Please use sample substances whose viscosity does not significantly exceed that of isopropanol at room temperature!

If your cleaning agents are the same as your sample substances, you can combine the *Verify Inlet Parameters*, *Perform Cleaning*, and *Check Baseline* procedures, which will significantly save on inspection time.

Perform Cleaning:
Select this check box to clean the inlet tract with cleaning agents.

Before analysis and after each measurement, the Elmathron measuring device calibrates its baseline, assessing the amount of impurities deposited inside from previous experiments and subtracting the averaged impurity amount from the measured composition of analyzed substances.

Unfortunately, if there the impurities are excessive, then it becomes quite difficult to guarantee good analysis sensitivity.

Accordingly, we recommend that you regularly clean both the entire inlet tract and the internal tract of the Elmathron device.

If you already know the composition of the impurities and have received recommendations for their removal, please enter two substances in the *Cleaning Substances* section in accordance with those recommendations.

If you do not have such recommendations, please select two simple substances that are as free from impurities as possible.

Usual cleaning substances include: distilled water (0.9 mPa·s/25^{o}C), acetone (0.3 mPa·s/25^{o}C, and low-molecular-weight alcohols: methanol (0.5 mPa·s/25^{o}C), ethanol (1.1 mPa·s/25^{o}C), or propanol/isopropanol (2.0 mPa·s/25^{o}C).

Please use cleaning agents whose viscosity does not significantly exceed that of isopropanol at room temperature!

Check Baseline:
Select this check box to perform baseline scoring and quantitative and qualitative chemistry assessments from which to generate recommendations for detailed cleaning of the inlet tract of the Elmathron device.

During experiments, analytes pass through the inlet tract and through the internal parts of the Elmathron measurement device. Some substances can be adsorbed during that passage and subsequently fall into the measurement area of the Elmathron device, creating an additional baseline.

It is impossible to accurately predict the behavior of all substances in advance, hence it is inevitable that some residual responses will be observed.

Before analysis and after each measurement, the Elmathron measuring device calibrates its baseline, assessing the amount of impurities deposited inside from previous experiments and subtracting the averaged impurity amount from the measured composition of analyzed substances.

Unfortunately, if there the impurities are excessive, then it becomes quite difficult to guarantee good analysis sensitivity.

Accordingly, we recommend that you regularly clean both the entire inlet tract and the internal tract of the Elmathron device.

Please use cleaning agents whose viscosity does not significantly exceed that of isopropanol at room temperature!

Speed/Accuracy Balance:
Here you can select the speed at which the inspection is conducted.

The fastest speed level *Fast* will allow you to quickly obtain necessary parameters and, if you have selected the cleaning option, will also carry out the cleaning.

Meanwhile, the options *Accurate* and *Very Accurate* will allow you to more reliably evaluate all parameters.

After choosing one or several types of inspection and the speed at which the inspection is to be carried out, the estimated time needed for conducting the inspection is reported as $\mathbf{T}_{estimated}$ which is a preliminary value.

Cleaning Substances:

If you already know the composition of the impurities and have received recommendations for their removal, please enter two substances in this section in accordance with those recommendations.

If you do not have such recommendations, please select two simple substances that are as free from impurities as possible.

Usual cleaning substances include: distilled water, acetone, or low-molecular-weight alcohols: methanol, ethanol, or propanol/isopropanol.

Next, you need to indicate the CID numbers of your selected cleaning agents.

If you plan to use a mixture as a cleaning agent, you must indicate the CID number of each constituent, separated by spaces or commas, along with the percentage in the mixture that it comprises, in parentheses.

For example, **176(1%) 962(89%) 6342(10%)** corresponds to a solution of 1% acetic acid (CID=176) and 10% acetonitrile (CID=6342) in water (CID=962). You can look up CID numbers in advance using the *Search for Molecules in the HugeMDB* screen 

For the inspection mode *Verify Inlet Parameters*, we recommend using only those substances which have 100% mutual mixing.

For the inspection mode *Check Baseline*, we recommend that *S1* and *S2* be mixtures of different chemical composition, in which no two substances are equal.

Cleaning Stages:

In this section you perform several consecutive actions, namely:

- placing the inlet of the inlet tract in air that is, if possible, not contaminated with any third-party gases;
- placing the inlet of the inlet tract in cleaning agent *S1* or *S2* as appropriate;
- pressing the **Run** button for the current stage to conduct the cleaning step. This also generates the estimated time $T_{estimated}$ which represents how long the cleaning is expected to take.

At the end of each stage, the **Run** button of the next stage becomes active. You must complete all seven stages of cleaning.

After completion, you will receive a brief report on the results of the inspection.

You can also compare the values of the inlet tract parameters and decide whether you should modify them, or, using the **Export to Calculator** button, export the obtained parameters *Total Inlet Volume*, *Extra-Detector Volume*, and *Total Inlet* $L/K_d/S$ to the calculator.

Estimated Parameters:
After the inspection, the *Estimated Parameters* section will automatically display the *Total Inlet Volume*, *Extra-Detector Volume*, and *Total Inlet* $L/K_d/S$ parameters, which you can compare with the values determined using the software calculator.

If the values differ significantly, then we recommend that you check for errors in the specifications entered for the inlet tract or in the connection.

Large differences in *Total Inlet Volume* are usually due to there being a large unaccounted-for volume in the inlet tract.

For example, in a union, such differences may result if the capillary is not fully connected or if the length or diameter of the capillary is entered incorrectly.

Large differences in *Extra-Detector Volume* are usually due to connection issues.

For example, in a union where a capillary is not fully attached, the resulting volume creates strong mixing of adjacent zones.

Large differences in *Total Inlet* $L/K_d/S$ usually result from an incorrectly specified filter type or filter parameters, or from degradation of the filter, which greatly reduces its throughput.

You can also compare the values of the inlet tract parameters and decide whether you should modify them, or, using the **Export to Calculator** button, export the obtained parameters *Total Inlet Volume*, *Extra-Detector Volume*, and *Total Inlet* $L/K_d/S$ to the calculator.

Baseline:
Some substances, for example heavy metal ions or polycyclic aromatic hydrocarbons, can linger for a very long time on the inner surface of the inlet tract and the inner parts of the measuring device.

The DNP NMR responses of such substances will constantly be added to the responses of subsequently measured substances, thereby creating a baseline and reducing the sensitivity of the measurement device.

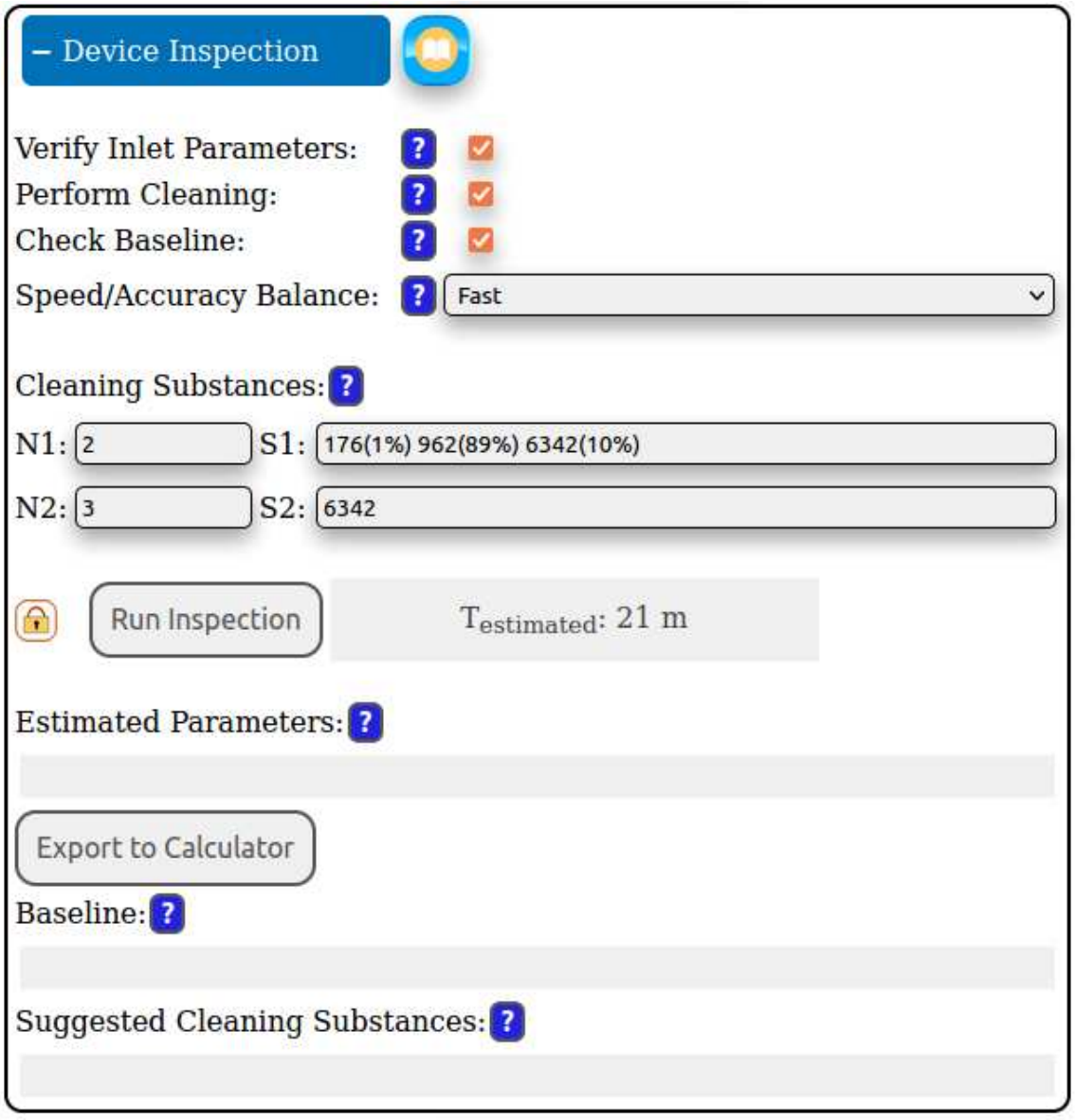
The *Baseline* field contains information on the quantitative and qualitative composition of the substances that make up the baseline, and also reports the expected measurement accuracy of substances similar or identical to those comprising the baseline.

This information is important for making decisions regarding cleaning of the inlet tract.

Suggested Cleaning Substances:
Based on the obtained baseline level, the contributing substances, and their concentrations, this section will display recommended cleaning solvents in the form of CID numbers and corresponding mixture percentages.

If you are not satisfied with the current baseline level, please select two solvents based on this recommendation and conduct an inspection with the *Perform Cleaning* and *Check Baseline* options selected.

8.3 Device Inspection at Measurements with Autosampler



The current information window contains useful recommendations on how to properly use the *Device Inspection* section to perform a preliminary check and ensure good accuracy of analyses using the Elegant NMR measuring system.

Attention! Do not conduct inspection at a temperature significantly different from room temperature (15-30^{o}C) !

Prompts are available regarding how to fill each input field and select experiment options. You can easily open these prompts by clicking the associated question symbol. To hide a prompt, click again either on the question symbol or anywhere in the prompt field.

Please read and follow the prompts carefully to make your chemical analysis as accurate as possible!

Verify Inlet Parameters:
Select this check box to confirm the reliability of the inlet tract for your measurement system.

For example, if the fitting in a union is not tightened securely, undesirable additional volume can be created within the union, in which case mixing of different analyte samples will occur.

We recommend that you perform this inspection if you are unsure of the performance and reliability of the inlet assembly, or if you notice any inconsistencies in measurement results.

During the inspection process, the Elmathron measuring device needs to take several samples of known substances. After each sample has been taken, the Elmathron will ask you to swap out for the next substance into which the inlet tract will be placed.

You will need to follow all such instructions and click each corresponding **Run** button to progress through all stages of the inspection.

Please use sample substances whose viscosity does not significantly exceed that of isopropanol at room temperature!

If your cleaning agents are the same as your sample substances, you can combine the *Verify Inlet Parameters*, *Perform Cleaning*, and *Check Baseline* procedures, which will significantly save on inspection time. When conducting an inspection, the Elmathron measuring device needs to take several samples of known substances, the tubes containing which must be placed in the autosampler.

Perform Cleaning:
Select this check box to clean the inlet tract with cleaning agents.

Before analysis and after each measurement, the Elmathron measuring device calibrates its baseline, assessing the amount of impurities deposited inside from previous experiments and subtracting the averaged impurity amount from the measured composition of analyzed substances.

Unfortunately, if there the impurities are excessive, then it becomes quite difficult to guarantee good analysis sensitivity.

Accordingly, we recommend that you regularly clean both the entire inlet tract and the internal tract of the Elmathron device.

If you already know the composition of the impurities and have received recommendations for their removal, please enter two substances in the *Cleaning Substances* section in accordance with those recommendations.

If you do not have such recommendations, please select two simple substances that are as free from impurities as possible.

Usual cleaning substances include: distilled water (0.9 mPa·s/25^{o}C), acetone (0.3 mPa·s/25^{o}C, and low-molecular-weight alcohols: methanol (0.5 mPa·s/25^{o}C), ethanol (1.1 mPa·s/25^{o}C), or propanol/isopropanol (2.0 mPa·s/25^{o}C).

Please use cleaning agents whose viscosity does not significantly exceed that of isopropanol at room temperature!

Check Baseline:
Select this check box to perform baseline scoring and quantitative and qualitative chemistry assessments from which to generate recommendations for detailed cleaning of the inlet tract of the Elmathron device.

During experiments, analytes pass through the inlet tract and through the internal parts of the Elmathron measurement device. Some substances can be adsorbed during that passage and subsequently fall into the measurement area of the Elmathron device, creating an additional baseline.

It is impossible to accurately predict the behavior of all substances in advance, hence it is inevitable that some residual responses will be observed.

Before analysis and after each measurement, the Elmathron measuring device calibrates its baseline, assessing the amount of impurities deposited inside from previous experiments and subtracting the averaged impurity amount from the measured composition of analyzed substances.

Unfortunately, if there the impurities are excessive, then it becomes quite difficult to guarantee good analysis sensitivity.

Accordingly, we recommend that you regularly clean both the entire inlet tract and the internal tract of the Elmathron device.

Please use cleaning agents whose viscosity does not significantly exceed that of isopropanol at room temperature!

Speed/Accuracy Balance:
Here you can select the speed at which the inspection is conducted.

The fastest speed level *Fast* will allow you to quickly obtain necessary parameters and, if you have selected the cleaning option, will also carry out the cleaning.

Meanwhile, the options *Accurate* and *Very Accurate* will allow you to more reliably evaluate all parameters.

After choosing one or several types of inspection and the speed at which the inspection is to be carried out, the estimated time needed for conducting the inspection is reported as $\mathbf{T}_{estimated}$ which is a preliminary value.

Cleaning Substances:
If you already know the composition of the impurities and have received recommendations for their removal, please enter two substances in this section in accordance with those recommendations.

If you do not have such recommendations, please select two simple substances that are as free from impurities as possible.

Usual cleaning substances include: distilled water, acetone, or low-molecular-weight alcohols: methanol, ethanol, or propanol/isopropanol.

Next, you need to indicate the CID numbers of your selected cleaning agents. If you plan to use a mixture as a cleaning agent, you must indicate the CID number of each constituent, separated by spaces or commas, along with the percentage in the mixture that it comprises, in parentheses.

For example, **176(1%) 962(89%) 6342(10%)** corresponds to a solution of 1% acetic acid (CID=176) and 10% acetonitrile (CID=6342) in water (CID=962). You can look up CID numbers in advance using the *Search for Molecules in the HugeMDB* screen 

For the inspection mode *Verify Inlet Parameters*, we recommend using only those substances which have 100% mutual mixing.

For the inspection mode *Check Baseline*, we recommend that *S1* and *S2* be mixtures of different chemical composition, in which no two substances are equal.

Please put the cleaning mixtures in two test tubes, add them to the autosampler so that they are in the autosampler's field of view, and verify that the autosampler's computer vision accurately recognizes the necks of the sample tubes.

Enter in the *N1* and *N2* fields the exact names of the samples as recognized by the autosampler.

The inspection will start after you click the **Run Inspection** button, and it will run in automatic mode. The estimated end time will be displayed next to the **Run Inspection** button.

After completion, you will receive a brief report on the results of the inspection.

You can also compare the values of the inlet tract parameters and decide whether you should modify them, or, using the **Export to Calculator** button, export the obtained parameters *Total Inlet Volume*, *Extra-Detector Volume*, and *Total Inlet* $L/K_d/S$ to the calculator.

Estimated Parameters:
After the inspection, the *Estimated Parameters* section will automatically display the *Total Inlet Volume*, *Extra-Detector Volume*, and *Total Inlet* $L/K_d/S$ parameters, which you can compare with the values determined using the software calculator.

If the values differ significantly, then we recommend that you check for errors in the specifications entered for the inlet tract or in the connection.

Large differences in *Total Inlet Volume* are usually due to there being a large unaccounted-for volume in the inlet tract.

For example, in a union, such differences may result if the capillary is not fully connected or if the length or diameter of the capillary is entered incorrectly.

Large differences in *Extra-Detector Volume* are usually due to connection issues.

For example, in a union where a capillary is not fully attached, the resulting volume creates strong mixing of adjacent zones.

Large differences in *Total Inlet* $L/K_d/S$ usually result from an incorrectly specified filter type or filter parameters, or from degradation of the filter, which greatly reduces its throughput.

You can also compare the values of the inlet tract parameters and decide whether you should modify them, or, using the **Export to Calculator** button, export the obtained parameters *Total Inlet Volume*, *Extra-Detector Volume*, and *Total Inlet* $L/K_d/S$ to the calculator.

Baseline:
Some substances, for example heavy metal ions or polycyclic aromatic hydrocarbons, can linger for a very long time on the inner surface of the inlet tract and the inner parts of the measuring device.

The DNP NMR responses of such substances will constantly be added to the responses of subsequently measured substances, thereby creating a baseline and reducing the sensitivity of the measurement device.

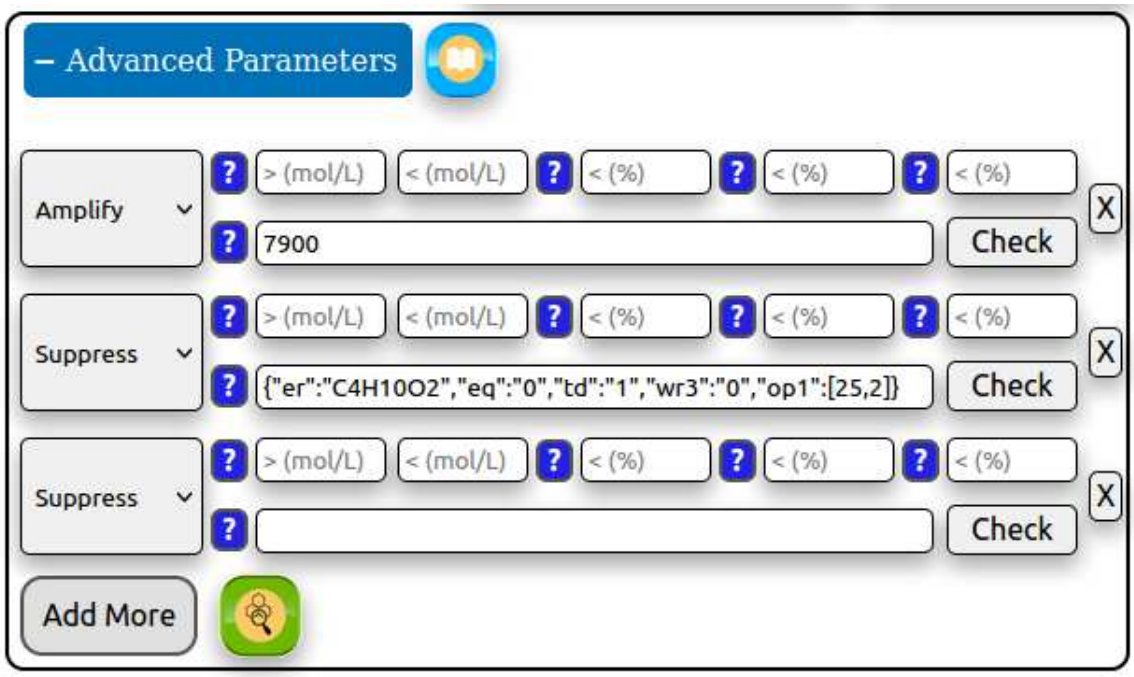
The *Baseline* field contains information on the quantitative and qualitative composition of the substances that make up the baseline, and also reports the expected measurement accuracy of substances similar or identical to those comprising the baseline.

This information is important for making decisions regarding cleaning of the inlet tract.

Suggested Cleaning Substances:
Based on the obtained baseline level, the contributing substances, and their concentrations, this section will display recommended cleaning solvents in the form of CID numbers and corresponding mixture percentages.

If you are not satisfied with the current baseline level, please select two solvents based on this recommendation and conduct an inspection with the *Perform Cleaning* and *Check Baseline* options selected.

8.4 Advanced Parameters



The current information window contains useful recommendations and examples of how to correctly enter parameters in the *Advanced Parameters* screen so as to significantly improve the quality of analysis. Prompts are available regarding how to fill each input field and select experiment options. You can easily open these prompts by clicking the associated question symbol. To hide a prompt, click again either on the question symbol or anywhere in the prompt field.

Please read and follow the prompts carefully to make your chemical analysis as accurate as possible! The Elmathron measuring device uses the method of dynamic nuclear polarization, in which microwave radiation corresponding to the Larmor frequency of electrons, has an envelope in the form of an NMR sequence. Company Elegant Mathematics received a patent for a method of generating such waves in 2020.

Irradiation of molecules with such a wave has the advantage of electron spins practically not interfering with the magnetization of nuclear spins. In practice, this method enables one-dimensional 1H spectra to be increased in sensitivity by several hundred times, and multidimensional heteronuclear spectra by hundreds of thousands of times.

This important fact allows Elegant NMR system to record multidimensional heteronuclear NMR spectra with good resolution while using permanent magnets. It is well known that multidimensional spectra require long accumulation times. However, if the approximate shape of a spectrum is known, it is possible to record multidimensional spectra sparsely rather than across the whole volume; this allows the Elegant NMR system to record multidimensional heteronuclear NMR spectra as quickly as if it were capturing a few one-dimensional spectra. If initially there is no information available regarding what substances are in the mixture being analyzed, then at first the system will have to record almost the complete multidimensional spectrum, and then process it in such a way as to elucidate what classes of substances are present. Then, it is feasible to proceed to making one and maybe several attempts to record a sparse multidimensional heteronuclear spectrum, from which it is then possible to obtain all the necessary information concerning the mixtures components.

Unfortunately, carrying out such a procedure may require a significant number of attempts and, as a consequence, consume a lot of the mixture and considerable time for analysis.

If you know the classes of substances that you plan to analyze, or if you have any additional information about the investigated substance, entering this information can significantly speed the analysis and help the Elegant NMR system in constructing the multidimensional NMR spectra. This additional information can be specified in:

- *Continuous Measurements* screen 
- *Measurements with Autosampler* screen 
- *Start Computations* screen 

which each contain a fold-out *Advanced Parameters* section. In the *Advanced Parameters* section, you can create one or more additional parameters, each of which determines whether a particular mixture component is included in the analysis.

For example, if you are analyzing a weak aqueous solution of several simple organic acids, you know that the analyzed mixture contains a lot of water, and you are not interested in its concentration. In this case, you would select the *Suppress* option and then provide information about the solvent, which is in this example water.

If the solution being investigated contains certain components of particular interest, for example acetic and formic acids, then you can create a line with each of these components and select the *Amplify* option.

Parameter 1

Enter the concentration range of the component to which the restriction applies, in *mol/L*.

If you do not specify a concentration range here, the restriction will apply to the entire concentration range.

You can also leave this field blank.

Parameter 2
Enter the maximum change in the component concentration (as a relative value); that is, this tells the artificial intelligence of the Elegant NMR system that in most experiments, the relative concentration of the selected component will change by amounts in the specified range.

You can also leave this field blank.

Parameter 3
Enter the expected accuracy of the relative concentration calculation for the mixture component to which this restriction applies, in *percent*.

Values significantly less than **one percent** can lead to infinitely long measurement times.

Please use this parameter with caution!

You can also leave this field blank.

Parameter 4
Specify the expected accuracy, in *percent*, with which the spatial geometry of the mixture component to which this restriction applies is calculated in the Euclidean norm based on the distances between atoms.

Values significantly less than **10 percents** can lead to infinitely long measurement times.

Please use this parameter with caution!

You can also leave this field blank.

Parameter 5
Here you can enter known information about the test mixture components.

For example, if you know the exact CID numbers of components, enter the list of numbers separated by commas or spaces.

It may be difficult to list all components under consideration, and you may instead have a set of criteria by which they can be characterized, such as the range of atom types, the presence of certain radicals, etc.

In such cases, you can first formulate a molecule type query in the *Search for Molecules in the HugeMDB* screen and check the query against the database.

If the expected results are returned, the query criteria can be imported into this field.

Criteria imported from a query will be displayed in the internal JSON format.

This JSON format is not intended for direct user editing, but you can double-check the query at any time by clicking the **Check** button. As already mentioned above, the Elmathron measuring device uses a method for constructing sparse multidimensional heteronuclear spectra with non-uniform sampling to detect substances and mixtures.

It is possible to record such spectra with very sparse data, and thus for the experiment time to be short. However, a situation may arise in which our method finds a substance with similar structure, but does not determine exactly what is needed due to missing data.

If we construct a complete multidimensional matrix for the heteronuclear spectra (7 and 8-dimensional spectra are built in the apparatus), then identifying substances will be much easier, but the experiment time can become infinitely long.

Specifying additional information in *Advanced Parameters* screen will allow for prediction of the types and structures of multidimensional spectra and hence the faster and more accurate solving of this problem without exceeding the maximum allowable time in the *Maximum Time* field.

We would like to remind that correctly-entered parameters allow you to perform chemical analysis hundreds of times faster while preserving consistent sensitivity and accuracy.

9 Search Records

The current information window contains useful recommendations and examples regarding how to correctly enter parameters in the *Search Records* screen in order to quickly search the database for results of prior experiments. Prompts are available regarding how to fill each input field and select experiment options. You can easily open these prompts by clicking the associated question symbol. To hide a prompt, click again either on the question symbol or anywhere in the prompt field.

Please read and follow the prompts carefully to make your chemical analysis as accurate as possible!

Attention! If after logging in you do not see the Elmathron device or autosampler you need, or data in the experiment database corresponding to any Elmathron device, then the username under which you logged in is not allowed to operate or use data from this device.

To obtain the rights, a superuser must correct the user account's access rights as listed in the *User Properties→Device Rights* field in *Settings* screen  All Elmathron devices and the server work independently of each other. Experimental data are recorded on Elmathron devices in the form of sequentially numbered records.

If there is an Ethernet connection between the Elmathron device and a server, the data are transferred to the server and, upon successful transfer, are then deleted from the internal device's memory.

As soon as the data arrives on the computing server, you can search and process it. Depending on the type of experiment, an Elmathron measuring device performs approximately one measurement every 10-200 seconds during its operation.

Each measurement is automatically assigned its own serial number, including instances of multiple measurements from the same sample. Then, each such number in the experiment database is associated with the unique name you assigned for the experiment, along with all current settings of the Elegant NMR system.

At the first measurement of a sample, the artificial intelligence of the system estimates which substances having what chemical groups are present in the mixture. In the course of subsequent measurements, a detailed analysis of each such substance is carried out using multidimensional DNP NMR with non-uniform sampling.

Further computer processing of all such measurements can significantly improve the sensitivity of the method.

After processing an experiment, you can get both the results of individual measurements and those from statistical processing of sequentially measured data.

Devices:
Here you can select one or several devices from the list of Elmathron measuring devices, to which you have access to search for the measurement results you are interested in.

List of Search Criteria:
Here you can select one or several search criteria with which to query the results database of the Elegant NMR system.

Enter or select different parameters on each line and then press the **Search Records** button  to start the search.

You can generate new lines for entering additional search criteria with the **Add More** button.

You can find more information about each search criteria in the *Search Records* information window by clicking on the **Help** button.

To delete an unneeded search line, click on the delete symbol at the end of that line.

The program searches in such a way that for each type of parameter you enter, at least one condition must be met.

For example, if you enter several lines representing different ranges of experiment numbers and several more with different *Experiment Name RegEx* criteria, all experiments will be found that fall within at least one experiment number range and that have names satisfying at least one regular expression.

In this case, all those experiments will be found, each of which satisfies at least one range of experiment numbers and at least one regular expression of the name of the experiments.

When entering numbers, the parameter entry field accepts the following:

- a single range with a hyphen, for example, 100-200;
- a single number to specify a single-valued parameter;
- or $>N$ or $<N$ to respectively select values greater or less than N.

Experiment Nr Range: Enter a range of ordinal numbers identifying experiments.

Time and Date: Enter the date and time range of the experiment in the format of day, month, year and hour.

Experiment Name RegEx: Enter a unique name for the experiment. *RegEx syntax* can be used for partial or multiple matching.

Substance CID: Enter one or several CID numbers of substances found in the analysis results, separated by spaces or commas. If several CIDs are entered on a single line, the program will search for experiments in which all of those substances were found. By entering two or more sets of CID numbers as separate criteria, you can find a set of experiments that contains substances matching the CID set in at least one of those lines.

Fluid Viscosity: Choose from the offered list of standard viscosities the value that the program should be guided by when searching experiments. To search on multiple viscosities, please open an additional line.

Maximum Volume: Enter a volume value or a range of values, or limit the volume search to amounts greater than or less than any given value, for example *<50 uL*. Include units when entering volume values: *nL, uL, mL, L*.

Maximum Sample Volume: Enter a sample volume value or a range of values, or limit the volume search to amounts greater than or less than any given value, for example *<50 uL*. Include units when entering volume values: *nL, uL, mL, L*.

Maximum Time: Enter a time value or range of values, or limit the time search to values greater than or less than any given duration, for example *<20 minutes*. Include units when entering time values: *seconds, minutes, hours, days, weeks*.

Mixture Lifetime: Enter a value or range of values representing the lifetime of a substance in the inlet tract, or limit the search to lifetimes greater than or less than any given value, for example <40 seconds. Include units when entering time values: *seconds, minutes, hours, days, weeks.*

Autosampler Method: Select an autosampler analysis method to specifically search for experiments using an autosampler.

Cleaning between Probes: Limit search results to autosampler experiments applying the selected inlet tract cleaning method between samples.

Several Attempts Allowed: Limit search results to autosampler experiments in which re-sampling was permitted.

List of Search Records:
After you press the **Search Records** button, the program will perform the search, and you will receive a list of matching experiments identified among the measuring devices you selected.

Each line corresponds to one experiment or experiment setting.

Using the mouse, you can highlight in a different color one or several lines of interest in order to prepare these experimental data for further active use in other program screens.

For example, if you determined one of the retrieved experiments to have been the most successful, and you want to utilize the same experiment settings, you can select that line and then click on the **Append to Continuous Measurements** or **Append to Measurements with Autosampler** button to send the experiment settings to the corresponding setup screen.

The selected results will be displayed automatically in that screen, and you can start an analysis by clicking on the **Run Continuous Measurements** or **Run Measurements with Autosampler** button as appropriate.

You can also view the results of a selected experiment without preliminary computer processing by clicking on the **Demonstrate Results** button which will take you to the *Results of Computations* screen 

Each instance of the web interface can display only one computer processing result at a time.

If computer processing of results is already underway in the present tab, that processing will be stopped and its output lost.

If you do not want to irretrievably terminate the processing, you can open another browser tab and access the experiment results there.

Selected experiments can be subjected to further correlation and more accurate numerical processing by clicking on the **Append to Start Computations** button.

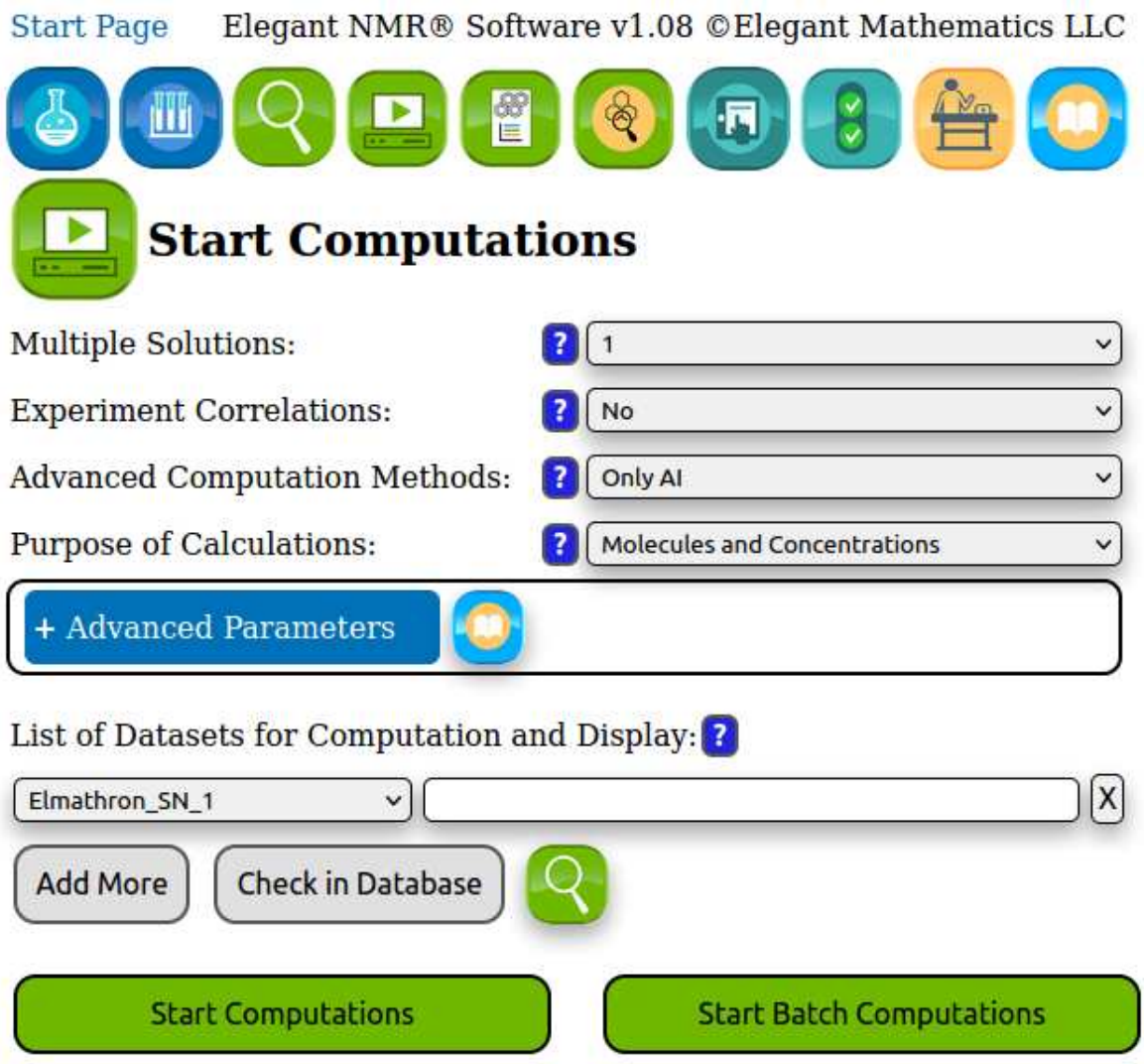
Their results will be automatically loaded in the *Start Computations* screen where you can then select the desired data processing method and start processing by clicking on the **Start Computations** button.

The options *Select All* or *Deselect All* allow you to select all search results for further actions or, conversely, to deselect all results.

To deselect one line, click on it once; the background of the line will change back to white, indicating it is no longer selectable.

The fields *Experiment Name* and *Device* are not interactive and not selectable.

10 Start Computations



The current information window contains useful recommendations and examples of how to correctly enter parameters in the *Start Computations* screen in order to carry out detailed computer modeling and processing of the measurement results obtained by the Elegant NMR system. Prompts are available regarding how to fill each input field and select experiment options. You can easily open these prompts by clicking the associated question symbol. To hide a prompt, click again either on the question symbol or anywhere in the prompt field.

Please read and follow the prompts carefully to make your chemical analysis as accurate as possible!

Attention! If after logging in you do not see the Elmathron device or autosampler you need, or data in the experiment database corresponding to any Elmathron device, then the username under which you logged in is not allowed to operate or use data from this device.

To obtain the rights, a superuser must correct the user account's access rights as listed in the *User Properties→Device Rights* field in *Settings* screen After retrieving experimental records through the *Search Records* screen and sending them to this screen, you can perform detailed computer simulations and so obtain the most accurate results.

In most cases, these calculations require significant computer resources and their completion can take a significant amount of time. Consequently, we recommend that you select the parameters for the computer simulation with care.

Multiple Solutions:

To improve the accuracy of the analysis, the Elegant NMR system can, at your request, obtain several solutions in such a way that the first solution is the most probable and the last is the least probable.

Thus, by choosing to seek multiple solutions you will receive additional information about the investigated substances.

Experiment Correlations:

If similar substances are present during different measurements, you can choose to perform a correlation analysis between those experiments.

Supported correlation scenarios are:

- No;
- Yes, between Each Experiment;
- Yes, between Datasets;
- Joint Correlations for the Same Time.

By default, the option *Yes, between Each Experiment* is selected, which performs correlation analysis of all experiments.

Selecting *Joint Correlations for the Same Time* is recommended when you used several Elmathron devices at the same time to continuously measure a complex chemical process at different points.

Advanced Computation Methods:
Here you can choose to carry out additional processing, with increased complexity of your results.

The options are:
- Only AI;
- AI and Molecular Mechanics (MM);
- AI, MM and Ab Initio;
- No.

By default, the *Only AI* option is selected.

You can also view the selected experiment's results without preliminary computer processing by choosing the *No* option here or by going to the *Search Records* screen and clicking the **Demonstrate Results** button; these actions have identical effects.

In rare cases, the Elegant NMR molecular database may not contain sufficient information on the conformations of molecules present in your test mixture.

Numerical simulation using molecular mechanics or ab initio may be utilized in this event, but such calculations can be very complex and take several hours, sometimes even several days.

We strongly recommend these options only be used after having searched the database using the *AI* and not achieving the desired results.

Each web interface can display only one computer processing result at a time. If you initiate a new calculation while another is already underway, that previous calculation will be terminated and lost.

If while a calculation is underway you close the web interface tab or the Internet connection to the server is interrupted for more than two minutes, the calculation will be stopped and the calculation results on the server will be permanently deleted.

If you want to start processing results and have them persist even after closing the web interface tab, then you need to click on the **Start Batch Computations** button.

After starting a batch computation, the current program window will display a list of processing results with the associated date of processing.

When the results are fully processed, you can view, visualize, and delete them.

Purpose of Calculations:
Here you can choose from a list how the results of processing are to be presented:
- Molecules and Concentrations;
- Drug Detection;
- Disease Detection.

In addition to results in the form of molecular structures and their concentrations, the Elegant NMR system supports a *Drug Detection* option, in which the belonging of found substances to classes of narcotic and prohibited substances is statistically determined.

The Elegant NMR system supports also a *Disease Detection* option in which the set of found substances is correlated with markers (detectors) of lung diseases. To optimize the time and accuracy of computer processing, you can additionally enter *Advanced Parameters*. Any additional information will improve and speed computer processing of the experimental results.

List of Datasets for Computation and Display:
Here each line list refers to one Elmathron measuring device, for which you enter one or several experiment numbers and/or number ranges separated by commas.

If you selected any correlation option under *Experiment Correlations*, then correlation analysis is conducted on the corresponding data.

For easy selection of experiment numbers or number ranges, you can click on the **Search Records** button to go to the *Search Records* screen and search on relevant criteria.

The search results can then be imported into the *List of Datasets for Computation and Display*.

The **Check in Database** allows you to confirm that the set of experiment ranges entered in each line is represented in the experiment database. After you have prepared the data processing request, click the **Start Computations** button to execute it.

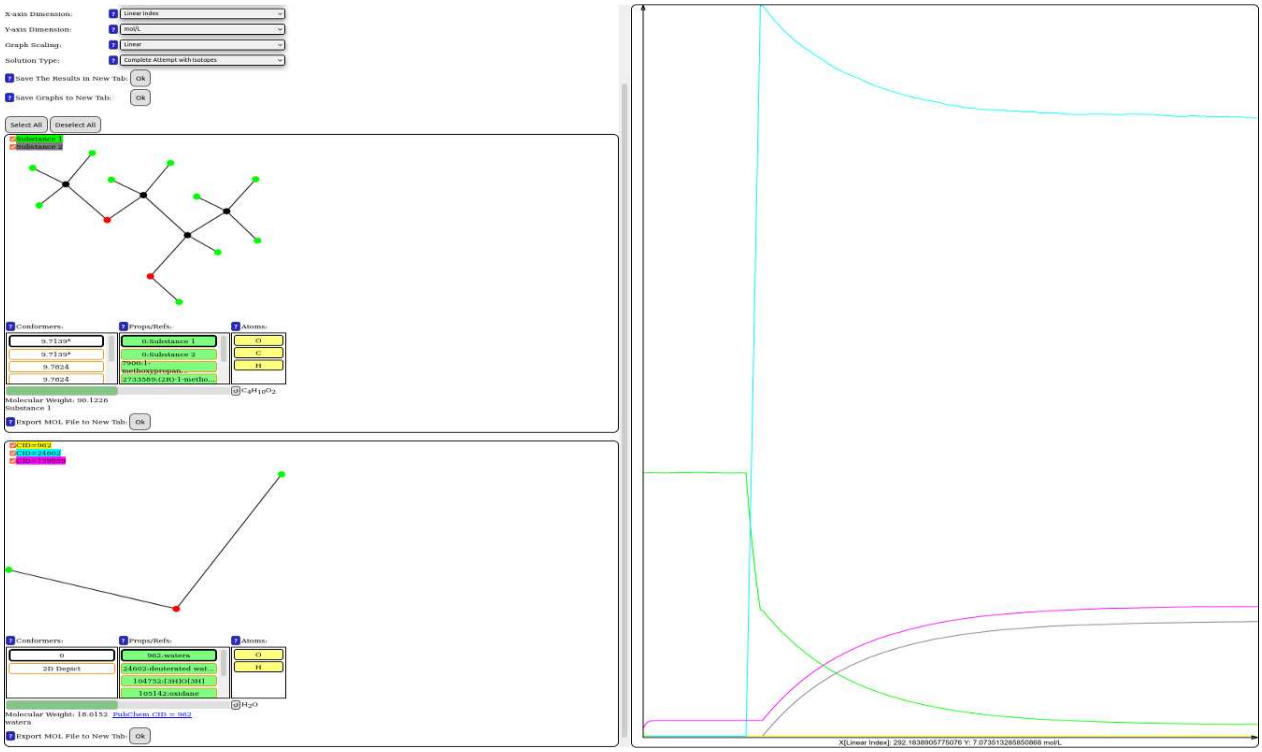
The computation time can be significantly long, and you may need to wait some time for the computation results to be generated. While this computation is processing on your server (data processing unit), calculation requests from other web clients may be running simultaneously, which can further increase the processing time.

When the processing is finished, the results can be viewed in the *Results of Computation* screen.

You can always save the results of a completed calculation into a separate static HTML file using the *Save Results to New Tab* option. The produced file includes a built-in visualizer for displaying molecular structures and concentration graphs, does not contain any third-party links, and can be used to save and transfer these results to a third-party storage system.

This file has a built-in visualizer for displaying molecular structures and concentrations graphs. You can use this file, which does not contain any third party links, to save and transfer these results to third party storage systems.

11 Results of Computations



The current information window contains useful recommendations and examples of how to correctly enter parameters in the *Results of Computation* screen in order to become acquainted with the findings from your experimental data and determine exactly what substances you analyzed. Prompts are available regarding how to fill each input field and select experiment options. You can easily open these prompts by clicking the associated question symbol. To hide a prompt, click again either on the question symbol or anywhere in the prompt field.

Please read and follow the prompts carefully to make your chemical analysis as accurate as possible! This screen allows you to graph the dependences of substance concentrations.

Graphs can be panned to the right or left by holding and dragging the mouse. Graph scaling is always vertical.

If you need to enlarge or reduce the horizontal dimension, then hold the mouse button and move the chart up or down.

If you click on a graph, the frame with the list of substances will automatically scroll to the substance corresponding to that graph.

Description Placement:

Here you can choose the placement of substance descriptions relative to the graphs:

- Top or Bottom: above or under graphs;

- Right or Left: to the right or left of graphs;
- Graph Only: show only graphs;
- Description Only: show only descriptions.

By default, the *Left* option is selected; that is, information is placed to the left of the graphs.

If you select the option to show only graphs, then you can return to the original view by clicking anywhere on a graph canvas.

X-axis Dimension:

The dimensions plotted along the x-axis depend on the parameters you selected in the *Start Computations* screen.

Available options are the following:

- Linear Index (default);
- Correlation Index;
- Measurement Time;
- Volume of Substance at Measurement Start;
- Time of Entry of a Sample with an Analyte into the Inlet Tract.

If you specified several experimental record ranges in the *List of Datasets for Computation and Display* of the *Start Computations* screen and selected the cross-correlation option, then the *Correlation Index* will correspond to the number of measurements in all specified records, which is assigned from the beginning for each experimental record range.

If you have selected to correlate on *Measurement Time*, this will be determined as elapsed time; that is, the time of a given measurement minus the time of the first measurement in each record.

Y-axis Dimension:

You can likewise choose from a list what dimension will be plotted along the y-axis:

- mol/L;
- mol;
- g/L;
- g.

By default, the *mol/L* option is selected.

Graph Scaling:

Graphs may have linear or logarithmic scaling along the y-axis.

In some cases, especially when both solvent and trace substances are present in the measurement mixture, it is preferable to choose logarithmic scaling.

By default, the *Linear* option is selected.

Solution Type:

If you performed a calculation with the *Multiple Solutions* condition, then selecting a *Solution Type* will allow you to choose which method's results are displayed:

- Complete Attempt without Isotopes;
- Complete Attempt with Isotopes;
- Approximate Attempt without Isotopes;
- Approximate Attempt with Isotopes.

If for some reason there is only one solution, you will not be able to select a different solution type here.

Each numerical simulation may have more than one solution, especially if the settings of the Elegant NMR system were less than perfectly correct and/or your data was very noisy.

By default, the first solution on the list is usually the most reliable, and all other solutions are a consequence of circumstances.

For example, the chemical composition of the test substance or mixture may be only partially determined partially for reasons such as low concentration, insufficient measurement time, insufficient amount of the measured mixture, etc.

Thus, by looking through and sorting out the solutions in the list, you can determine which is the most suitable for your problem and develop an understanding of how to most correctly analyze such mixtures in the future.

Save The Results in New Tab:
You can save the results of processing experiments you are interested in by clicking on the **Ok** button.

All results currently displayed in the visualizations on the *Results of Computations* screen will be transferred to a new browser tab, where you can save them as a separate file in HTML format.

All possible actions on the current page remain after saving, and you can alter the plots, view substance information, and view graphs of dependencies at any time.

You may also save data for each molecule in the form of a MOL file.

Save Graphs to New Tab:
By clicking on the **Ok** button, you can save graphed data in spreadsheet form to a separate tab of your browser.

You can then save this spreadsheet to your file system as a text document by right-clicking to bring up a pop-up menu and then select *Save Page As*. You can view the processed results in the form of a list with visualizations of the molecules detected in your experiments.

For three-dimensional molecular structures, the program supports molecular rotation for viewing its spatial structure from different angles.

You can also rotate the molecule with the mouse in its visualization field and start or stop automatic rotation by pressing the **Run/Stop Rotation** button.

Furthermore, clicking on a molecule in the structure will highlight it and display the following information:

- distance between atoms;
- torsion angle values;
- values of the angles between bonds in the molecule.

This information appears as a line of text at the bottom of the visualization area after you have selected appropriate atoms.

You have the option to further export the results to the MOL file. If you have installed third-party programs that support the MOL file format, you can also use data about conformers or enantiomers saved in that manner for your own purposes, with a link to the source. Additional information about each found molecule can be obtained through a special table with buttons having different states.

This table contains three columns concerning the molecule and its conformers:

- *Conformers*: a column listing conformers;
- *Props/Refs*: a column listing CID numbers;
- *Atoms*: a column listing atoms and isotopes.

Black borders on buttons in the table indicate which items are currently being visualized.

Conformers:

The *Conformers* column lists the molecule's conformers and enantiomers by formation energy in ascending order.

Upon clicking on the button corresponding to a conformer or enantiomer, its structure will be displayed in the visualization area associated with the molecule.

If, upon selection of a conformer, an **asterisk *** appears to the right of its formation energy, then that conformer has a mirror enantiomer, which is also marked with the same asterisk. If no asterisk appears, then the conformer is spatially invariant to its mirror image; that is, it does not have an mirror enantiomer.

The **Depict 2D** button (if present) switches the molecule's 3D visualization to 2D.

This column is linked to the column of CID numbers (*Props/Refs*) by the green priority selection slider at the bottom of the table.

The slider has two positions: when to the left, buttons in the column with conformers and enantiomers have priority, and when to the right, buttons with CID numbers have priority.

Each conformer or enantiomer corresponds to one or more CID numbers, and, similarly, each CID number corresponds to one or more conformers or enantiomers.

Upon changing the priority, you can see which conformer or enantiomer the CID numbers correspond to, and which CID number corresponds to which conformer or enantiomer. Namely,

those that match will be colored green, and can be selected; those that do not match will be grayed out, and cannot be selected.

This means that those that match, will be colored green, and can be selected; and those that do not match, will be grayed out, and cannot be selected.

Props/Refs:
The *Props/Refs* column presents the currently known CID numbers for the molecule, sourced from the PubChem database, in the form of active buttons.

Upon clicking on any button with a CID number, the nomenclature name of the molecule and an active link to PubChem with the CID number are displayed below the table.

At the same time, the *Atoms* column changes to a list of atoms appropriate to the chosen CID number.

In some cases, buttons with the entry *0: Substance ...* may appear in this column. These indicate molecules identified from the Elegant NMR internal database that, at the moment, do not have CID numbers.

This column is linked to the column of conformers and enantiomers by the green priority selection slider at the bottom of the table. Each conformer or enantiomer corresponds to one or more CID numbers; similarly, each CID number corresponds to one or more conformers or enantiomers.

The slider has two positions: when to the left, buttons in the column with conformers and enantiomers have priority, and when to the right, buttons with CID numbers have priority.

Each conformer or enantiomer corresponds to one or more CID numbers, and, similarly, each CID number corresponds to one or more conformers or enantiomers.

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This means that those that match, will be colored green, and can be selected; and those that do not match, will be grayed out, and cannot be selected.

Atoms:
The *Atoms* column lists all atoms included in the visualized molecule shown above the table.

Atoms are presented as element symbols inside active buttons that can be selected by clicking, upon which their color changes.

The buttons have three possible states, indicated by color:

- *yellow* means that the selected atoms will be represented with different colors depending on atom type;
- *white* means that the selected atoms will be displayed as text symbols;
- *gray* means the selected atoms are hidden from the visualization.

In some cases, when a molecule has at least isotopic variants or variants with charged atoms, corresponding additional buttons with isotopes and charged atom symbols may be present in this column.

Furthermore, clicking on a molecule in the structure will highlight it and display the following information:

- distance between atoms;
- torsion angle values;
- values of the angles between bonds in the molecule.

This information appears as a line of text at the bottom of the visualization area after you have selected appropriate atoms. Each molecule has an associated check box that allows you to hide or show the corresponding graph image.

For convenience, the color of the check box field matches the color of the corresponding graph in the graphs image field.

This option is implemented for ease of perceiving the results of processing experiments. When a large amount of information is processed, many dependence graphs will be present in the graph image area; this color-coding aids in tracking those dependencies that interest you.

Export MOL File to New Tab:
Search results may be readily exported to the MOL file format.

First, select a conformer and CID (*Props/Refs*) of interest from the table and then click on the **Ok** button.

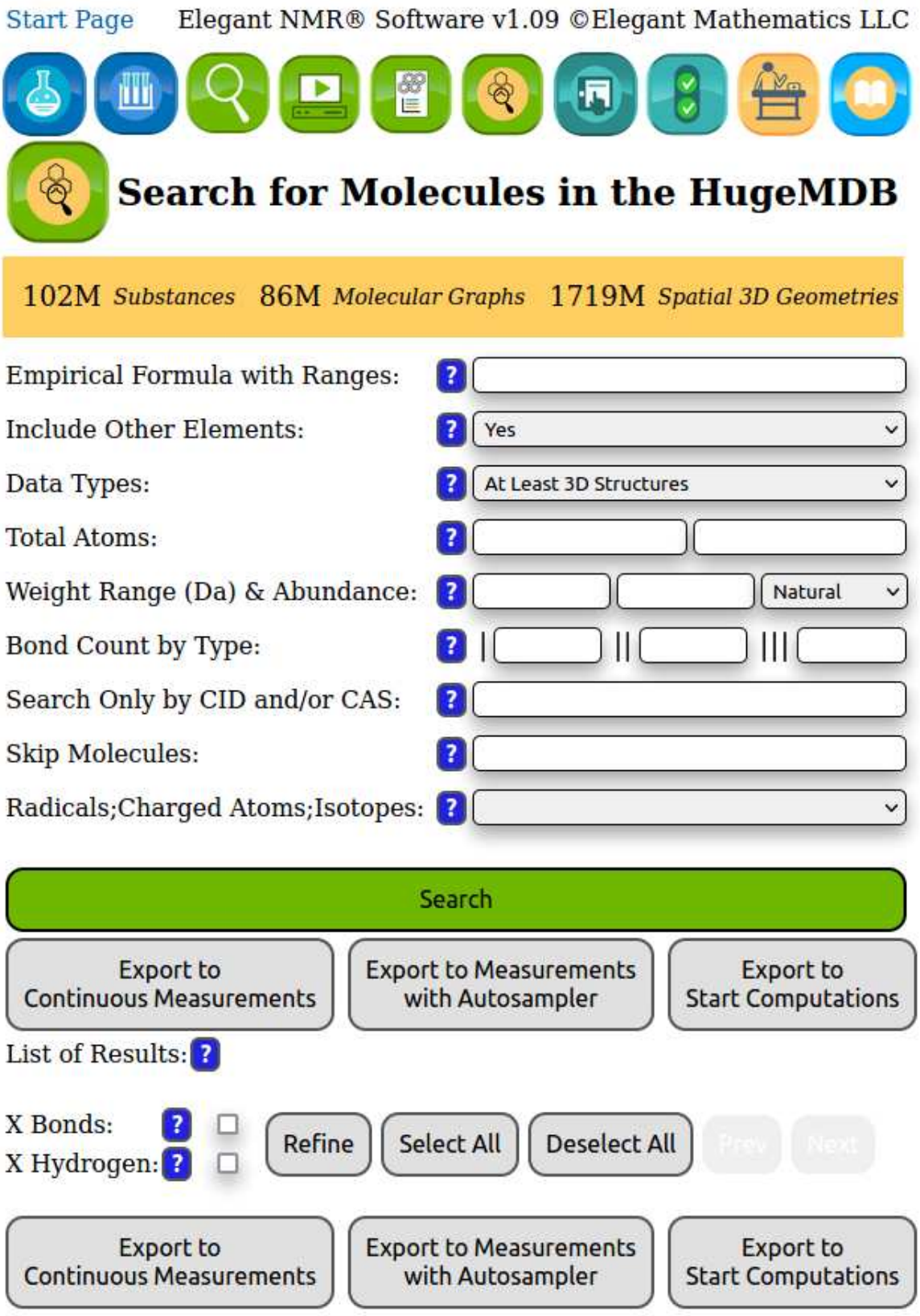
Then, the MOL file information for that conformer will be displayed in an additional tab of your browser.

After that, in an additional tab of your browser, information will appear in the form of MOL File about the selected conformer.

You can save this file by right-clicking to bring up a pop-up menu and then selecting *Save Page As*.

You have the right to further use the saved data about the conformer for your own purposes, with reference to the source from which those data were received, if you have installed third-party programs that support the MOL file format. The set of calculation results and their displays will remain unchanged until you either request a new calculation be performed or click the **Demonstrate Results** button in the *Search Records* screen 

12 Search for Molecules in the HugeMDB



The *Search for Molecules in the HugeMDB* capability is an integral part of the *Elegant NMR*

Software v1.11 and is designed to conduct fast and efficient searches for molecules and their spatial structures.

The web interface of the program works on all computer systems and architectures, including all modern mobile devices and tablets with JavaScript-enabled browsers.

Computational algorithms for searching and processing spectra and molecular structures are installed on a specialized high-performance Linux server with GPU/Nvidia CUDA support that has minimal vulnerability to computer trojans and viruses.

The Elegant Mathematics algorithms used to develop this program comprise:

- *Tensor Decomposition Algorithms and Multivariate Approximation Methods*: Detailed in the issued patents US10733092B2, US10733092B2, US10733092B2, and subsequent divisional applications, including the application US17019263;
- *Molecule Comparison and Recognition Algorithms* based on patent application US16695200;
- *Algorithms for Spectral Recognition of Molecular Structures*, which are state of the art and are detailed in patent pending applications filed by Elegant Mathematics LLC.

Using the search program is completely free and does not require special user registration.

The database of substances queried by the search is based on open data compiled in the world's largest database of chemical compounds, PubChem (the National Center for Biotechnology Information (NCBI)); it contains about 100 million chemical compounds.

Building from this basis, Elegant Mathematics LLC has formed a large set of conformers of chemical structures and plans to continually supplement the database with new experimental data and the results of numerical modeling using molecular mechanics and *ab initio* quantum mechanical calculations.

The number of 3D molecular structures included in the Elegant NMR Software database, including all enantiomers, conformers and enantiomeric conformers, already exceeds **1.7 billion**! Using the search tool, you can quickly find the following:

- Data on the chemical and structural composition of molecules and their conformers and enantiomers, as well as their molecular weight.
- Visualizations of three-dimensional models of molecules and their conformers and enantiomers.
- Data on the distances between atoms in molecules, the values of the angles between bonds, and the values of torsion angles.
- CID numbers of molecules, conformers, and enantiomers, along with further links to useful information.

In the near future, electron distribution density for each conformer will also be added.

You can save the search results as a separate file in HTML format. You can also export the results to a MOL file and then use them for your own purposes with a link to the source. If you already have information about the substances you are searching for, such as the CID and/or CAS numbers of substances or the approximate chemical composition of compounds,

you can simplify your search by entering that information into the appropriate input fields. Prompts are available regarding how to fill each input field and select experiment options. You can easily open these prompts by clicking the associated question symbol. To hide a prompt, click again either on the question symbol or anywhere in the prompt field. If the search parameters are incorrect or entered incorrectly, the program will report *Nothing found*.

Empirical Formula with Ranges:
Enter a set of atoms that are included in the molecule.

It is possible to do so with a range for each type of atom, in which case you write the range immediately after the corresponding atom symbol, indicating the range with a hyphen.

For example, entering **C12-24H30** will allow you to find all molecules that have **30** hydrogen atoms and anywhere from **12** to **24** carbon atoms.

All symbols of chemical elements should be written in Latin letters, as is customary in the periodic table of chemical elements.

The first letter of the name is capitalized, and the second is lowercase if present. The program will automatically change the case of first letters entered in lowercase. It also limits the use of extraneous characters.

The number of atoms may be zero, and a range may start from zero.

In this case, the program will search for molecules that do not contain that element.

In the input field, element symbols may be separated by spaces, or you can write the symbols cheek-by-jowl as in the example above.

This field may be empty only if you have entered molecule CID and/or CAS numbers in other input fields, as those numbers take priority.

Include Other Elements:
Here you can choose to include in the search other elements that may also be present in the molecules.

If the *Yes* option is selected (which is also the default), the search will consider molecules having elements not specified by you in the *Empirical Formula with Ranges* field.

Otherwise, if the *No* option is selected, the program will only search for those molecules comprised of the elements entered in the *Empirical Formula with Ranges* field.

Data Types:
Here you can select what types of molecular structures to search for:

- *At Least 3D Structures*: return only those molecules for which there is at least one three-dimensional structure.

- *At Least 2D Structures*: return only those molecules for which there is at least one two-dimensional structure.
- *Any Structures*: return all molecular structures without limits.

By default, the *At Least 3D Structures* option is used.

If *At Least 2D Structures* is selected, you will get results with a predominance of molecules having two-dimensional structures and without additional options.

For three-dimensional molecular structures, the program supports molecular rotation for viewing its spatial structure from different angles.

You can also rotate the molecule with the mouse in its visualization field and start or stop automatic rotation by pressing the **Run/Stop Rotation** button.

Furthermore, clicking on a molecule in the structure will highlight it and display the following information:

- distance between atoms;
- torsion angle values;
- values of the angles between bonds in the molecule.

This information appears as a line of text at the bottom of the visualization area after you have selected appropriate atoms.

Total Atoms:
Here you can enter values that limit the total number of atoms in molecules.

The first input field represents the minimum number of atoms in your molecules of interest, and the second field the maximum number of atoms.

You can leave either or both of these fields blank.

Weight Range (Da) & Abundance:
Here you can enter limits on the molecular weight, in *Daltons*.

The first input field represents the minimum weight of your molecules of interest, and the second field the maximum weight.

You also have the opportunity to choose an isotope distribution: *natural* or *isotopic* abundance.

When using the natural abundance of isotopes, the entered molecular weight values correspond to the sums of the atomic masses of all constituent atoms (averaged for our planet).

When using the isotopic distribution, the entered molecular weight values correspond to the sums of the atomic masses of any stable isotopes. If a given element has no stable isotope, then the isotope with the maximum lifetime is used.

For example, when referencing the natural distribution of isotopes in nature, the molecular weight of water will correspond to 18.01526 Da.

In contrast, the molecular weight of a water molecule that consists of two atoms of deuterium and one atom of [18]O will be 22.02736 Da.

Bond Count by Type:
Here you can enter ranges constraining the numbers of single, double, and triple bonds in returned molecules.

Each range should be entered as a hyphenated number pair *from-to* or as a single number.

If **0** is specified in one or more fields, then the corresponding type of bond must not be present in the molecule.

You can also leave one or several fields blank, in which case that bond type will not be considered as a search criterion.

Search Only by CID and/or CAS:
If you already know the CID (PubChem ID) and/or CAS numbers of your molecules of interest, please enter them in this input field, separated by commas or spaces.

You can also use the internal molecular structure number used for reference within the Elegant NMR Software database, termed a *Molecular ID*, which is prefixed by the letter *M* in front of the number. These IDs can be entered alongside CID and/or CAS numbers.

Attention! If you fill in this field, the search tool will prioritize the CID, CAS, and Molecular ID numbers, ignoring any other search criteria.

Skip Molecules:
In the event that your search returns more hits than can be immediately displayed in the search results page, this field allows you to bypass the first *N* results for easier viewing.

For example, to go to the thousandth molecule, you can enter **999** in this field and so immediately start viewing the results for the thousandth molecule and beyond.

By default, up to **50** search results are shown per page.

Radicals;Charged Atoms;Isotopes:
Here you can choose one or several options from the proposed list of isotopes, radicals and charged atoms.

The options you select will appear in the field below in the form of buttons with formulas of radicals, isotopes, charged atoms, and special symbols.

Each button can be used as inclusion, exclusion, or ignored criteria, which functions can be changed with a click:

- *green checkmark*: the selected atom type must be present in the molecule;
- *red stop symbol*: the selected atom type must not be present in the molecule;
- *no symbol beside the formula*: the criterion is not used.

All unused buttons can be removed by clicking on the **Remove Unmarked** button. After you have completed all the required input fields, you can start your search for molecules by clicking on the **Search** button.

If you perform chemical analysis of substances with the Elegant NMR measuring system, you are able to send all entered parameters from the search screen to other program screens, namely:

- *Continuous Measurements*
- *Measurements with Autosampler*
- *Start Computations*

To perform such an export, use the appropriate button: **Export to Continuous Measurements** or **Export to Autosampler** or **Export to Start Computations**.

After export, this data will be automatically displayed in a special input line of the *Advanced Parameters* section.

Be careful, *Skip Molecules* option cannot be exported!

You can then apply either *Suppress* or *Amplify* mode to use this data in your analysis or processing of results.

List of Results:

After the program has performed a molecule search, you will be presented with a list of found molecules, their structural visualizations, and additional useful information about each molecule and its structure.

You can refine your search using the **Refine** button.

First, select from the results list those molecules to be refined, then click the **Refine** button, which will automatically appear as additional buttons with the corresponding CID numbers in the field covering radicals, charged atoms, and isotopes.

Then, you can run the refined search by clicking on the **Search** button again. If you want to use search results in measurement or computation settings, first check appropriate boxes in the visualization area and then, depending on the type of experiment, click on the appropriate button: **Export to Continuous Measurements** or **Export to Autosampler** or **Export to Start Computations**.

The CID numbers of the selected molecules will be automatically copied into an input line under *Advanced Parameters*.

X Hydrogen:

Allows you to exclude hydrogen atoms in molecules upon subsequently clicking **Refine** button.

In selecting this check box mode and your molecules of interest from the search results, you allow the program to ignore all hydrogen atoms that are in those molecules.

To see *Example 2*, which documents how to correctly use this option for searching, go to the information window in the *Search for Molecules in the HugeMDB* screen by clicking on the **Help** button.

You can also choose not to use this option.

X Bonds:
Allows you to exclude types of bonds upon subsequently clicking **Refine** button.

In selecting this check box mode and your molecules of interest from the search results, you allow the program to ignore the types of bonds between atoms in those molecules.

To see *Example 2*, which documents how to correctly use this option for searching, go to the information window in the *Search for Molecules in the HugeMDB* screen by clicking on the **Help** button.

You can also choose not to use this option.

Refine:
Using the additional option *Refine* to improve search results significantly increases the search time, more so than for any other search criteria; therefore, we recommend using this option only if other search criteria do not return the result you are looking for!

For example, if the list of radicals, charged atoms, and isotopes contains both a benzene ring and an acetylene group, a search using **C6** (benzene ring) and **-C#C-** (triple bond between two carbons) criteria will be significantly faster than one using 241H and 6326B.

Save Results in New Tab:
All results currently displayed in the visualization area will be transferred to a new browser tab, where you can save them as a separate file in HTML format.

You have the right to use this file with a link to its source for various purposes. For example, sending by e-mail, saving on your mobile device or computer, embedding in a presentation, etc.

All possible actions regarding the visualization on the current page remain after saving, and you can view all information on the selected molecule at any time.

You also have the opportunity to save the data for each molecule in the form of a MOL file. Additional information about each found molecule can be obtained through a special table with buttons having different states.

This table contains three columns concerning the molecule and its conformers:

- *Conformers*: a column listing conformers;
- *Props/Refs*: a column listing CID numbers;
- *Atoms*: a column listing atoms and isotopes.

Black borders on buttons in the table indicate which items are currently being visualized.

Conformers:

The *Conformers* column lists the molecule's conformers and enantiomers by formation energy in ascending order.

Upon clicking on the button corresponding to a conformer or enantiomer, its structure will be displayed in the visualization area associated with the molecule.

If, upon selection of a conformer, an **asterisk *** appears to the right of its formation energy, then that conformer has a mirror enantiomer, which is also marked with the same asterisk. If no asterisk appears, then the conformer is spatially invariant to its mirror image; that is, it does not have an mirror enantiomer.

The **Depict 2D** button (if present) switches the molecule's 3D visualization to 2D.

This column is linked to the column of CID numbers (*Props/Refs*) by the green priority selection slider at the bottom of the table.

The slider has two positions: when to the left, buttons in the column with conformers and enantiomers have priority, and when to the right, buttons with CID numbers have priority.

Each conformer or enantiomer corresponds to one or more CID numbers, and, similarly, each CID number corresponds to one or more conformers or enantiomers.

Upon changing the priority, you can see which conformer or enantiomer the CID numbers correspond to, and which CID number corresponds to which conformer or enantiomer. Namely, those that match will be colored green, and can be selected; those that do not match will be grayed out, and cannot be selected.

This means that those that match, will be colored green, and can be selected; and those that do not match, will be grayed out, and cannot be selected.

Props/Refs:

The *Props/Refs* column presents the currently known CID numbers for the molecule, sourced from the PubChem database, in the form of active buttons.

Upon clicking on any button with a CID number, the nomenclature name of the molecule and an active link to PubChem with the CID number are displayed below the table. At the same time, the column *Atoms* changes to a list of atoms appropriate to the chosen CID number.

This column is linked to the column of conformers and enantiomers by the green priority selection slider at the bottom of the table. Each conformer or enantiomer corresponds to one

or more CID numbers; similarly, each CID number corresponds to one or more conformers or enantiomers.

The slider has two positions: when to the left, buttons in the column with conformers and enantiomers have priority, and when to the right, buttons with CID numbers have priority.

Each conformer or enantiomer corresponds to one or more CID numbers, and, similarly, each CID number corresponds to one or more conformers or enantiomers.

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This means that those that match, will be colored green, and can be selected; and those that do not match, will be grayed out, and cannot be selected.

Atoms:
The *Atoms* column lists all atoms included in the visualized molecule shown above the table.

Atoms are presented as element symbols inside active buttons that can be selected by clicking, upon which their color changes.

The buttons have three possible states, indicated by color:
- *yellow* means that the selected atoms will be represented with different colors depending on atom type;
- *white* means that the selected atoms will be displayed as text symbols;
- *gray* means the selected atoms are hidden from the visualization.

In some cases, when a molecule has at least isotopic variants or variants with charged atoms, corresponding additional buttons with isotopes and charged atom symbols may be present in this column.

Furthermore, clicking on a molecule in the structure will highlight it and display the following information:
- distance between atoms;
- torsion angle values;
- values of the angles between bonds in the molecule.

This information appears as a line of text at the bottom of the visualization area after you have selected appropriate atoms.

Export MOL File to New Tab:
Search results may be readily exported to the MOL file format.

First, select a conformer and CID (*Props/Refs*) of interest from the table and then click on the **Ok** button.

Then, the MOL file information for that conformer will be displayed in an additional tab of your browser.

After that, in an additional tab of your browser, information will appear in the form of MOL File about the selected conformer.

You can save this file by right-clicking to bring up a pop-up menu and then selecting *Save Page As*.

You have the right to further use the saved data about the conformer for your own purposes, with reference to the source from which those data were received, if you have installed third-party programs that support the MOL file format. **Now we invite you to consider several examples of using the search tool to retrieve molecules and their associated information from the molecular database.**

Example 1:
In this first example, we will search for glucose.

It is known that glucose has four sequentially-located -CH(OH)- groups and no COOH group.

First, let's enter the empirical glucose formula **C6H12O6** in the field *Empirical Formula with Ranges*.

Next, select two functional groups from the *Radicals;Charged Atoms;Isotopes* list: **COOH** and **[C(O)]4** (i.e. four sequential -CH(OH)- groups).

After their selection, buttons with the symbols of these groups will appear in the additional field.

Click on the button with the COOH group so that a red stop symbol appears on it, and then click on the button **Search**.

We will receive a list of about 20 search results, the first of which will be glucose.

Then we select its first conformer, followed by four successive atoms, thereby obtaining the associated torsion angle and all other angles.

Upon moving on to the second conformer, you can see that the angle values change accordingly.

Example 2:
In this second example, we will search for caffeine derivatives whose substituents do not contain carbon or nitrogen.

We know that the caffeine molecule contains five- and six-membered heterogeneous rings.

We also know its formula, **C8H10N4O2**, which first needs to be entered in the field *Empirical Formula with Ranges*.

Then, select from the list *Radicals;Charged Atoms;Isotopes* rings **X 5**, **X 6**, **C5 C6**.

lick on the corresponding buttons with symbols **C5** and **C6** so that both have red stop symbols, and then execute the search with the **Search** button.

In the list of search results, find the caffeine molecule and select the *X Hydrogen* option to ignore hydrogens in the subsequent refining search.

Clicking on the **Refine** button will automatically produce a new button marked **2519H** in the additional field for radicals. The search tool will now use the caffeine skeleton to refine the search without considering hydrogen.

Next, we enter **C8N4** in the *Empirical Formula with Ranges* field to explicitly indicate that there should be no additional carbon or nitrogen in the returned molecules.

Select *Yes* in the *Include Other Elements*.

We then repeat the search with the **Search** button and get a list of currently known caffeine derivatives whose substituents do not contain carbon or nitrogen.

For each molecule in the results, we can select a conformer and look at its structure, rotate it in three-dimensional space, survey the known isotopic variants,s and, if necessary, follow the corresponding link to PubChem for further information.

We can also generalize the search for caffeine derivatives to allow substitutes that may contain carbon. To do this, enter **C8-12N4** in the *Empirical Formula with Ranges* field and repeat the search by clicking on the **Search** button.

Example 3:

In the third example, we will repeat the scenario from **Example 2** but now select both the X Hydrogen option and the *X Bonds* option.

After doing so, click on the **Refine** button. This will automatically create a button under the field *Radicals;Charged Atoms;Isotopes* with the text **2519HB**.

The search tool will now use the caffeine skeleton to refine the search without considering hydrogen and without taking into account types of bonds.

Click on the **Search** button to execute the refinement.

In addition to the results we obtained in the second example, the present results now also include non-aromatic purine bases with a non-planar 5-6-membered structure, such as *1,3,7-trimethyl-4,5,8,9-tetrahydropurine-2,6-quinon*. We thank you for your interest in our molecule search tool and hope that it will be useful for you!

We would like to hear your feedback for improving and supplementing the search functions.

To send us your feedback and suggestions, please use the contact information in the Contacts section of our main website.

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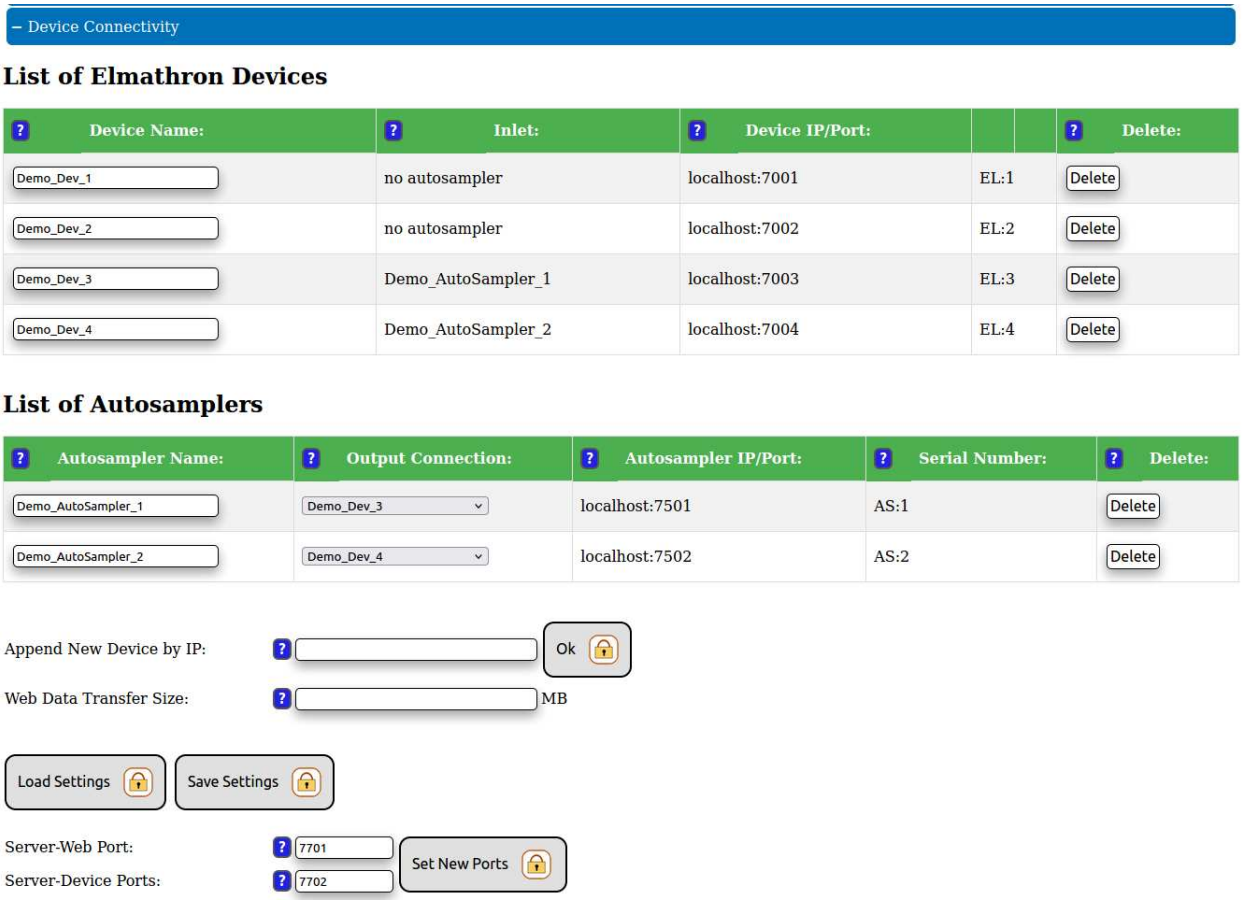
Disclaimer The information used by the *Search for Molecules in the HugeMDB* tool that is included in the *Elegant NMR Software v1.11* is partially based on data from the PubChem database.

Elegant Mathematics LLC does not participate in the creation of the PubChem database and does not guarantee its accuracy and relevance. Elegant Mathematics LLC is not responsible for any errors, omissions or other deficiencies in the content (any information) contained either in the PubChem database or in the Search tool. Also, Elegant Mathematics LLC cannot be held liable for any damage incurred by users of this tool in connection with the use of the aforementioned content or in connection with any other actions of users involving the aforementioned content.

13 Settings



The current information window contains useful recommendations on those operating parameters that must be specified for the Elegant NMR measuring system in the *Settings* screen, especially in cases where the measuring system includes several Elmathron devices and several autosamplers for conducting simultaneous analysis with all data stored in a common database of experimental results for subsequent processing. Prompts are available regarding how to fill each input field and select experiment options. You can easily open these prompts by clicking the associated question symbol. To hide a prompt, click again either on the question symbol or anywhere in the prompt field.

Please read and follow the prompts carefully to make your chemical analysis as accurate as possible!

Attention! If after logging in you do not see the Elmathron device or autosampler you need, or data in the experiment database corresponding to any Elmathron device, then the username under which you logged in is not allowed to operate or use data from this device.

To obtain the rights, a superuser must correct the user account's access rights as listed in the *User Properties→Device Rights* field in *Settings* screen All components of the Elegant NMR system communicate with the computation server via sockets, and each device must receive its own IP Address from your local network.

You can always rearrange, change, delete, or add component devices to the general configuration of the Elegant NMR system. When adding a device, all that you need is the IP address allocated to it by your Ethernet network, which you enter in the special field *Append New Device by IP*.

All devices of the Elegant NMR system have their own serial numbers. When a new IP address is entered in the *Append New Device by IP* field and a system device is successfully found at that address, the server will immediately automatically populate its information in the corresponding table column in the *Settings* screen.

You can also load the settings of your Elegant NMR system's component devices from your server at any time by pressing the button **Load Settings**.

Changes to settings are not recorded until you click the **Save Settings** button.

Device Name:
In this field, you assign a personal name to the Elmathron measuring device.

The experiment database is linked to each Elmathron device by the device's serial number, so any change in this field will also update its name in the database.

Inlet:
By default, each Elmathron device is configured to intake the test mixture in continuous mode.

You can also connect an autosampler to automatically supply the mixture to the Elmathron device.

To connect an autosampler to a device, you must first change the *Output Connection* for the autosampler to the appropriate Elmathron device in the following *List of Autosamplers* table.

This will automatically update the corresponding *Inlet* settings.

Device IP/Port:
Each Elmathron measuring device must have its own IP address for integration into the Elegant NMR system, or an address assigned through the Domain Name Service (DNS).

Each new device's address will be automatically listed in this table upon entering it in the *Append New Device by IP* field.

Serial Number:
Each Elmathron measuring device has its own unique serial number, which cannot be changed by the user.

This number is used to identify measurement results in the computation server.

Delete:
If an Elmathron device is no longer being used, its table row can be deleted.

In this event, the results of measurements conducted on that device will remain in the experiment database.

The device and its settings can be restored for use by entering its IP address of in the *Append New Device by IP* field.

Autosampler Name:
In this field, you assign a personal name to the autosampler.

Any change to the personalized name will update the autosamplers entry in the experiment database.

Output Connection:
This field indicates whether the autosampler is connected to an Elmathron measuring device.

Autosampler IP/Port:
Each autosampler must have its own address to be embedded in the Elegant NMR system.

The connection is enacted using the DHCP protocol, or by assigning a static IP address in the router to which the autosampler is connected.

Each new autosampler's address will be automatically listed in this table upon entering it in the *Append New Device by IP* field.

Serial Number:
Each autosampler has its own unique serial number, which cannot be changed by the user.

This number is used to identify measurement results in the computation server.

Delete:
If an autosampler is no longer being used, its table row can be deleted. In this event, the autosampler can be re-added to the *List of Autosamplers* table by entering its IP address in the *Append New Device by IP* field.

You can add the autosampler to the *List of Autosamplers* table again if you add its IP address in the *Append New Device by IP* field.

Append New Device by IP:
In this field, you can enter the IP address associated with a new Elmathron measuring device or autosampler.

At the time of entry, the devices must be connected to your local network.

If your system administrator has chosen two different IP or domain addresses to support both Ethernet and WiFi connections, please enter both addresses, separated by a space. If

it is customary to use the DHCP protocol in your local system, and your DHCP assigns a device a new number each time it is turned on, it will be more convenient for you to use an alphabetic name that your system administrator assigns the device.

In most cases, this identification is based on the MAC number of the device's network card.

We offer two ways for you to connect devices to your local network: via 1 GBit/s Ethernet and via WiFi. The two methods use different network cards and different names, which can lead to confusion when allocating an IP address on your local subnet.

If the resources of your local subnet allow, you can allocate static IP addresses to devices.

Web Data Transfer Size:
Enter the maximum size of data packets allowed for transmission between the computation server and the web interface.

This value can be determined both by the speed of downloading the results from the server to your web interface, and by the volume of the result data.

If you want to visualize very large amounts of data, this limit needs to be set to a higher value.

If you use a smartphone with only a small amount of internal memory, you will not be able to draw very large data on the screen.

Hence, we recommend entering a packet size that is no more then 1/10 of the total RAM on the device you use to access the web interface.

Server-Web Port:
A dedicated port is used for communication between the web interface and the computing server, with a default value of **7701**.

In this field, you can change that port number.

This action can be performed only if you have the right to do so and there is no padlock next to the **Set New Ports** button.

Be careful: changing to a new port may result in the loss of experimental and calculated data if Elmathron devices, autosamplers, or the server are currently performing any action.

Server-Device Ports:
Dedicated ports are used for communication between the computer server and the Elmathron devices or autosamplers.

In this field, you specify the lower limit of the range of ports.

The available ports above that number must be at least the total number of devices in the system, and the port numbers must be sequential.

This action can be performed only if you have the right to do so and there is no padlock next to the **Set New Ports** button.

Be careful: altering the device port range may result in the loss of experimental and calculated data if Elmathron devices, autosamplers, or the server are currently performing any actions. The Elegant NMR system implements standard multi-user access for resource management.

The following gradation of access rights is implemented:

- *user*: has access only to those resources that are specifically permitted and has no right to influence the access of other users,
- *super user*: in addition to what is allowed for a regular user, can also change the access rights of any other user and register or delete new users.

Logged in as:
You must provide your username to log in.

By default, the name *guest* is used, which login provides access only to demo devices and their database.

Upon starting the server for the first time or after full initialization of the user table, the phrase *new user required* will be written in this field. You should skip entering a username here in that case.

Instead, you need to go to the next section *User Properties*, and complete information for the first user with superuser rights.

After three successive password entry failures, the IP address of your computer will be blocked from entering a password for 15 seconds; after five attempts, for 5 minutes; and after a seventh attempt, for three hours.

Attention! If you are leaving the workplace and there may be a risk of someone having unauthorized access to the system, press the **Exit** button to log out.

In this event, your chosen system settings will remain in the web interface, but no one will be able to use them for measurements.

If you want to reset all experiment settings, the browser **Reload** button will refresh and completely reset the web interface.

After reloading, you will need to enter your username and password again to make further changes.

Closing the web interface window will log you out automatically without saving any settings.

If for some reason the connection with the server is interrupted for more than two minutes, the web interface automatically switches your access level to that of the *guest* user.

Login:
You must provide your username to log in.

You should skip entering here the username if the *new user required* entry appears in the *Logged in as* and *Userprop for Modifications* fields.

Password:
You must provide your password for the username to log in.

You should skip entering here the username if the *new user required* entry appears in the *Logged in as* and *Userprop for Modifications* fields.

After three successive password entry failures, the IP address of your computer will be blocked from entering a password for 15 seconds; after five attempts, for 5 minutes; and after a seventh attempt, for three hours.

Userprop for Modifications:
Here you can specify the name of a user whose access rights you plan to change, or else enter the name of a new user.

After first starting the server or completing initialization of the user table, the phrase *new user required* will appear in this field, upon which you need to enter information concerning the first user with superuser rights.

If you are logged in with superuser rights, then you can select any user and modify associated personal data and access rights.

If you are logged in as a regular user, you can only select your username, and that only when you have the right to change your profile.

The new user option can be selected and a new user created only after entering the superuser login and password at the bottom of this screen.

If you have superuser rights, you can specify a new username, or leave the field empty to delete all information about this user.

Deleting a user does not automatically affect the presence of associated experiments and results in the experiment database. Experiment data can always be deleted separately by a user having superuser rights.

Login:
If you have superuser rights, you can specify a new username, or leave the field empty to delete all information about this user.

Deleting a user does not automatically affect the presence of associated experiments and results in the experiment database. Experiment data can always be deleted separately by a user having superuser rights.

After deleting a user, another user with superuser rights can always delete his experiment data.

Password:
The password must contain at least 8 characters, and must satisfy the following criteria: at least one uppercase letter, at least one lowercase letter, and at least one number or punctuation symbol.

Repeat Password:
You must repeat your password for the username to log in.

Name:
You can provide your name, or leave this field blank.

Surname:
You can provide your surname, or leave this field blank.

Group:
You can provide your working group's name, or leave this field blank.

Lab:
You can provide your laboratory's name, or leave this field blank.

Department:
You can provide your faculty's name, or leave this field blank.

Sudo Allowed:
Selecting this checkbox gives a user permission to modify the personal data and access rights of any user.

That is, by selecting this checkbox, you create a superuser.

If you, being a superuser, uncheck this box for yourself, then you will become a regular user.

If, at that moment, there is only one superuser in your system, the system will ask if you really want to proceed so that your system cannot accidentally end up with no superuser.

Modifications Allowed:
Selecting this checkbox gives a user the right to modify personal data.

Reboot Allowed:
Selecting this checkbox gives a user the right to restart the server.

Shut Down Allowed:
Selecting this checkbox gives a user the right to shutdown the server.

Upgrades Allowed:

Selecting this checkbox gives a user the right to install software updates.

Number of Running Computations:
Here you can limit the number of computational calculations that this user can have running simultaneously.

Number of Stored Computations:
Here you can limit the number of computational calculations that this user can hold on the server.

Device Rights:
Here you select an Elmathron device or autosampler by serial number or name, specify the date and time interval over which the access rights will be in force, and specify access rights to the device and the measurements performed.

You can specify dates both in the past and in the future. Dates in the past are needed for accessing stored data, while dates in the future are needed to access the devices and make new measurements.

At the end of the access rights line, you can specify who, other than you and any superuser, will have access to the measurements:

- *None*: just you and superusers
- *Other*: all users except guest
- *All*: all users, including guest

SUDO Login:
Here you re-enter the username under which you logged in.

This additional security is necessary to prevent a third party from changing your settings in an open browser window.

After specifying the *SUDO Login/Password*, the system will continue to operate under the previous settings for another three minutes.

This is convenient if you immediately notice an error and need to fix it, or if you decide to create or modify several users.

This additional entry of credentials does not extend to normal login/password operations, but is only utilized to increase security when creating new and modifying existing users.

SUDO Password:
Here you re-enter the user password corresponding to the username in *SUDO Login*.

After specifying the *SUDO Login/Password*, the system will continue to operate under the previous settings for another three minutes.

Reset & Maintenance

If you have permission to shut down and restart the server or update the software, you can invoke these commands in the *Reset & Maintenance* section.

Full Reset Key:
This key is necessary if you have completely lost user information and can no longer log in as a superuser.

You can find this key on the last page of the technical documentation, after the *RESET* label, or you can request it directly from the manufacturer.

After entering the key and clicking on the button **Restore Factory Settings and Reset Passwords**, the entire user table will be deleted.

Then you can log in and create a new first user with superuser rights, and thereafter continue working.

In re-initializing the user table, all data on experiments will be saved, but all records of user names, passwords, and access rights will be completely deleted.

14 Device and Server Status

In the *Status of All Devices and Server* screen, you can view the current status of the Elegant NMR measuring system and, if necessary, stop the execution of any experiment on a chosen device.

This screen also presents important information on:
- the current configuration of the measuring system;
- which devices are functioning and how successfully;
- what experiments are presently being carried out on the measuring devices.

Attention! Violations of the equipment operation rules may cause technical malfunctions to arise in the operation of the Elegant NMR measuring system.

For example, the following emergency situations may occur:
- The pressure at the inlet of your vacuum line rises above the permissible value denoted on the technical data sheet.
- A strong magnetic field source or ferromagnet comes into the immediate vicinity of the Elmathron device.
- Strong acid, magnetic fluid, fluid with particles, glue, fast polymerizing substances enters the inlet of the Elmathron measuring device.

In such situations, the main icon of the **Devices and Server Sratus** screen  will change its color to red: 

15 FAQ

Q: What is the magnetic strength in Tesla?

A: We use very weak magnets, only 1 T, because DNP in liquids only works well with magnetic fields less than 1 T. In turn, DNP improves the signal-to-noise ratio for one-dimensional spectra by about 400 times, and almost 100,000 times for multidimensional spectra. Therefore, the sensitivity of 1D is approximately as if we were capturing spectra at 100 MHz, and the sensitivity of 2D+ is approximately as if we were capturing spectra at 400 MHz.

Q: Can I get 1D spectra from Elegant NMR system?

A: The ability of the Elegant NMR measuring system to automatically interpret heteronuclear DNP NMR spectra on an adaptive grid completely disrupts the status quo in which 7- and 8-dimensional DNP NMR spectra, having sparsity values less than 0.1%, are very difficult not only to interpret, but even to visualize.

In the Elegant NMR system, such spectra are identified with reference to a huge database containing about 1.7 billion spatial molecular structures.

7-8-dimensional spectra can be projected onto one-dimensional slices and then visualized. We will implement this approach in the expert mode of the Elegant NMR software for reference purposes.

Q: Do we need to use external MW source for DNP?

A: No, Elegant NMR System is equipped with internal DNP source according to recently patented technology US 10773092 B2.

Q: Do you have HPLC/GCMS inside, or how you separate unknown mixtures?

A: We do not separate molecules, we separate signals. In classical HPLC, for separation to occur, we need the substances to be separated to form complexes with a stationary phase and the energy of formation of such complexes is significantly different. It is often possible to find a stationary phase that would orientate the substances to be separated well, but would not separate these mixtures well enough, for instance, because of the insufficient number of theoretical plates. In our apparatus we do not separate substances, namely, we orient them differently. This orientation affects the two-dimensional NMR spectra and it is possible, without separation, to obtain slightly different HSQC or NOE spectra, and on the basis of their correlations, to get relative concentration and pure spectra of the substances themselves.

The patent pending technology US 16/695,200 is fully implemented inside Elegant NMR system.