Z-Dis MUX

Multi-Channel Dissolution Monitor

Software Specification & Manual

(Revision 0.9)

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Contents

1. Hardware and software system specification

The Z-Dis MUX Dissolution Monitor Software will be designed and compiled using exclusively National Instruments™ LabView™ development system (current release 4.01). The software is to be programmed under and designed for MS Windows NT 4.0. The software will not be portable (without recompilation) to other operating systems.

Being a Win NT 4.0 application, the Z-Dis MUX Dissolution Monitor Software will require the following minimum hardware and software environment:

- IBM compatible Pentium™ (150 MHz or better recommended) with at least 32 MB RAM (64 MB recommended)
- 2 serial interfaces plus (!) mouse port
- about 50 MB of free capacity on an NTFS formatted (to enable file security features of NT) harddisk (100 MB+ recommended)
- SVGA graphics card
- Mouse

- MS Windows NT™ 4.0 (logged on to a NT network)
- NT graphics mode set to 1024 x 768 x 256 colors, small fonts (!)
- A suitable printer (Laserjet type) and a suitable storage device (harddisk) must be logged on to the network for remote protocol printout and data storage. The machine running Z-Dis MUX must have access to the network printer and storage device.

    Maximum raw data storage (every measured spectrum, parameters, results) for a 20-point run will typically require about 500-700kByte. This could sum up to a typical monthly total (2-6 runs /day, 7 days / week) of approximately 30-50 Mbyte. Thus a standard 1-2 Gbyte harddisk will be sufficient for at least a 1-2 years of data storage.

- No Eco-PC (Power savings etc.) settings installed or activated (*)

    *Because **Z-DIS MUX** is designed for long duration runs it is strongly recommended to uninstall or disable, respectively, any Eco-PC settings of your PC (the likes of e.g. processor shut-down if no input is made by mouse or keyboard etc.)*

- The MCS spectrometer, the VanKel Dissolution Bath and the DiCon GP700 multiplexer must be properly connected to their respective interface ports of the PC

2.   Installation and File Structure

2.1   Installation

In order to enable the PC to communicate with the MCS spectrometer unit via the plug-in PC card the device driver for the spectrometer (kernel mode driver) must be properly installed on the system. The **MCS 500 kernel mode driver** is delivered on a separate disk together with the complete system.

The **Z-Dis MUX software** will be delivered on 3.5" disks complete with a standard installation routine. To start the installation:

- insert disk 1 into the floppy drive of your PC
- run ZDISMXnn.EXE to install the software (nn.. release number)

The software will now be installed, the required directories etc. will be automatically created.

If an older release of the software is already installed on your system the old INI file settings will be read and reused in the new installation. A registry group will be created holding the required icons.

2.2   Directories, Files and Access rights

The **installation** must be carried out having **Administrator access rights** in NT. The software can be installed into any directory. This directory will contain subdirectories for parameter files, local data files and routine check (validation) protocols.

The access to these files (and also to the applications INI file) can be limited using the log-in security features of NT/Z-DIS MUX (see below).

In order to employ the log-in routine of NT as the primary user determination and to make use of the built-in security mechanisms of NT ZEISS suggests to have the Z-Dis MUX software installed and maintained by an (Administrator level) IT person and operated by the (User level)

lab personnel. The rights to delete or even modify acquired raw data and to manipulate vital Z-Dis system data will be restricted to Administrator level.

In any case the PC running Z-Dis MUX must have access to the network printer and data storage, if required.

2.3 Data files

The measured spectra will be stored in the ZEISS native ASPECT plus data file format

For a description of the ZEISS ASPECT plus data file format see Supplement D..

All results of a run

for every sample point:

- Time, sample and standard reading,
- % Diss of vessels 1-6,
- Min Diss Result
- Max Diss Result
- Mean Diss Result
- Temperature (°C) , flag according USP (specified temperature +/- 0.5°C)
- Stirring rate (rpm) , flag according USP (specified rpm +/- 4%)

together with additional information (including an optional text descriptor field)

• Batch No.	• Raw File Names
• Product	• Stability Y/N
• Compound	• Stabiltiy Conditions
• Strength	• Time Points
• Media	• Condition
• Media Volume	• performed by
• Basket/Paddle	• Analyst
• Method Name	• Approved by

will be stored in form of a result ASCII file which can be used and edited e.g. in MS Excel™. In addition a printed protocol (according to) can be generated on any active system printer.The required additional information (that is not part of the applied method file but describes the individual run) will be prompted for (dialog box) at the beginning of a run.
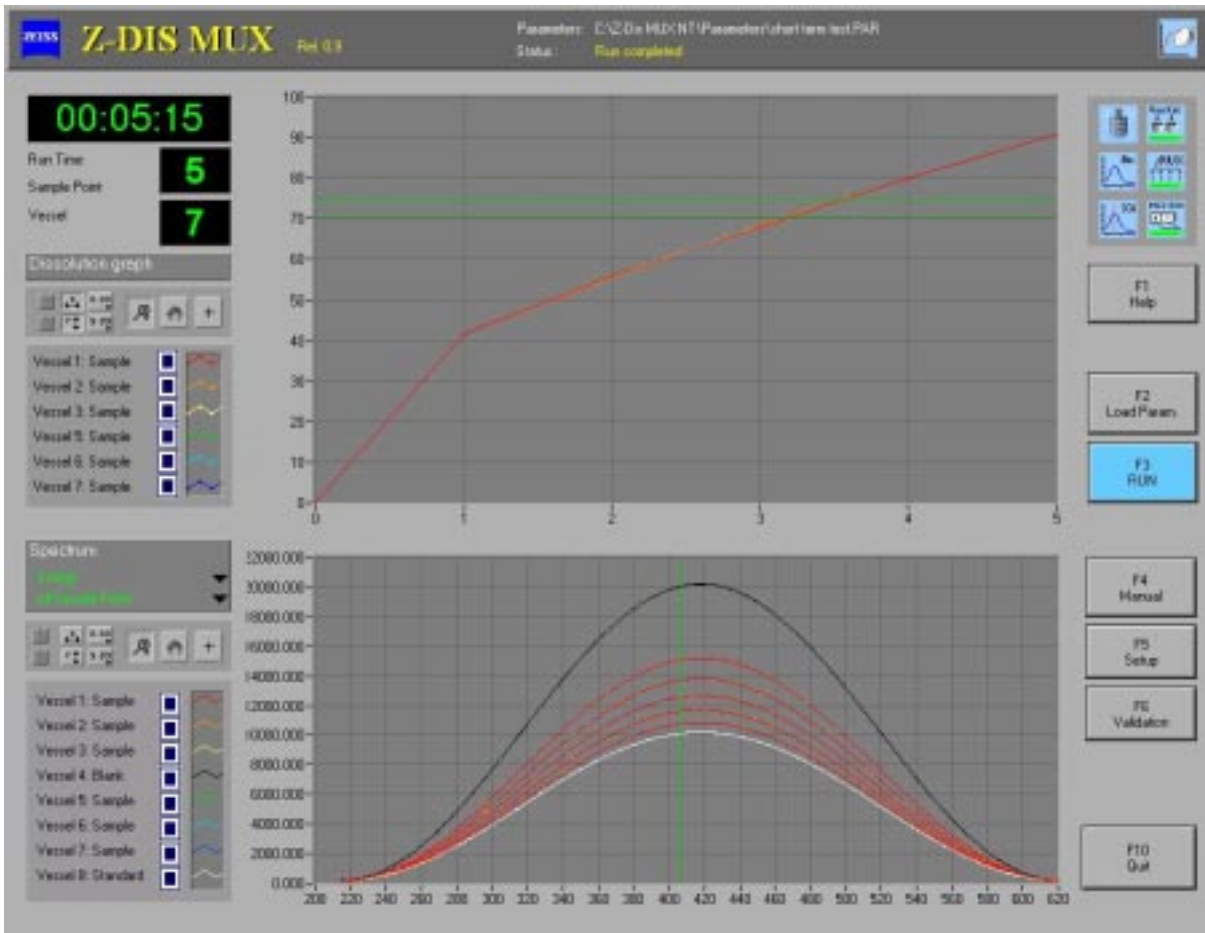
3.   General system design

The following diagram shows the arrangement of components in the complete Z-DIS MUX system.

MCS 500

GP 700 MUX

Dissolution Testing
Station VK 7000

Heater/Circulator VK 750
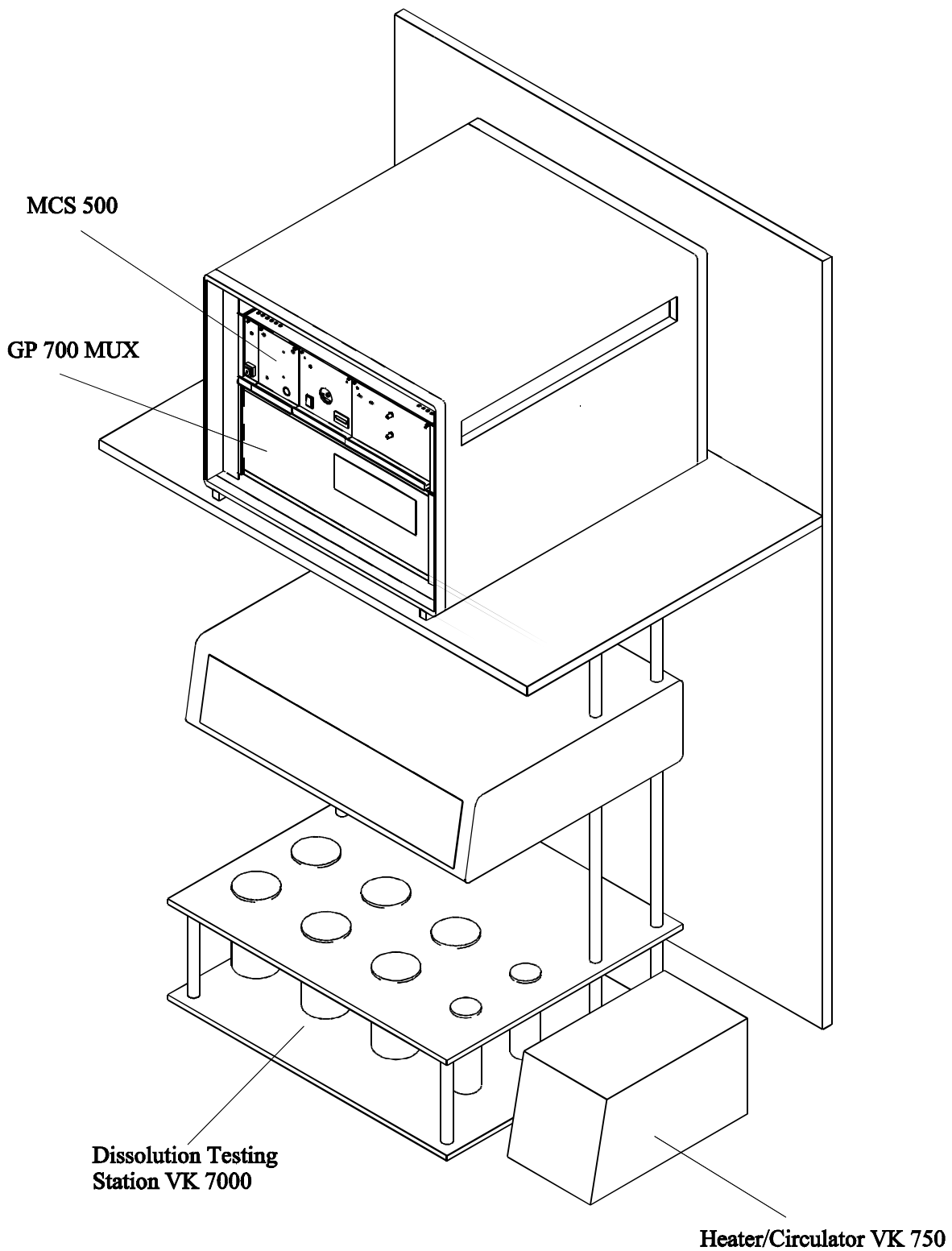
4. Automatic Dissolution Testing

4.1 The Main Screen

This screen displays the essential data during the dissolution run.

On the right side (top) the status of the devices and essential method selections are indicated. The buttons on the right side open up secondary screens like On-line help, Manual Mode, Technical Set-up and Device Check & Validation.

The controls of this screen (submenu buttons, graph selectors) will be individually enabled or disabled according to the access level of the currently logged-in operator. (See 4.1 access rights)

The filename and path of the current parameter file are displayed in the Headline Bar of this window. Two graphs (dissolution curves and spectra display) represent the measured data.

For a description of the graph manipulation handles (left of the graphs) see Supplement C.

Short description of main screen controls and indicators:

Dissolution Graph   displays the dissolution curves for any single or all of the dissolution vessels. The vessels to be displayed can be specified in the checkbox array left of the dissolution graph.

Spectra   displays the spectra for any single or all of the dissolution vessels. The vessels to be displayed can be specified in the checkbox array left of the dissolution graph (to avoid overloading the graph maybe this should be restricted to radio button type, i.e. spectra of one vessel at a time)

Energy/Absorbance/2nd Deriv: This switch can be used to toggle between the display of the raw energy spectra, the background corrected absorbance spectra and their second derivs.
Single / All sample points: This switch can be used to toggle between the display of the last measured spectrum of a vessel and an overlay of the spectra of all measuring points, i.e. the concentration series

Time   shows the current duration of the dissolution run [hh:mm:ss]. This counter is started at the first sample reading of the run

Sample Point   indicates the current sample point
F1 Run / Stop   After a confirmation prompt the dissolution run will be started, F2-F5 buttons will be disabled. Pressing this button again will stop the dissolution run. (All data produced by then will be stored)

F2 Load Paras   Load a method file (parameters) produced in Manual Mode
F3 Manual Mode   Manual Measurement and Parameter Set-up
F4 Setup   Technical set-up (COM Port settings, Passwords etc.)
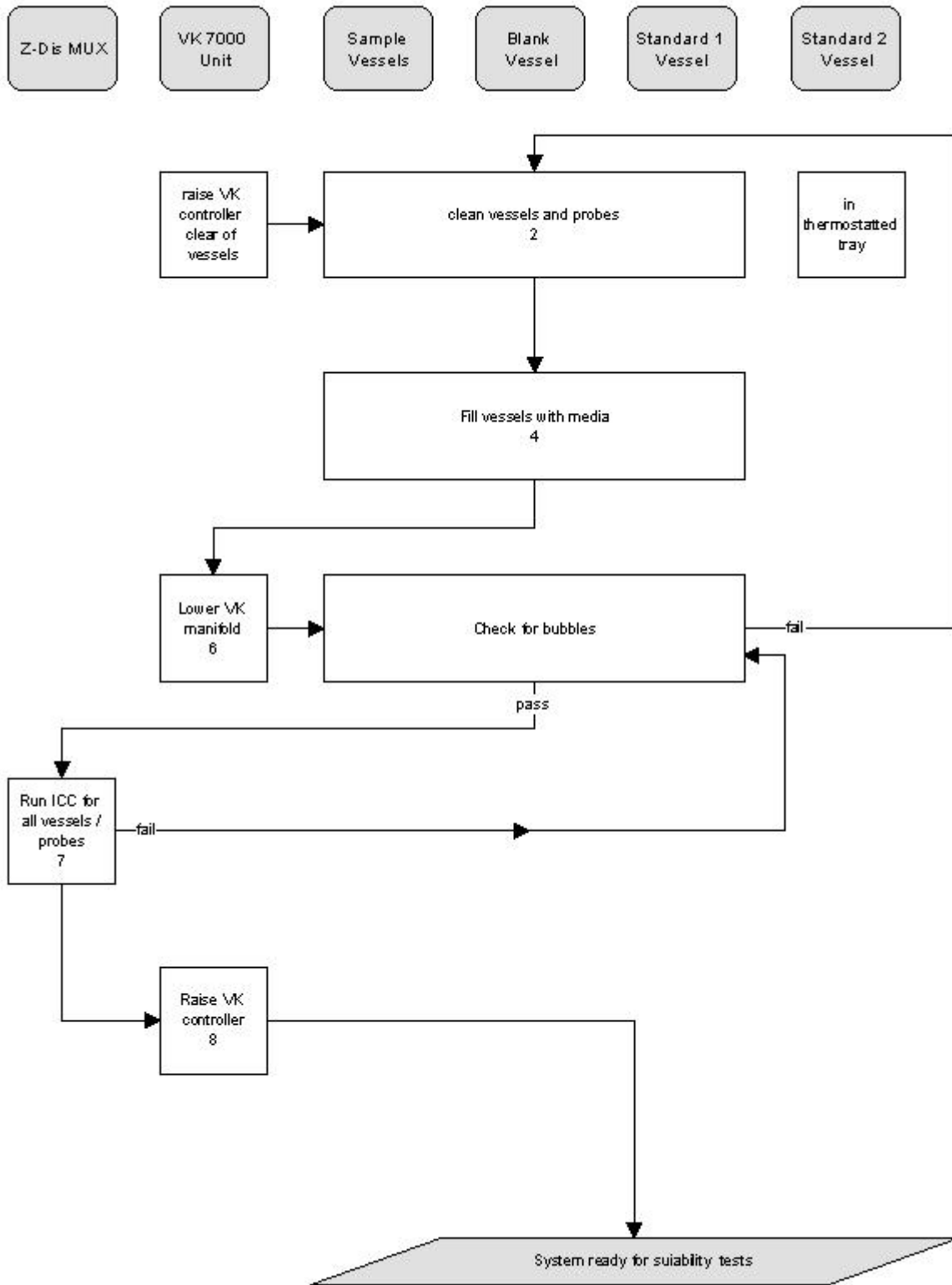**F5 Validation**   Collection of routine checks to confirm functionality of : Multiplexer, Bath, Spectrometer, Data Evaluation Module (and maybe Probes). Validation reports will be generated, printed and stored.
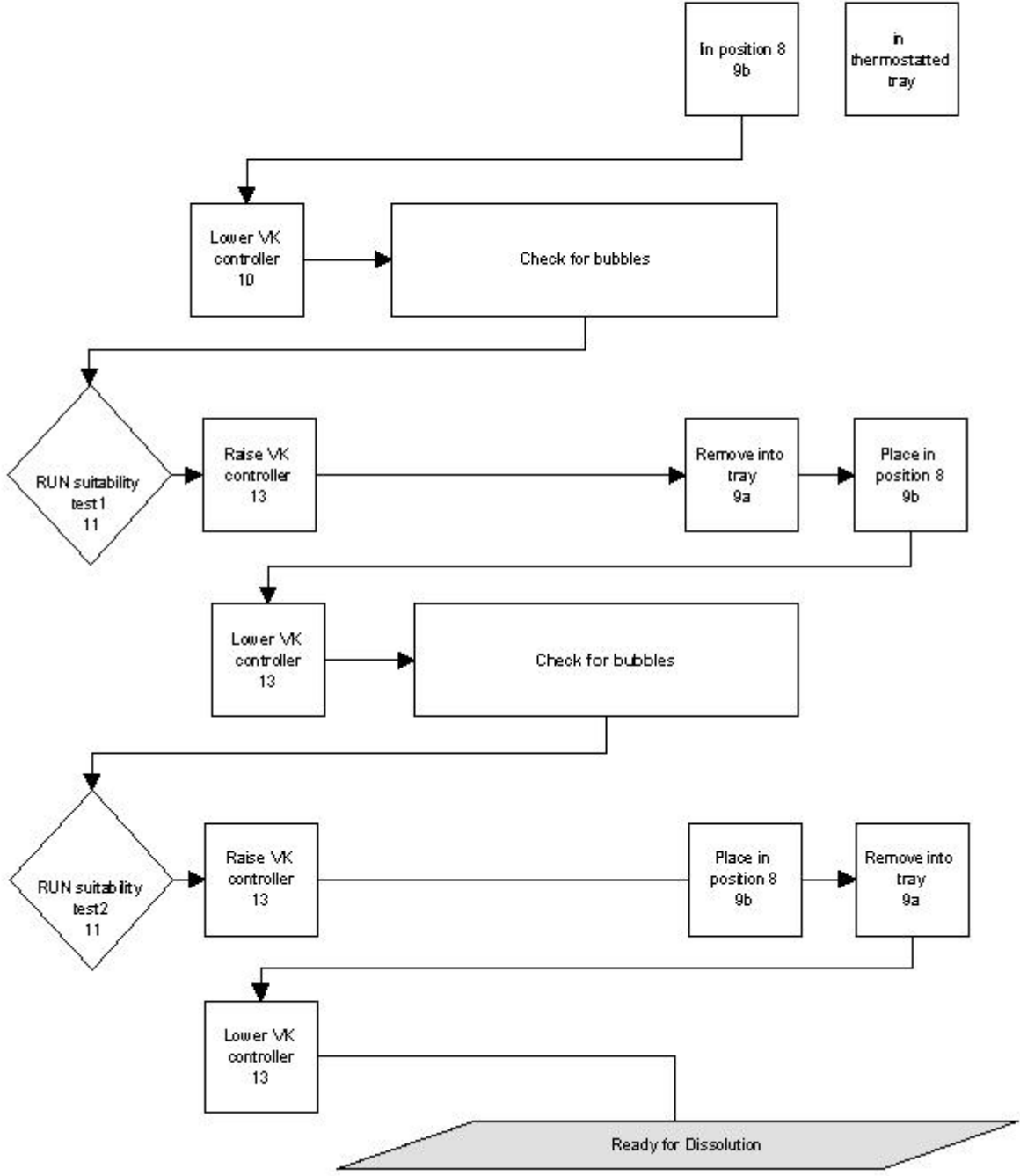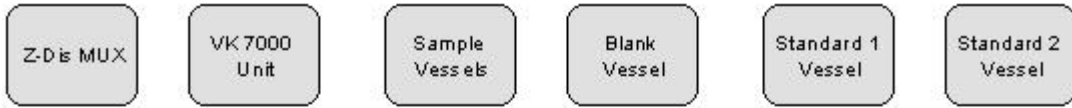
F10 Quit   After a confirmation prompt the Z-Dis MUX software will be ended.
All displays are continuously updated while the dissolution run is performed.

4.2   The Dissolution Run

The Automatic Dissolution run (F1 Run) follows a defined routine which is described in the
following table.

Step	Dialog Box	Description
1		Initialisation of MUX (COM, Time), Spectrometer (Port, Integration time, averaging) and Bath (COM).
2	Run Info Dialog Box	The program prompts for additional information describing the run.
3...8	Insert Tablet / Basket Nr. [1..6][OK]	In a specified interval (currently depending on the MUX settling time) the operator is prompted to insert tablets / baskets. The time of confirmation is recorded as the zero time point for the run of the corresponding vessel.
9..n		For every sample point:at SP – 20 seconds blank and standard measurement is repeated.Then read 6 sample spectra and the current temperature and rpm data from the bath. The concentration (%Diss) is determined from the current blank/standard calibration and displayed in the dissolution graph
n+1	Run completed[OK]	Store all acquired data, (local or remote), print protocol, indicate the completion of the run. The whole sequence can now be repeated with the next method.

```
┌──────────┐  ┌──────────┐  ┌──────────┐  ┌──────────┐  ┌──────────┐  ┌──────────┐
│ Z-Dis MUX│  │ VK 7000  │  │ Sample   │  │ Blank    │  │Standard 1│  │Standard 2│
│          │  │ Unit     │  │ Vessels  │  │ Vessel   │  │ Vessel   │  │ Vessel   │
└──────────┘  └──────────┘  └──────────┘  └──────────┘  └──────────┘  └──────────┘
```

┌──────────────┐   ┌─────────────────────────────────┐   ┌──────────────┐
│ raise VK   │───▶│ clean vessels and probes   │   │ in   │
│ controller   │   │ 2   │   │ thermostatted│
│ clear of   │   │   │   │ tray   │
│ vessels   │   └─────────────────────────────────┘   └──────────────┘
└──────────────┘

┌─────────────────────────────────┐
│ Fill vessels with media   │
│ 4   │
└─────────────────────────────────┘

┌──────────────┐   ┌─────────────────────────────────┐
│ Lower VK   │───▶│ Check for bubbles   │──── fail
│ manifold   │   │   │
│ 6   │   └─────────────────────────────────┘
└──────────────┘   pass

┌──────────────┐
│ Run ICC for │
│ all vessels /│──── fail
│ probes   │
│ 7   │
└──────────────┘

┌──────────────┐
│ Raise VK   │
│ controller   │
│ 8   │
└──────────────┘

System ready for suiability tests

```
┌──────────┐  ┌──────────┐  ┌──────────┐  ┌──────────┐  ┌──────────┐  ┌──────────┐
│ Z-Dis MUX│  │ VK 7000  │  │  Sample  │  │  Blank   │  │Standard 1│  │Standard 2│
│          │  │  Unit    │  │ Vessels  │  │  Vessel  │  │  Vessel  │  │  Vessel  │
└──────────┘  └──────────┘  └──────────┘  └──────────┘  └──────────┘  └──────────┘
```

In position 8
9b

in thermostatted tray

Lower VK controller
10

Check for bubbles

RUN suitability test1
11

Raise VK controller
13

Remove into tray
9a

Place in position 8
9b

Lower VK controller
13

Check for bubbles

RUN suitability test2
11

Raise VK controller
13

Place in position 8
9b

Remove into tray
9a

Lower VK controller
13

Ready for Dissolution

Z-Dis MUX

VK 7000 Unit

Sample Vessels

Blank Vessel

Standard 1 Vessel

Standard 2 Vessel

Start run
14

Method = Baskets ?

no → Drop Tablets into vessels
15

yes

Add baskets
16

Run all sample points
17

Store results, create report & printout
19

Ready for Next cycle

4.3 The Run Info Dialog

This section will be completed, when the assignment of all parameters to either method or individual run is clarified. (J.M.)

4.4   Inter-Channel Calibration

The immersion probes have different transmission curves. In order to compensate for these transmission differences energy measurements are taken from all channels and are used to calibrate the raw energy measurements in the channels.

The smallest automatically adjusted integration time is determined from all channels.

$$E_{1...8}(\lambda)$$

Bubble detection: *If the determined integration time is too high or if it takes the system too long to determine the integration time a bubble is assumed to be in the respective probe. A warning message is issued and you may repeat the ICC after you have cleared the respective channel. If the determined ICC factor exceeds a given value (as specified in the Run Info dialog) the same assumption is made by the program.*

Using the determined common integration time (in order to avoid saturation in any of the channels) energy measurements are taken from all channels at the same measuring conditions.

The channel N that yields the highest output value (counts) is selected as reference for the other channels. The ratio ("ICC factor", which in fact is a function of the wavelength, not a factor as such) is computed for every channels as

$$ICC_{1...8}(\lambda) = \frac{E_N(\lambda)}{E_{1...8}(\lambda)}$$

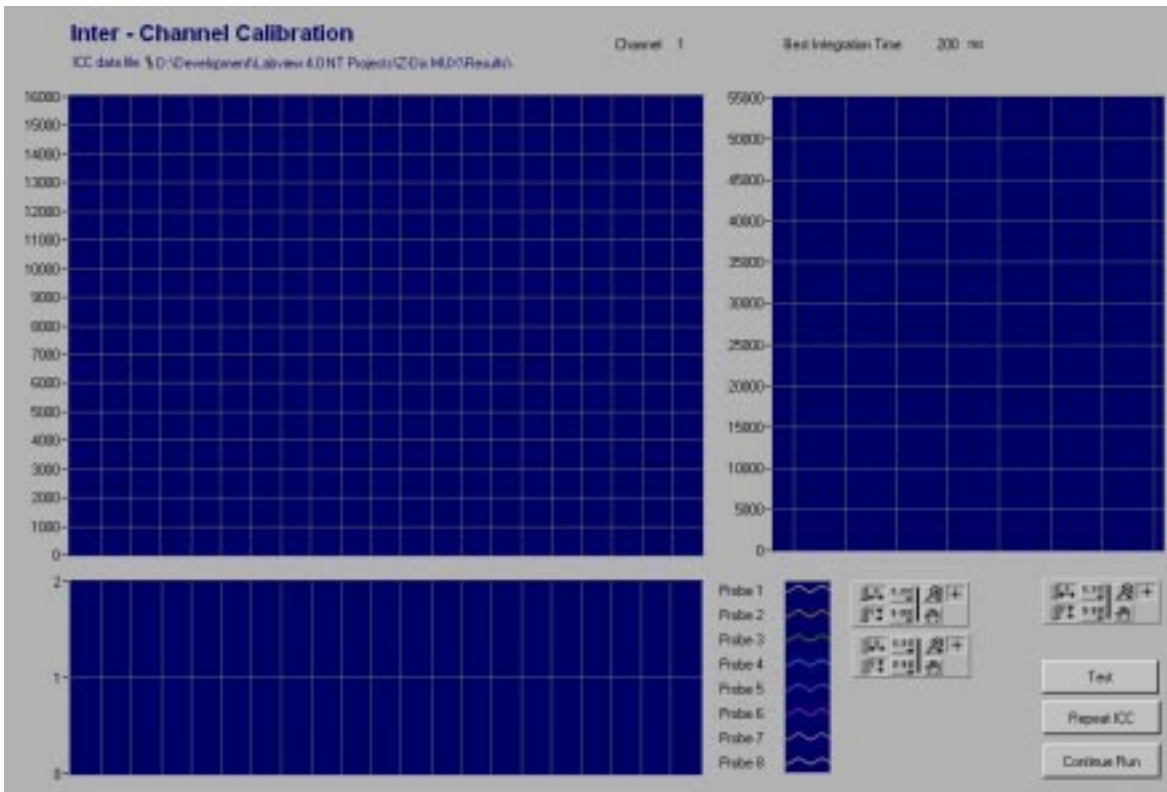Of course $ICC_N = 1$ for all λ.
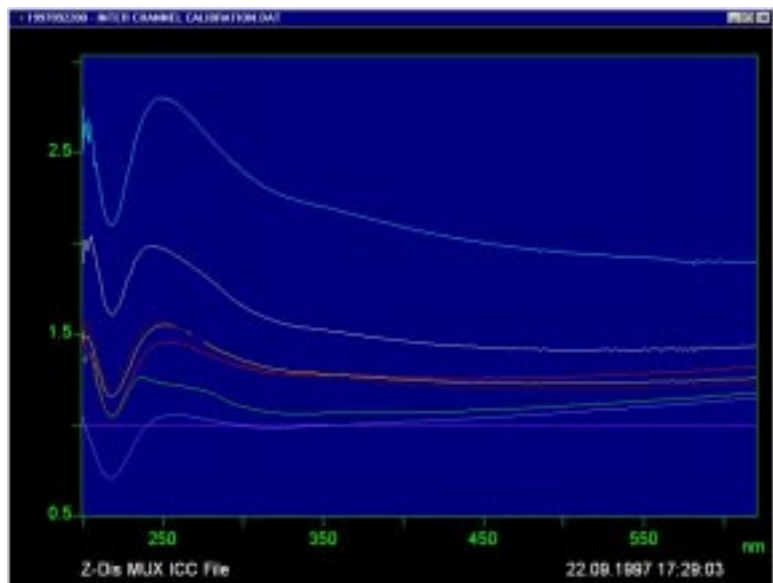
Example set of ICC curves:

These ICC curves are multiplied to every new energy measurement

$$E_{1..8}^{used}(\lambda) = ICC_{1...8}(\lambda) \cdot E_{1...8}^{measured}(\lambda)$$

in order to compensate for the transmission differences. So, being normalised to one energy level, the energy spectra are now used to compute the absorbance spectra from sample and reference channel etc.

Spectrum graph	The upper left graph displays the energy spectra that are taken from the 8 channels
ICC graph	Below this the computed ICC factor curves will be displayed.
Test	After the ICC is completed you can run a test measurent on all 8 channels to see the accuracy of the ICC correction.
Test spectrum graph	The corrected spectra will be displayed in the right side graph. The spectra should now be sufficiently congruent.
Repeat ICC	If required (bubbles), the ICC can be repeated.
Continue Run	Confirm ICC and continue

4.5   *System Suitability Test*

The System Suitability test is performed before the run.

The user is prompted to fill Vessel 8 with Standard 1. Then a blank and Standard reading is taken.

Now the user is prompted to fill Vessel 8 with Standard 2. A Standard reading is taken, the ratio of both standard readings is computed and the difference of the ratio and 100% is compared to the Maximum allowed difference as specified in the Run Info dialog. The SST is flagged accordingly.

A series of 6 readings is now taken from vessel 8. The %RSD is computed and compared to the Maximum allowed %RSD as specified in the Run Info dialog. The SST is flagged accordingly.

For the calculations used in SST see chapter 4.5.

The results of the SST are stored in the Dissolution Result file (4.5) and added to the Dissolution report (4.6). The measured standard spectra (energy raw data) are stored in spectra files and can be viewed etc. with the Aspect+ software.

The results of the system suitability test are displayed in a message box. Upon confirmation the dissolution run continues.

4.6 Calculations used in Dissolution run

Spectra are measured in counts (diode), representing the energy input **I(λ_i)** onto the diode array.

The wavelengths λ_i represented by the diodes are computed during the initialisation of the device from non-linear coefficients. These coefficients are provided by the manufacturer and stored in the MCS spectrometer's internal EEPROM in the course of calibration and system integration of the device. Because of the spherical characteristics of the spectral imaging these λ_i are non-equidistant values, they differ slightly from an exact equidistant series of wavelength values. In the course of the computation of absorbance spectra and values derived from them (concentrations etc.) the λ_i are recomputed to an array of equidistant λ_i values.

Blank & Background Spectrum

$$E^{Blank,Bckgr}(\lambda_i) = I^{Current}(\lambda_i) - I^{Dark}(\lambda_i)$$

Standard & Sample Spectrum :

$$E^{Std,Sample}(\lambda_i) = I^{Current}(\lambda_i) - I^{Dark}(\lambda_i)$$

Absorbance Spectrum :

$$Abs^{Standard,Backgrnd}(\lambda_i) = -\log\left(\frac{E^{Standard,Backgrnd}(\lambda_i)}{E^{Blank}(\lambda_i)}\right)$$

$$Abs^{Sample}(\lambda_i) = -\log\left(\frac{E^{Sample}(\lambda_i)}{E^{Background}(\lambda_i)}\right)$$

$$Abs^{Std,Sample}(\overline{\lambda}_i) = linInterpolation(Abs(\lambda_i))$$

2nd Deriv of Absorbance:

$$Der^{Std,Sample}(\overline{\lambda}_i) = SGderiv(SGsmooth(Abs^{Std,Sample}))$$

SGsmooth   numerical smoothing operation according to Savitzky-Golay (see Appendix of Z-Dis Software Manual)

SGderiv   numerical 2nd derivative operation according to Savitzky-Golay (see Appendix of Z-Dis Software Manual)

Standard & Sample Reading

$$Rd^{Std,Sample} = Abs^{Std,Samplet}(\lambda_{evaluation})$$

resp.

$$Der^{Std,Sample} = Abs^{Std,Samplet}(\lambda_{evaluation})$$

The spectral value at the fractional index of $\lambda_{evaluation}$ is computed by linear interpolation.

Standard Response:

$$\operatorname{Re} s^{Std1,2} = \frac{Rd^{Std1,2}}{Conc^{Std1,2}}$$

resp.

$$\operatorname{Re} s^{Std1,2} = \frac{Der^{Std1,2}}{Conc^{Std1,2}}$$

Std Ratio 2 & Ratio 1

$$Ratio = \frac{\operatorname{Re} s^{Std1}}{\operatorname{Re} s_1^{Std2}} \times 100$$

Pass/fail

$$Ratio \to \overset{?}{<>} 100 \pm NomRatio$$

%RSD Std2

$$\% RSD = \frac{\sigma\left(Rd_{2,\ldots,7}^{Std2}\right)}{\mu\left(Rd_{2,\ldots,7}^{Std2}\right)} \times 100$$

with

$$\sigma(x) = \sqrt{\frac{1}{n-1}\sum_{i=0}^{n-1}(x_i - \mu(x))^2}$$

and

$$\mu(x) = \frac{1}{n}\sqrt{\sum_{i=0}^{n-1} x_i}$$

%Dissolution

$$\% Diss^{Sample} = \frac{Rd^{Sample}}{\operatorname{Re} s^{Std1}} \times \frac{Volume}{Dosage} \times 100$$

4.7   Dissolution Run Result & Data Files

Excerpt from example data log file:

```
....... Raw data stored in : M:\ARCHIVE\ZDIS_MUX\DATA96\S0105V00.R01 etc ;
M:\ARCHIVE\ZDIS_MUX \DATA96\B0105BCK.R01 ;
M:\ARCHIVE\ZDIS_MUX \DATA96\R0105STD.R01


Standard Concentration = 1,20000 mg/ml
Nominal Volume = 500 ml
Formulation = 500
Calibration Wavelength = 400,00 nm

Background Absorbencies

....

Corrected Sample OD

....

RESULTS

....
```

The results of a run will be stored in plain ASCII files. These files can be re-printed, viewed, or imported into Excel, Word etc. any time.

4.8   Dissolution Run Report

Each Method will produce a separate report. In any case an ASCII data file is created, if Auto-Print is enabled in the Technical Setup menu, the report will be printed after the run on the currently selected system printer. The printer must be pre-selected before the use of the system.

The **page header** includes :
- Method, ARD reference number, Operator, Date & Time of the run
- Location and name of all data files
  (standard, blank & sample spectra, ICC data, SST spectra)
- Location and name of parameter files

The **footer** includes:
- Version, page n of m

The **report data** include:
- Standard concentrations
- System suitability responses, RSD of System suitability
- Standard responses, response of last standard, ratio of standards
- Table of dissolution results, for every sample point:
    time, Mean, Min, Max, bath temperature, rpm & USP flag
    for every sample vessel:
        result, rpm, vessel temperature & USP flag
- Individual vessel plots (like in the robotic software) including Q, Q+5, Q_{time} marker
- Mean Min Max plot (like in the robotic software) including Q, Q+5, Q_{time} marker
- Additional information to describe the run (see 2.3)

The layout of the report sheets will be designed as close as possible to the reports produced by the Zeiss / Zymark Robotic Dissolution System.

5. Manual Operation of the System

5.1 The Manual Screen
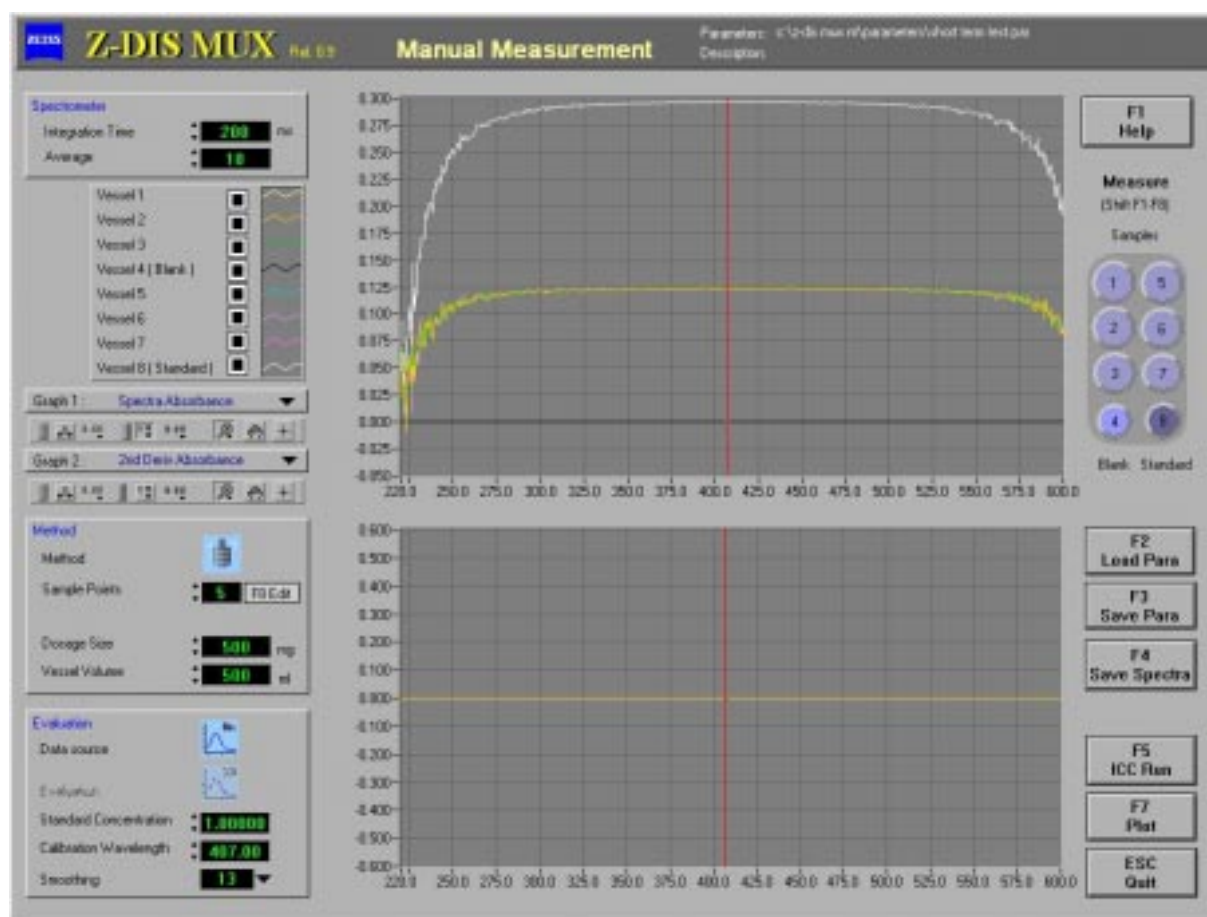
The Manual Module is used to create and evaluate parameter files for the automated dissolution runs. It allows you to observe the complete spectra and their 2nd derivatives in order to find the best calibration wavelength, integration time and other settings for the special analytical problem.

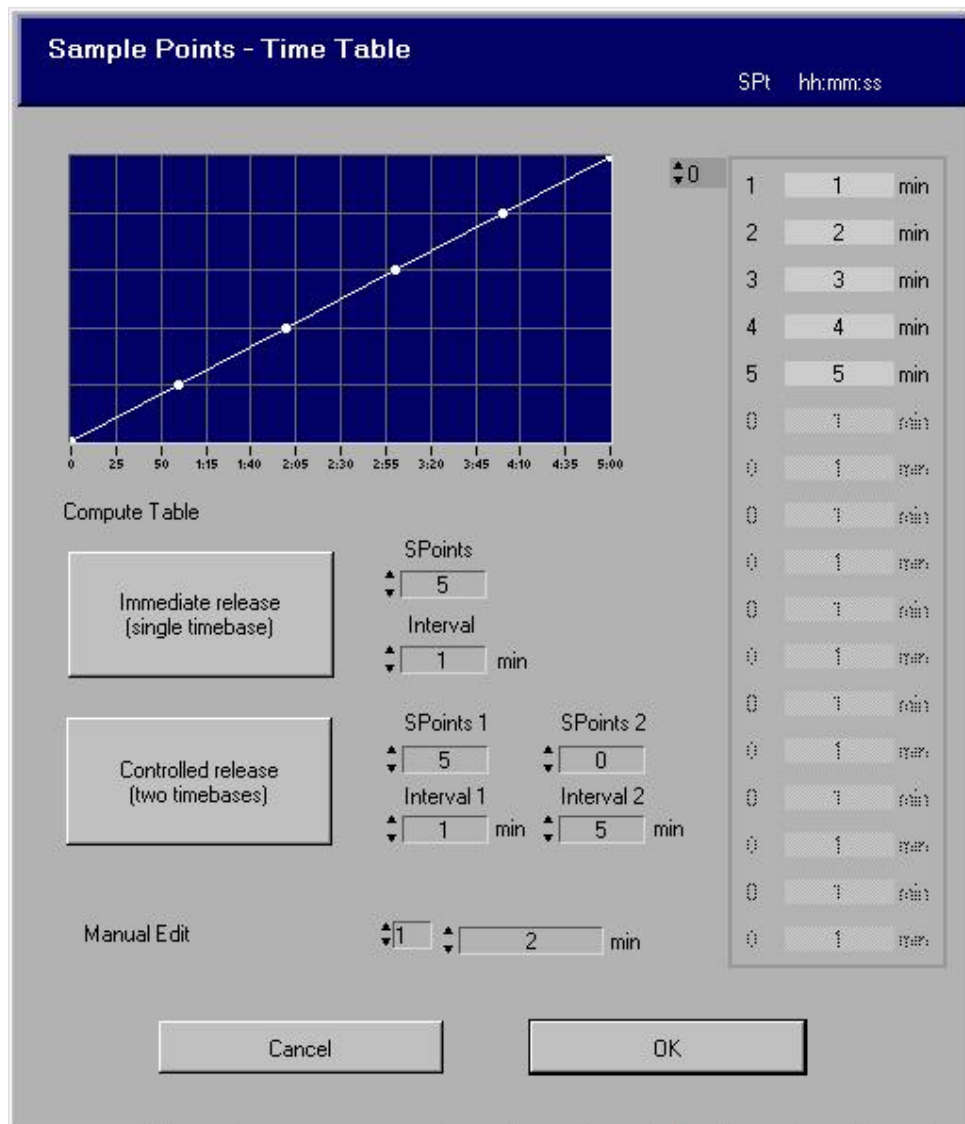The filename and path of the current parameter file are displayed in the Headline Bar of this window.

For a description of the graph manipulation handles (upper right of the graphs) see Supplement C.

Short description of Manual screen controls and indicators

Integration time	Integration time of the MCS 500 diode array spectrometer.
Average	Number of spectra to be averaged by the spectrometer in each measurement.
Method	Icon switch paddles / baskets
Sample Points	Number of sample points (measurements)
	Edit : Calls a dialog box, that allows the operator to define the sample points. The sample point table (Nr, Time) can be filled automatically (Immediate release, Controlled release) with predefined segments corresponding to a total time and the number of sample points, or, respectively, can be edited manually.
Standard Conc.	Specifies the concentration of the standard that will be measured (F5 Standard) and that will be used for the automatic run. The value is required to compute the concentration of a sample measurement.
Dosage Size	Specifies the dosage size that is required to compute the concentration (%Diss) of a sample measurement.
Vessel Volume	Specifies the vessel volume that is required to compute the concentration (%Diss) of a sample measurement.
Data Source	Icon switch to toggle between usage of Absorbance spectra or 2nd deriv of Abs.
Calibration wavelength	Specifies the wavelength at which to compute the calibration curve. The current calibration wavelength is indicated by a red line cursor in the graphs.
Smoothing	Determines the number of measuring points included in the smoothing algorithm for the computation of the 2nd derivative.
F1 Help	On-line help
F2 Load Para	Load a method (parameter set)
F3 Save Para	Save a method (parameter set). File dialog box will be displayed in any case (thus works as both Save/Save as)

F4 Save Spectra	Stores the currently displayed spectra in ASPECT+ file format.
Sample, Blank, Standard[Shift F1 - F6]	Blank measurement. The obtained spectrum will be stored as blank (reference) for manual standard and sample measurements.Standard measurement. The obtained spectrum will be stored as Standard for evaluation of manual sample measurements. Sample measurement. The obtained spectra are blank-(reference-) corrected. If a valid standard has been measured, or a MCA model is employed, the concentration(s) is(are) computed and displayed.
F5 ICC Run	Performs the inter-channel calibration to update the correction factors for the differences of the individual channels
F7 Plot	Plot current spectra and deriv graphs.
F10 Quit	Quit Manual Module.
Spectra	Displays measured spectra
2nd Deriv	Displays 2nd derivative of standard and sample spectra

5.2 Edit Sample Point Table

This dialog can be used to define and edit the series of samplepoints for the dissolution run.

The table is presented as a graph and on the right sight of the dialog box.
Use the two buttons to create two different types of sample point series.

Immediate Release: n sample points are created with the specified interval

example: SP 3   Interval 5 ->   5, 10, 15 min

Controlled Release: n+m sample points are created with the specified intervals

example: SP 4 4   Interval 5 10 -> 5,10,15, 20,30,40,50,60 min

In addition the time table can now be manually edited.

5.3   *Calculations used in Manual Module*

Spectra are measured in counts (diode), representing the energy input $I(\lambda_i)$ onto the diode array.

The wavelengths λ_i represented by the diodes are computed during the initialisation of the device from non-linear coefficients. These coefficients are provided by the manufacturer and stored in the MCS spectrometer's internal EEPROM in the course of calibration and system integration of the device. Because of the spherical characteristics of the spectral imaging these λ_i are non-equidistant values, they differ slightly from an exact equidistant series of wavelength values. In the course of the computation of absorbance spectra and values derived from them (concentrations etc.) the λ_i are recomputed to an array of equidistant λ_i values.

Blank Spectrum :

$$E^{Blank}(\lambda_i) = I^{Current}(\lambda_i) - I^{Dark}(\lambda_i)$$

Standard & Sample Spectrum :

$$E^{Std,Sample}(\lambda_i) = I^{Current}(\lambda_i) - I^{Dark}(\lambda_i)$$

Absorbance Spectrum :

$$Abs^{Std,Sample}(\lambda_i) = -\log\left(\frac{E^{Std,Sample}(\lambda_i)}{E^{Blank}(\lambda_i)}\right)$$

$$Abs^{Std,Sample}(\overline{\lambda}_i) = linInterpolation(Abs(\lambda_i))$$

2nd Deriv of Absorbance:

$$Der^{Std,Sample}(\overline{\lambda}_i) = SGderiv(SGsmooth(Abs^{Std,Sample}))$$

SGsmooth   numerical smoothing operation according to Savitzky-Golay
                  (see Appendix of Z-Dis Software Manual)
SGderiv   numerical 2nd derivative operation according to Savitzky-Golay
                  (see Appendix of Z-Dis Software Manual)

Standard & Sample Reading

$$Rd^{Std,Sample} = Abs^{Std,Samplet}(\lambda_{evaluation})$$

resp.

$$Der^{Std,Sample} = Abs^{Std,Samplet}(\lambda_{evaluation})$$

The spectral value at the fractional index of $\lambda_{evaluation}$ is computed by linear interpolation.

Concentration:

$$Conc^{Sample} = \frac{Rd^{Sample}}{Rd^{Std}} \times Conc^{Std}$$

$$Conc^{Sample} = \frac{Der^{Sample}}{Der^{Std}} \times Conc^{Std}$$

5.4 Z-Dis MUX parameter file format

A parameter file contains all necessary parameters for a complete dissolution run. The parameter files are stored in plain ASCII (use notepad or any other ASCII viewer)Example:

```
[GENERAL]
FileID=Z-Dis MUX Dissolution Monitor Parameter File
Time=21.11.1995/12:26:49
Origin= Z-Dis MUX Dissolution Monitor  V n.nn
Note=

[Spectrometer]
IntegrationTime=25
Accumulation=20

[Method]
Method=0
SamplePoints=3
SampleTimes=10;110;210
StdConc=1.0003
DosageSize=500
VesselVolume=300
MaxBackgroundAbs=0.0002
CalibWavelength= 400.00
...
[Evaluation]
UseDeriv=0
Smooth=8
CalibWavelength= 400.00

[MCA]
..(special settings for MCA modelling & evaluation)
```

6. Technical setup

6.1 The setup screen

The Technical setup screen includes controls for several software settings.

Directories

Validation Data	Report files produced in the Validation submenu
ICC Data	Inter-channel correction data
Manual Data	data files generated in the manual mode
Parameter Files	Parameter sets (Methods) for dissolution runs
Multivariate Models	Multivariate model and calibration files referred to from multivariate
(not used in this release)	methods (parameter sets)

Spectral Raw Data   All raw spectra produced during a dissolution run

Dissolution Results   Storage of the Dissolution Reports on a network PC or, respectively, in a
                           local backup directory, if the network path is not accessible

Settings

Store dissolution results   Generate result file of the run (basis for report)

Store spectral raw data   Store all raw spectra produced during a dissolution run

Auto-Print   Print Dissolution Report automatically at the end of each Dissolution run.

Emulation   Enables Device emulation of Bath, MUX or spectrometer for off-line
                                demonstration purposes

Probes present   In case of any of the sample probes missing, the probe can be disabled
                                here, the system will still be able to perform runs.

COM Ports

GP 700, VK 7000   COM port settings for MUX and VanKel Bath

6.2   Passwords

In this dialog, the password list can be modified along with the assigned access rights.

To add a new password enter the name and the password and assign an access level.

To remove a password from the list delete both name and password and the corresponding line will be removed.

Z-Dis MUX access level hierarchy:

level		access to
0	Administrator	everything
1	Chief operator	everything, except technical parameters (no access to Technical Parameter Setup)
2	Operator	Load predefined methods and monitor automatic measurement only

7. Validation

7.1 The Validation screen

The Validation screen gives access to special check and validation routines to create regular reports on the status of hard- and software.
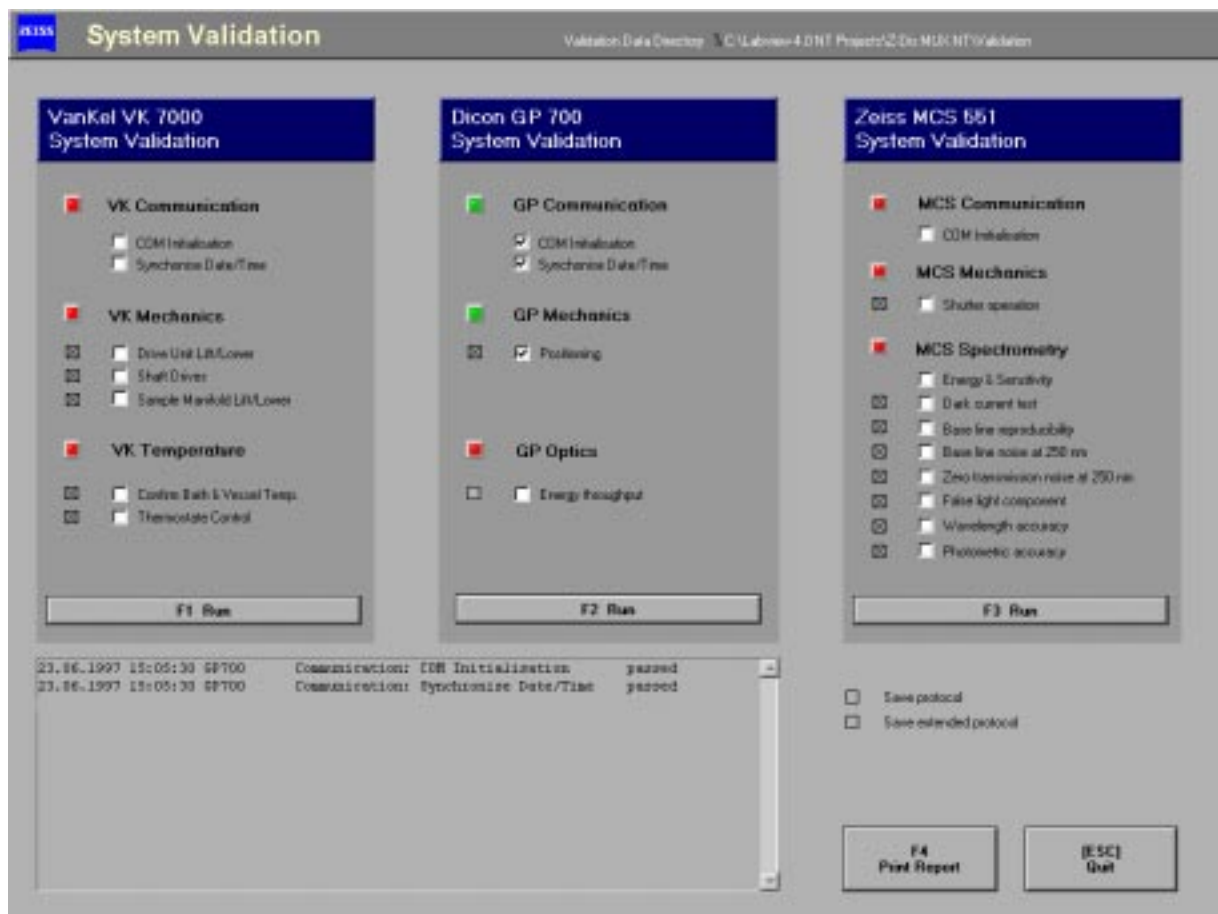
Most of the individual test routines (except for some required basic tests) can be included/excluded by checking/unchecking the corresponding checkboxes. The test routines will be performed in the given order. Test routines that run for a more than a few seconds will display their own progress window, displaying essential information, temperature curves, spectra etc. The test series can be cancelled any time.

Two types of reports can be created. The standard report lists date & time, device, test identification and completion for every individual device test. This protocol is displayed on-line to follow-up the progress. This report can be stored and printed.

An extended protocol holds additional information, especially for the MCS spectrometer device, like durations, limits, actual values, measured spectra etc. For the first release of Z-Dis MUX this extended information is for storage and evaluation by Zeiss only. It will be made open and printable as soon as possible.

The created validation reports can be printed and / or stored in a special validation directory. This directory can be specified in the Technical Setup menu.

7.2 Description of VK7000 test routines

Communication: Initialisation

The serial communication with the VK 7000 unit is initialised according to the COM port settings specified in the Technical Setup menu. A number of test commands is sent and acknowledgement is checked.

Communication: Synchronise Date & Time

The serial communication with the VK 7000 unit is once more checked by downloading the PC's current date and time to be set on the VK7000, and afterwards verifying it, thus synchronising the internal clocks of both the devices.

Mechanics: Drive Unit Lift/Lower

The drive unit of the VK 7000 is automatically moved down, up and down again in order to ensure the proper function of drive and limiting switches.

Mechanics: Shaft Drives

The paddle spin velocity is sequentially set to 50, 100, 150 and 200 rpm and the actual rpm value is read and displayed.

Mechanics: Sample Manifold Lift/Lower

The sample manifold is automatically moved down, up and down again in order to ensure the proper function of the manifold drive.

Temperature: Confirm Bath & Vessel Temperature(*)

The current temperatures of bath and sample vessels as send by the VK7000 are displayed. They can be checked with an external temperature. Any required VK7000 calibrations of the thermosensors could / should be performed now. The current temperature readings must be confirmed by pressing the OK button.

Temperature: Thermostatting(*)

The nominal bath temperature is set to 36°C. The temperatures of bath and sample vessels as read by the VK7000 are displayed in a temperature–time graph. The test routine finishes when the bath temperature reading is 36°C. This test can take a couple of minutes, depending on the initial bath temperature. If the thermostatting of the VK7000 pump unit works properly, a linear increase of all temperatures can be observed.

(*) Please note that due to technical reasons (VanKel) the vessel thermistors will start sending temperature data only from about 30°C and above.

7.3   Description of GP700 test routines

Communication: Initialisation

The serial communication with the GP 700 unit is initialised according to the COM port settings specified in the Technical Setup menu. A number of test commands is sent and acknowledgement is checked.

Communication: Synchronise Date & Time

The serial communication with the GP 700 multiplexer unit is once more checked by downloading the PC's current date and time to be set on the GP700, and afterwards verifying it, thus synchronising the internal clocks of both the devices.

Mechanics: Positioning

The multiplexer is moved into all 8 positions and the signal is checked to ensure proper positioning of the fiber switch.

Optics: Energy throughput (*)

The multiplexer is moved into all 8 positions and the signal is measured without multiplexer and with the multiplexer inserted in the optical path.

(*) This test requires optical fibres to be rearranged at the spectrometer in order to measure the energy throughput without multiplexer.

7.4   Description of MCS 500 series test routines

The device test and validation routines implemented in this section are a direct implementation of parts of the Zeiss PA 224210-7121.000 internal Quality Test instruction as applied in the production facility.

Some of the validation routines require only the measuring beam to be covered-up (dark current etc.), some require special filters (and therefore a simple cell holder and two fibres). These filters must be available to perform the corresponding tests.

NaNO$_2$ solution cell for false light test, cell holder and monofibres.

Filter-Set (HELLMA 666.000) with Holmiumoxide & Standard filters for wavelength and photometric validation
Communication:

Initialisation

The communication with the MCS 500 series spectrometer via the PC interface card is initialised. The firmware is downloaded and a number of test commands is sent and acknowledgement is checked.***Mechanics:*** ***Shutter operation***The shutter is opened and closed several times and the energy throughput is monitored.

Spectrometry: Energy and Sensitivity

The test routine automatically determines an optimum integration time for all the following tests (approx. 85% of the dynamic range). The resulting energy curve is displayed and evaluated according to factory specifications.

Spectrometry: Dark current test

Amount and uniformity (peak-to-peak noise and overall values) of the dark current signal of the spectrometer are checked according to factory specifications. The measuring beam must be covered (insert filter into cell holder turned by 90°) for this measurement. The dark current signal is displayed.

Spectrometry: Baseline reproducibility

The reproducibility of the spectral baseline in the range from 215 – 620 nm is determined. After a reference measurement 10 sample measurements are performed and displayed, and the baseline stability is checked according to factory specifications.

Spectrometry: Baseline noise

The noise of the spectral baseline at 250 nm is determined.
After a reference measurement 50 sample measurements are performed and displayed, and the measurement value at 250 nm is displayed in a graph. Finally the results (peek-to-peek) are checked according to factory specifications.

Attention! It takes this test about 20 s to complete. Cell holder and optical fibres must not be moved during the test!

Spectrometry: Zero-transmission noise

The zero-transmission noise at 250 nm is determined. On request the measuring beam must be covered (insert filter into cell holder turned by 90°) for this measurement.
After a reference measurement 50 sample measurements are performed and displayed, and the measurement value at 250 nm is displayed in a graph. Finally the results (mean value, standard deviation) are checked according to factory specifications.

Attention! It takes this test about 20 s to complete. Cell holder and optical fibres must not be moved during the test!

Spectrometry: False light component

The false light component at 240 and 340 nm will be determined using $NaNO_2$ solution. After a reference measurement a measurement of the $NaNO_2$ solution will be performed. The resulting spectrum will be displayed and the false light component is evaluated according to factory specifications.

Spectrometry: Wavelength accuracy & reproducibility

The wavelength accuracy is determined using a Holmiumoxide filter.

The wavelength accuracy is checked 10 times at 4 different wavelengths with the peek position being determined by a 20-point interpolation between the spectral points. The resulting spectrum is displayed and the wavelength accuracy is evaluated according to factory specifications.

The wavelength reproducibility is checked as the largest wavelength difference between these measurements and can be further investigated by long-time comparison of the validation results.

Spectrometry: Photometric accuracy

The photometric accuracy is checked using a standard filter set (Pm10) with defined reference values. After a reference measurement the standard filters are measured and the measured absorbancies are evaluated according to factory specifications and the defined values of the standard filters.

8.   Project History

Release 1.0 due : xx.06.98	First delivery release
Release 0.9 released: 05.05.98	Release According to User Interface Design Review P.Rogers' visit to Jena - clear graph at beginning of run - added zero point to dissolution graph - real time clipped to +/- 15 sec - added Qt, Q, Q+5 to dissolution graph - removed background check - disabled any Multi-component features - SST is default, 1 std 1 reading, 1+6 std 2 readings - 1 minute accuracy in SP edit - sp edit: linear only, but two time bases - Qt default 30 min, Q+5 default 75 % - removed component names from run info - define Qt, Q, Q+5 in run info - Std 1Conc, Std2 Conc in run info - carrys over best integration time from ICC - infinty test included - flags SP results acc. to USP rpm +- 4%, T 37 +- 0.5 °C
Review 3.98	Phil Rogers (Pfizer) on site review at Zeiss, user interface design review
Release 0.8 released : 2.98	Preliminary test release for Multicomponent Analysis not brought forth, archived at OEM-M2, further work from R 0.72
Release 0.4 - 0.72 released : 4.97 – 3.98	Zeiss on-site test and demos
Release 0.2 released 21.04.1997	Revised and Signed Software Specification by Zeiss
Review 02.04.97	Comments on Software Spec by Pfizer (FAX 2/4/97)
Release 0.1 released 20.12.1996	Proposal of software specification by Zeiss

Supplements

Algorithm for smoothing and derivatives according to Savitzky-Golay

Smoothed spectra and their derivatives are computed according to the Savitzky-Golay algorithm. This fast numerical procedure provides the new data points using a set of predefined coefficients.

$$y_j^{new} = \frac{1}{coeff_{n+1}} \cdot \sum_{i=1}^{n} \left(y_{j+i-(n+1)/2}^{old} \cdot coeff \right)$$

The spectra to be processed must be of equidistant. type, i.e. the x-data points must be evenly spaced by ΔX. The standard SG coefficients are computed for a ΔX of 1.

The coefficients have been computed according to R. Ludwig [see "Methoden der Fehler- und Ausgleichsrechnung"; VEB Deutscher Verlag der Wissenschaften, Berlin 1969].

Coefficients for smoothing, using n points

Coefficients for derivatives (n=9)

i	n=5	n=7	n=9	n=11	n=13	n=17	n=21	n=25		i	1st	2nd	3rd	4th
1	-3	-2	-21	-36	-11	-21	-171	-253		1	-4	28	-14	14
2	12	3	14	9	0	-6	-76	-138		2	-3	7	7	-21
3	17	6	39	44	9	7	9	-33		3	-2	-8	13	-11
4	12	7	54	69	16	18	84	62		4	-1	-17	9	9
5	-3	6	59	84	21	27	149	147		5	0	-20	0	18
6	35	3	54	89	24	34	204	222		6	1	-17	-9	9
7		-2	39	84	25	39	249	287		7	2	-8	-13	-11
8		21	14	69	24	42	284	342		8	3	7	-7	-21
9			-21	44	21	43	309	387		9	4	28	14	14
10			231	9	16	42	324	422		10	60	462	198	143
11				-36	9	39	329	447						
12				429	0	34	324	462						
13					-11	27	309	467						
14					143	18	284	462						
15						7	249	447						
16						-6	204	422						
17						-21	149	387						
18						323	84	342						
19							9	287						
20							-76	222						
21							-171	147						
22							3059	62						
23								-33						
24								-138						
25								-253						
26								5175						

The described algorithm is used in the ZEISS software to produce smoothed spectra and their derivatives.

Labview Graph Handles
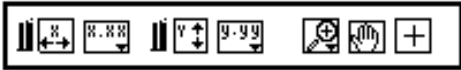
The graph palette has controls for panning (scrolling the display area of a graph) and for zooming in and out of sections of the graph.

If you press the x **autoscale button**, LabVIEW autoscales the X data of the graph. If you press the y autoscale button, LabVIEW autoscales the Y data of the graph. If you want the graph to autoscale either of the scales continuously, click on the lock switch, shown at the left, to lock autoscaling on.

The **scale format buttons** give you run-time control over the format of the X and Y scale markers respectively.

You use the remaining three buttons to control the **operation mode** for the graph.

Normally, you are in **standard** operate mode, indicated by the plus or crosshatch. In operate mode, you can click in the graph to move cursors around.

If you press the **panning tool**, shown to the left, you switch to a mode in which you can scroll the visible data by clicking and dragging sections of the graph.

If you press the **zoom tool**, shown at the left, you can zoom in on a section of the graph by dragging a selection rectangle around that section. If you click on the zoom tool and hold for a moment, you get a pop-up menu you can use to choose some other methods of zooming. This menu is shown in the following illustration.
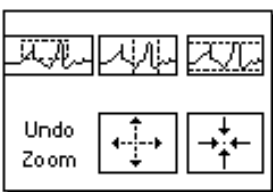
A description of each of these options follows.

Zoom by rectangle.

Zoom by rectangle, with zooming restricted to x data (the y scale remains unchanged.

Zoom by rectangle, with zooming restricted to y data (the z scale remains unchanged).

Undo
Zoom

Undo last zoom. Resets the graph to its previous setting.

Zoom in about a point. If you hold down the mouse on a specific point, the graph continuously zooms in until you release the mouse button.

Zoom out about a point. If you hold down the mouse on a specific point, the graph continuously zooms out until you release the mouse button.

Note: For the last two modes, zoom in and zoom out about a point, shift clicking zooms in the other direction.

Zeiss ASPECT plus data file format

author: E.Stein
released :   08.06.95

General remarks

- The header of the data file is similar to a windows-INI-file. To read a data file it is necessary to interpret the sections GENERAL and DATA.
  Every entry has to start at the beginning of a line. The section keywords are enclosed in square brackets ('[' and ']') and immediately followed by a CR/LF.

- The keywords in the sections must befollowed immediately by an equal sign and then by the corresponding value of the respective keyword (in GENERAL section). In theDATA section the equal sign is to be followed immediately by a CR/LF. Here the first byte of the data has to stand on the beginning of the next line. After the last byte of data a CR/LF is to be appended.

- All data are 4-Byte IEEE float values. ASPECT will accept values in the range (-1.0 E15 .... 1.0 E15) only.

- The section GENERAL is always the first section in the data file.

- Several more sections and keywords are defined for internal use and may occur in the data files.

- The data file should be opened in binary mode.

Format

[GENERAL]

TITLE=	small note of up to 50 characters

TYP=

	0	old DOS-aspect format,
	1	old DOS-aspect format,
	2	old DOS-aspect format,
	3	old DOS-aspect format,
	4	current data file format

TIME=	date and time as a string in the format:
	dd.mm.yyyy/hh:mm:ss
XUNITS=	unit of the abscissa values
YUNITS=	unit of the ordinate values
ZUNITS=	unit of the cycle values
FIRSTX=	start value of measurement range as string
LASTX=	end value of measurement range as string
NPOINTS=	number of measurement values per cycle as string
NCYCL=	number of cycles as string

[DATA]

ZDATA=	cycle values in a field of float values (data type float). The size of the field (number of elements) is specified by keyword NCYCL. ZDATA is not necessarily included in the data file, even if the number of cycles is greater than 1 !
XDATA=	abscissa values in a field of float values. The size of the field is specified by keyword NPOINTS. The abscissa values are the same for all cycles.
YDATA=	measurement values in a field of float values. The size of the field is NPOINTS * NCYCL. The cycle values are stored in subsequent order (cycle 1, cycle 2, ...)