



PARIS (Proteomic Analysis and Resources Indexation System) VERSION 2.0 User's Guide

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PARIS (Proteomic Analysis and Resources Indexation System)

VERSION 2.0



User's Guide

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1.INTRODUCTION.....	4
2.CONTACT AND TECHNICAL ASSISTANCE.....	5
3.SYSTEM REQUIREMENT.....	5
4.INSTALLATION.....	5
4.1 FILES DISTRIBUTED WITH THIS PACKAGE.....	5
4.2 CLIENT SIDE INSTALLATION.....	6
4.3 SERVER SIDE INSTALLATION.....	6
5.INTERFACE	8
5.1 LOG PANEL.....	8
5.2 LOGIN AND LOGOUT.....	9
5.3 DATA QUERY.....	10
6.MULTI-GEL VISUALIZATION.....	13
7.DATA EXPLORATION AND ANALYSIS.....	13
7.1 SMART LIST	14
7.2 IMAGE ENHANCEMENT.....	15
7.3 SPOT PROPRIETIES PANEL.....	15
8.VISUAL DATA CORRECTION AND GEL ANNOTATION.....	16
9.GEL-WIDE PROTEIN DIFFERENTIAL EXPRESSION ANALYSIS.....	25
10.INTRA/INTER GEL RELATION EXPLORATION	28
11.GEL ANALYSIS IN THE CONTEXT OF THE METABOLIC PATHWAY.....	35
12.DATA ENTRY.....	37
13.PUBLICATIONS.....	41

1. INTRODUCTION

PARIS (*Proteomic Analysis and Resources Indexation System, version 2.0*) is an open source, freely available software system for analysing and managing data from 2D electrophoresis centred proteomics technologies. It stores information about experiments and analysis procedure, allows the user to search and navigate in genomic and proteomic data, supports visual verification and validation of the analysis results, and provides tools for cross multi-experiment and multi-experimenter data validation and exploration.

Based on a 3-tier architecture, **PARIS** consists of a *PostgreSQL* based database server, an integrated search engine and a graphical user interface. The database server manages data regarding experimentation, including sample preparation through biological interpretations of the results while passing by parameter settings of used analysis procedure. It also stores information necessary to connect with external genomic and proteomic resources such as *GenBank*, *SWISS-PROT*, and *KEGG*.

The search engine analyses the queries formulated by biologist, provides fast, highly selective access to internal and external data sources, and structures the search results. From information provided by the biologist, it defines a search strategy taking into account the availability of local data and external sources, starts appropriate processing, and structures the provided information in order to facilitate its reading and interpretation. An important feature that distinguishes **PARIS** from other proteomics data management system is that queries implemented in **PARIS** are not limited in means for accessing the needed entries in the database, they can also help users to discover relations that were not explicitly noticed in the data but can be derived from them.

Based on Java 2D Graphics API, the graphical interface enables users to visualize, to compare, and to correct and validate the analysis results. It provides basic functions for image manipulation such as zooming, scrolling, region-of-interest (ROI) selection and image contrast enhancement as well as spot emboss and contour detection. Other functions give helps to understand the relationships which exist in the proteomic data. The spot where the mouse cursor is over is highlighted, and the associated genomic and proteomic information is displayed. Given a term such as spot, protein, physiochemical characteristics, etc, we can retrieve the gels having relationships with this term, display the gels in a set of windows, and highlight, by using pseudo-colours, particular relationships such as spot matching, protein isoforms, etc.

PARIS is particularly designed for maximizing the system usefulness. It assists the users to formulate their queries. Users can either select queries from an established list or compose queries by combining pre-established queries. Complex queries can be formulated from elements directly selected on the images and be previewed before being submitted to the search engine.

2. CONTACT AND TECHNICAL ASSISTANCE

If you have any questions about this system or need technical support, please contact Christophe.Caron@jouy.inra.fr or Juhui.Wang@jouy.inra.fr. We will highly appreciate your opinions and comments.

3. SYSTEM REQUIREMENT

For a client side installation, you just need Java(TM) SE Runtime Environment 1.4 or later (with Java Web Start).

For a server side installation, the following packages are necessary in addition to the previously mentioned Java environment:

- *AXIS* 1.4 or later (<http://ws.apache.org/axis/>).
- *PostgreSQL* 7.2.3 or later (<http://www.postgresql.org/>).
- *APACHE Tomcat* 5.5.12 or later (<http://tomcat.apache.org/>).

PARIS has been tested on *Mandrake Linux 8.0*, *Mandriva 10.0*, *Redhat Enterprise 4.4* and *Windows XP Professional*. Although we're not sure **PARIS**'s compatibility when working with other operating systems or other vendors' Java implementation, and strongly recommend to use the tested environments, **PARIS** should be able, theoretically speaking, to run on any platforms with a suitable Java environment installed.

4. INSTALLATION

4.1 Files distributed with this package

```
|-- bin
|   |-- client
|   |   |-- index.html
|   |   |-- lib
|   |   |-- myKeys
|   |   |-- paris.jnlp
|   |   |-- paris_client.jar
|   |   |-- splashScreen.jpg
|   |-- database
|   |   |-- add_match.sql
|   |   |-- add_spot.sql
|   |   |-- create-paris.sh
|   |   |-- create-user.sh
|   |   |-- paris.sql
|   |   |-- remove_spot.sql
|   |   |-- reverse_match.sql
|   |   |-- update_match_ratio.sql
|   |-- server
|   |   |-- config_bd.xml
|   |   |-- paris_server.war
|-- src
|   |-- client
|   |   |-- main
|   |   |-- test
|   |-- database -> ../bin/database
|   |-- server
```

`-- main

4.2 Client side installation

A) Installing and configuring Java Web Start

Be sure that Sun Microsystem's Java Runtime Environment with *Java Web Start* has been installed on your computer.

Setup the Java Web Start MIME type (JNLP) for your web browser. By example, if you use Mozilla browser, you should set the corresponding items in the *Edit->Preferences->Navigator->Applications* section as follows. The file extension should be "jnlp", MIME Type should be set into "application/x-java-jnlp-file", and the application handler should be the *javaws* executable file of Java Web Start found in your file system.

B) Visiting our demonstration system

We have set up a live demonstration system and would highly recommend you to try it before installing your own copy. To try the demonstration system, just go to **PARIS**'s web site (<http://w3.jouy.inra.fr/unites/miaj/public/imaste/paris/>) and click on the associated hyper link. **PARIS** will be automatically loaded and launched via Sun Microsystem's Java Web Start. The demonstration system's database is named "*demo_paris*", and both the user name and password to accede to the demonstration database are "*demo_paris*".

4.3 Server side installation

*Notice: You must have administrator privilege for your system to install **PARIS** server.*

A) Database installation

PARIS's back-end data storage is based on a *PostgreSQL* database. It must be installed and configured on your system before you operate to install the **PARIS** system. This preliminary procedure involves three stages: creating the databases, setting up the user's privileges, and making communications between the database and the components of **PARIS**. The provided install script `$PARIS_HOME/bin/database/create_paris.sh` will create a database according to the data model defined in **PARIS**, and the script `$PARIS_HOME/bin/database/create_paris.sh` will create three users "paris_admin", "paris_root" and "paris_read"

B) Web Services configuration

PARIS is designed to support interoperable component interaction over network. Axis, an Apache implementation of Web Services, has been used to achieve this aim. So, you must also install an APACHE HTTP server and the Axis related components before preceding the installation of PARIS itself.

After finishing the installation of APACHE and Tomcat, modify the database connection configure file `$PARIS_HOME/bin/server/config_bd.xml` according to your local PostgreSQL settings, and replace the modified file into the directory `$CATALINA_HOME/webapps/axis/WEB-INF/classes/`.

Once the preceding steps were done, deploy the file `$PARIS_HOME/bin/server/paris_server.war` with the help of the Tomcat manager whose default port is `8080/manager.html`, and restart Tomcat.

C) Java Web Start configuration

To enable Java Web Start launching, copy the files from `paris-2.0/bin/client` of the distribution package into the `htdocs` directory of your HTTP server, and edit the file `paris.jnlp` as follows:

1. Change the URL in the jnlp codebase attribute to the appropriate URL for your web server.

```
<?xml version="1.2" encoding="utf-8"?>
<jnlp
  spec="1.0+"
  codebase="http://genome.jouy.inra.fr/paris/" href="paris.jnlp">
  <information>
    <title>PARIS2D</title>
    <vendor>INRA</vendor>
    <homepage href="http://w3.jouy.inra.fr/unites/miaj/public/imaste/paris/" />
    <description>Proteomic Analysis and Resources Indexation
System</description>
    <description kind="short"> PARIS is a system to manage data from 2D
electrophoresis centred proteomics analysis </description>
    <icon href="splashScreen.jpg" />
    <icon kind="splash" href="splashScreen.jpg" />
  </information>

  <security>
    <all-permissions/>
  </security>

  <resources>
    <j2se version="1.4.+" initial-head-size="32m" max-heap-size="256m" />
    <jar href="paris_client.jar" main="true" />
    <jar href="lib/axis.jar" />
    <jar href="lib/jaxrpc.jar" />

    <jar href="lib/saaj.jar" />
    <jar href="lib/commons-logging-1.0.4.jar" />
    <jar href="lib/wsdl4j-1.5.1.jar" />
    <jar href="lib/commons-discovery-0.2.jar" />
    <jar href="lib/axis-ant.jar" />

  </resources>

  <application-desc main-class="fr.inra.jouy.bia.paris.client.gui.Paris" />
</jnlp>
```

2. Restart the web server.

5. INTERFACE

The user interface of **PARIS** is composed of four parts, as indicated in the picture **Fig. 1**: the **Main Window**, the **Navigation Panel**, the **Thumbnail Panel**, and the local **File Browser**. The **Main Window** constitutes the working space, it shows the main images that we are analysing. A **Tool Bar** is attached to the **Main Window**, it allows you to choose the appropriate tools used for the undergoing analysis task. On the left side of the page is a **Navigation Panel** that makes easier your travel inside the gel images such as zooming, moving, and focusing, etc. The **Thumbnail Panel** lists all gels found in the **PARIS** servers, which match your query criteria. These thumbnails give you a general survey of the results of your research, and allow you to choose the gels on which you would like to deep different analyses before all data are fetched from the servers to the client machine. As windows explorer, the **File Browser** is used to describe and to explorer the directories and files managed by your local operating system. With the **File Browser**, you can load files and gels from your local operating system and compare them with the files and gels stored in the **PARIS** servers, and save your analysis results into your local file system.

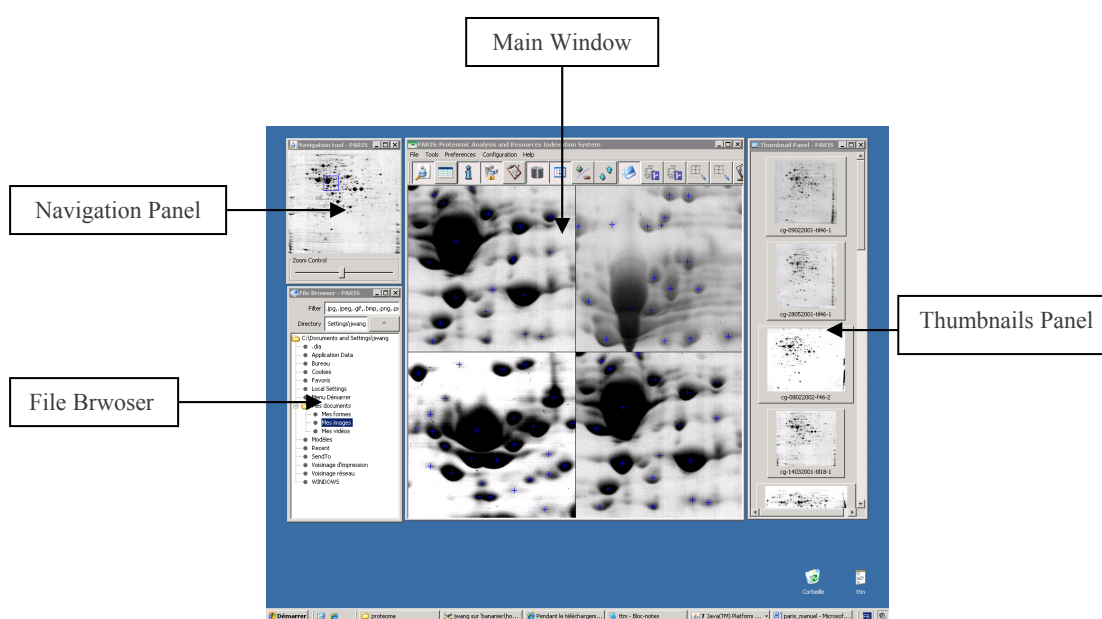


Fig. 1 - The main user interface.

5.1 Log Panel

The **Log Panel** can be opened by clicking on the **Log Icon** from the **Tool Bar** of the **Main Window**. It shows you the errors and messages about your operations. The messages are printed in three colours. Blue indicates that your job has been successfully completed; red

indicates errors; and black suggests a general message. Clicking on the *Clear List* button will erase the old messages.



Fig. 2 – The Log Icon on the Tool Bar of the Main Window.

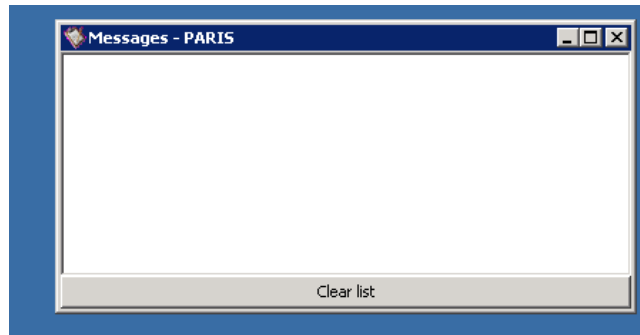


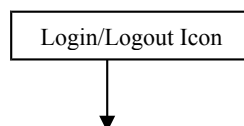
Fig. 3 – The Log Panel.

5.2 Login and Logout

PARIS uses a UNIX-like user group management policy to manage the data access control issue. Users are divided into three groups: data ``owner", owner's group and other users not in the previous groups. Thanks to this policy, the data providers can decide whether to keep their data private or on the contrary to open their data to others members of the communities.

To accede to **PARIS**, you need an account on the **PARIS** server to which your **PARIS** client is attached. If you are only client of the **PARIS** system, ask the administrator of your **PARIS** server to open an account for you. Your account will be protected with a user name and a password. Click the **Login/Logout Icon** on the **Tool Bar** of the **Main Window**, and a login/logout pop-up window will be opened. Choose your data server from the multi-choice list and type your user name and password. If you don't have an account yet, you can still try **PARIS** with a demonstration account provided by default with **PARIS** installation. Both the user name and the password of this demonstration account are "*demo_paris*". The data server to which the demonstration account is authorized to accede is also named "*demo_paris*".

To close a session, just click on the **Login/Logout Icon** of the **Tool Bar**. Once the login/logout pop-up window was opened, click on the "*logout*" button.



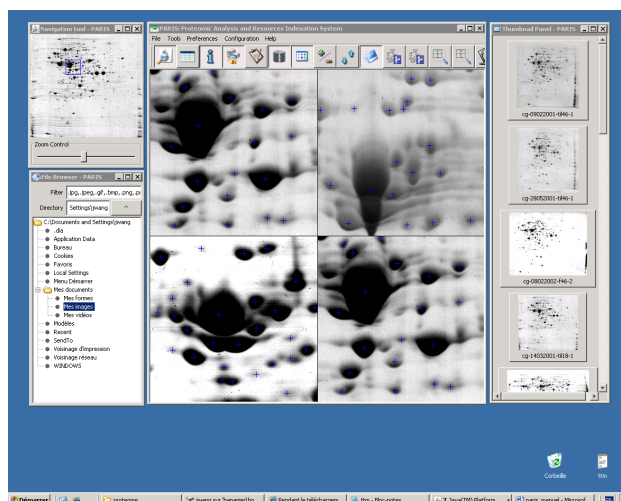


Fig. 4 - Login/logout icon on the tool bar.

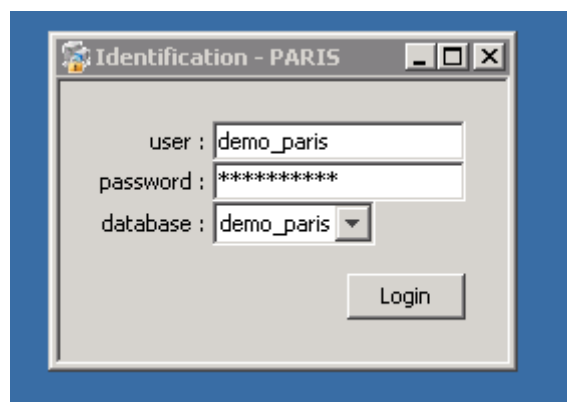


Fig. 5 - Login Window.

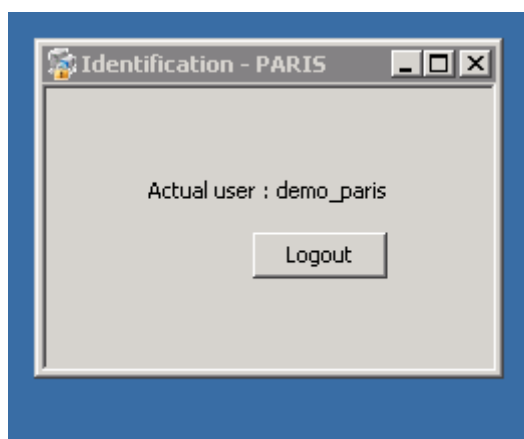


Fig. 6 - Logout Window.

5.3 Data Query

Before everything, **PARIS** is a gel centred proteomics analysis data management system. One of its most fundamental functions is data storage and retrieval. You can search, from the data servers, gels according to different criteria such as gel name, author, gene name, scanned date,

strain, medium, and key words. You can also combine the previously mentioned criteria via an **Advanced Search Panel**.

To accede to the **Data Query Panel**, just click on the **Data Search Icon** on the tool bar of the **Main Window** as indicated in **Fig. 7**.



Fig. 7 – The **Data Search Icon** on the **Tool Bar** of the **Main Window**.

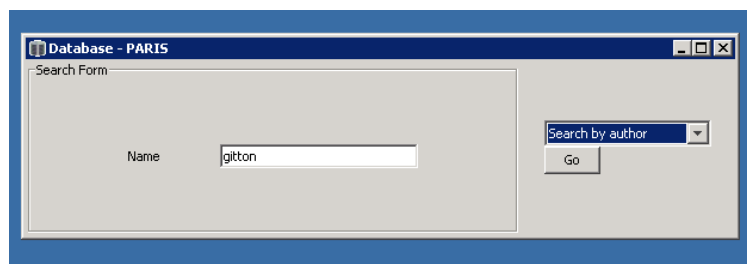
A screenshot of a web application window titled "Database - PARIS". It contains a "Search Form" with a text input field labeled "Name" containing the text "gitton". To the right of the input field is a dropdown menu labeled "Search by author" and a "Go" button.

Fig. 8 - Search gels according to gels' author. In this example, all gels made by experimenter *Gitton* will be retrieved from the data servers, and a survey of the retrieved results will be displayed in the **Thumbnail Panel**.

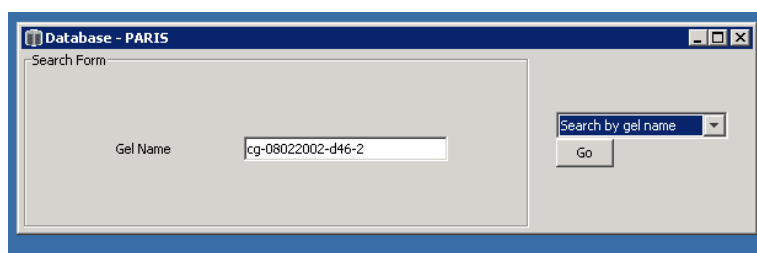
A screenshot of a web application window titled "Database - PARIS". It contains a "Search Form" with a text input field labeled "Gel Name" containing the text "cg-08022002-d46-2". To the right of the input field is a dropdown menu labeled "Search by gel name" and a "Go" button.

Fig. 9 - Search gels according to gel's name. In this example, only the gel named "cg-08022002-d46-2" will be retrieved.

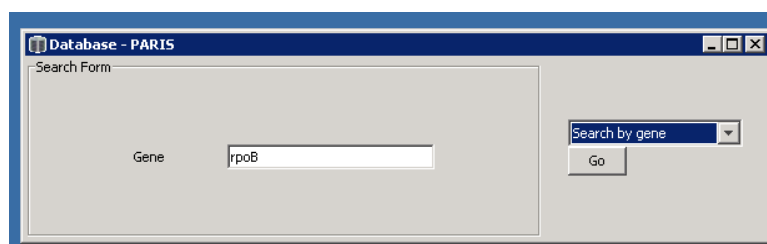
A screenshot of a web application window titled "Database - PARIS". It contains a "Search Form" with a text input field labeled "Gene" containing the text "rpoB". To the right of the input field is a dropdown menu labeled "Search by gene" and a "Go" button.

Fig. 10 - Search gels according to gene name. In this example, all gels in which the expression of gene *rpoB* was observed will be retrieved.

Database - PARIS

Search Form

Scanner Date: 08-02-2002

Search by scanner date

Go

Fig. 11 - Search gels according to the date of gel scanning. In this example, all gels scanned on February 8th 2002 will be retrieved.

Database - PARIS

Search Form

Strain: IL1403

Search by strain

Go

Fig. 12 - Search gels according to biological strain. In this example, all gels relating to experiments on strain *IL1403* (a strain of the *L. Lactis*) will be retrieved.

Database - PARIS

Search Form

Medium: M17

Search by medium

Go

Fig. 13 - Gel search according to bacteria culture conditions. In this example, all gels carried out in the culture condition named *M17* will be retrieved.

Database - PARIS

Search Form

Keywords: Lactose

Search by keywords

Go

Fig. 14 - Gel search according to keywords. In this example, all gels for which the word *Lactose* was found in the associated data will be retrieved.

Database - PARIS

Search Form

Item: Keywords

Value: Lactose

Operator: ☐ and ☐ or ☒ not

all
:and:Gene:rpoB
:and:Strain:IL1403
:not:Keywords:Lactose

Advanced search

Go

Fig. 15 - The **Advanced Search Panel** is used to formulate complex queries. In this example, we try to retrieve the gels which contains the product of gene *rpoB*, carried out on bacteria strain *IL1403*, and whose associated data does not contain the word *Lactose*.

6. MULTI-GEL VISUALIZATION

The number of gels that can be visualized at once in the **Main Window** is limited to 4. If you need to visualize more gels, you have to use the **Multiple View Tool** which can be accessed via the **Tool Bar** of the **Main Window**. The **Multiple View Tool** gives you the possibility to visualize any number of images with lost of functionalities (only visualization related functions are accessible from the multiple view mode).

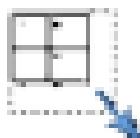


Fig. 16 - Icon for acceding to the **Multiple View Tool**.

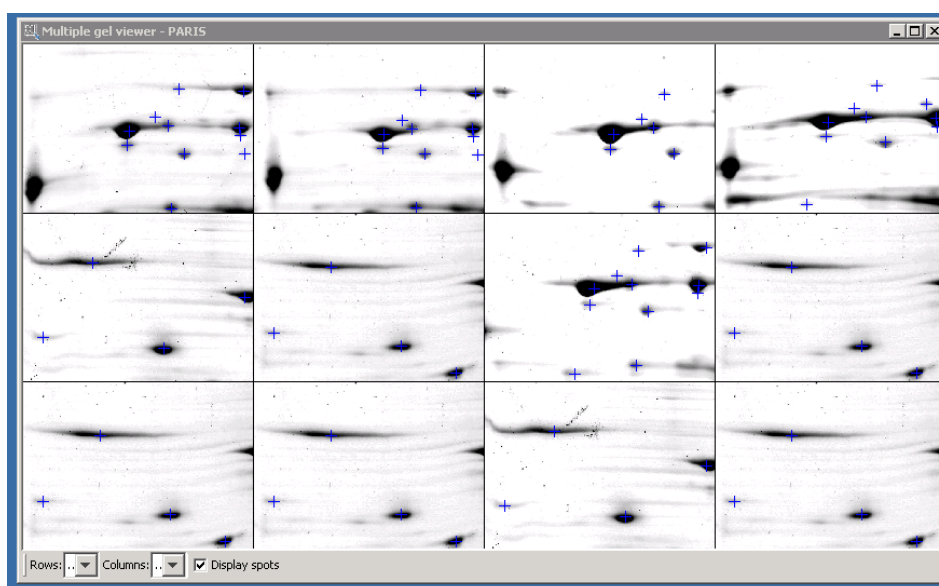


Fig. 17 – The tool for multiple gel visualization.

7. DATA EXPLORATION AND ANALYSIS

One of the most important and value-added features of the system **PARIS** is its capability to help the biologist to analyse their data. **PARIS** provides several build-in tools for electrophoresis gel centred data analysis. These tools will be switched on when you have loaded the gel images into the **Main Window** from the **Thumbnail Panel**. To load the image into the **Main Window**, select the image of interest in the **Thumbnail Panel** with the left button of the mouse, drag and drop it into one of the four frames of the **Main Window**. By default, the top-left image frame contains the reference gel. That is to say, by default, all pair wise gel comparison will be carried out regarding to this gel, and the **Navigation Panel** is also

anchored on this gel. Notes that the **Main Window** can only contain four images. If you have to analyse more images simultaneously, please refer to the Section 6.

7.1 Smart List

PARIS is equipped with a feature called **Smart List** that allows you to put the information about the spots contained in a gel into a table, and to ease the navigation between the gel and the table. To activate the **Smart List**, just place the cursor on an image contained in the **Main Window**, click on the right button of the mouse, and choose the item “*View spot list from this gel*” from the pop-up list as shown in the following pictures.

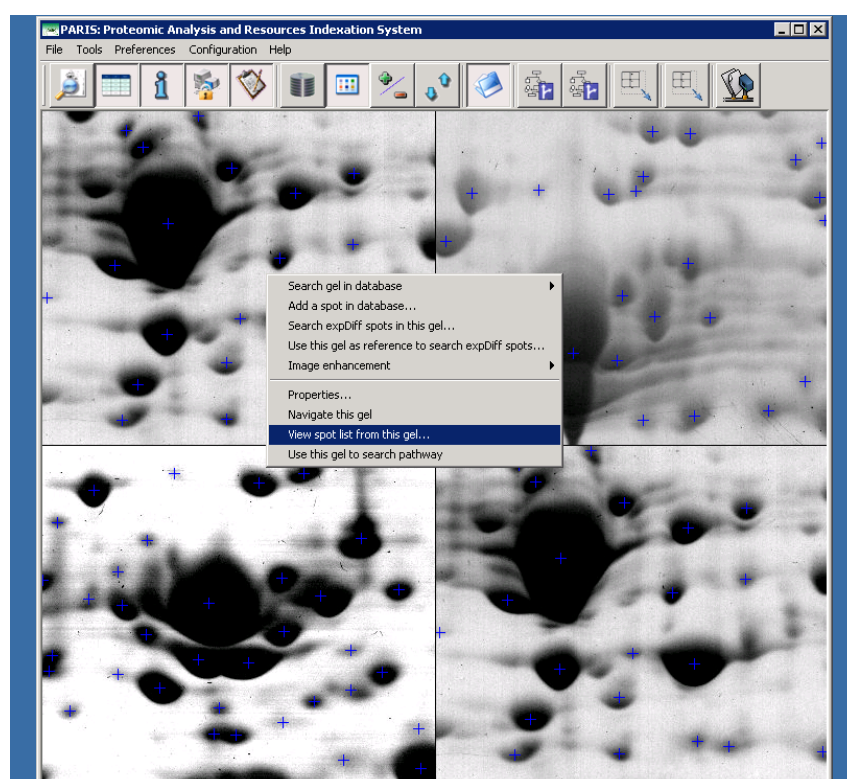


Fig. 18 - View the spots contained in an image with a Smart List.

Spot ID	Gene Name	Experiment...	Experiment...	Relative Vol...	z3Q	Identification	Annotation ...	Area	Gel ID	x	y
1	rpoB	142 308	4,56	15 802		0 ms-maldi	experiment	131	27	517	95
2	dpsA	141 233	4,63	231 235		0 ms-maldi	experiment	1 092	27	591	98
3	pycA	126 812	5,287	78 005		0 ms-maldi	experiment	647	27	1290	141
4	adhE	113 521	5,572	136 502		0 ms-maldi	experiment	1 038	27	1593	186
5	leuS	113 245	4,994	84 071		0 ms-maldi	experiment	524	27	978	187
6	secA	109 992	5,094	105 989		0 ms-maldi	experiment	865	27	1085	199
7	pfl	100 406	5,038	36 539		0 ms-maldi	experiment	298	27	1025	237
8	pheT	100 168	4,811	50 580		0 ms-maldi	experiment	444	27	784	238
9	pfl	100 168	5,006	11 347		0 ms-maldi	experiment	88	27	991	238
10	clpC	99 457	6,02	21 508		0 ms-maldi	experiment	274	27	2069	241
11	pcrA	95 319	5,306	24 992		0 ms-maldi	experiment	283	27	1310	259
12	pnpA	95 096	4,905	32 425		0 ms-maldi	experiment	281	27	884	260
13	pfl	93 330	5,069	10 749		0 ms-maldi	experiment	83	27	1058	268
14	pfl	93 112	5,123	5 646		0 ms-maldi	experiment	41	27	1115	269
15	pfl	92 462	5,095	25 896		0 ms-maldi	experiment	166	27	1086	272
16	clpE	91 818	4,902	20 405		0 ms-maldi	experiment	171	27	880	275
17	clpB	90 967	4,991	4 708		0 ms-maldi	experiment	50	27	975	279
18	typA	87 059	4,844	254 710		0 ms-maldi	experiment	1 293	27	819	298
19	yciC	84 893	5,501	22 975		0 ms-maldi	experiment	289	27	1517	309
20	fusA	84 507	4,736	831 789		0 ms-maldi	experiment	3 555	27	704	311
21	hndE	83 740	5,135	138 181		0 ms-maldi	experiment	860	27	1128	315

Fig. 19 - Smart List generated from the top left image. Double click on a spot from the list will centre and highlight the corresponding spot on the image of the **Main Window**.

7.2 Image Enhancement

We also provides **PARIS** with some image manipulation tools to improve the visual quality of the gel images. These include brightness/contrast enhancement, image sharpening, spot contour detection and image blurring. You can accede to these functionalities in the same manner as for **Smart List**: just place the cursor on an image and click on the right button of the mouse. A pop-up list for image enhancement will be opened. To cancel the processing carried out on the images and restore the original ones, select the item “*Restore*” from the image enhancement pop-up list.

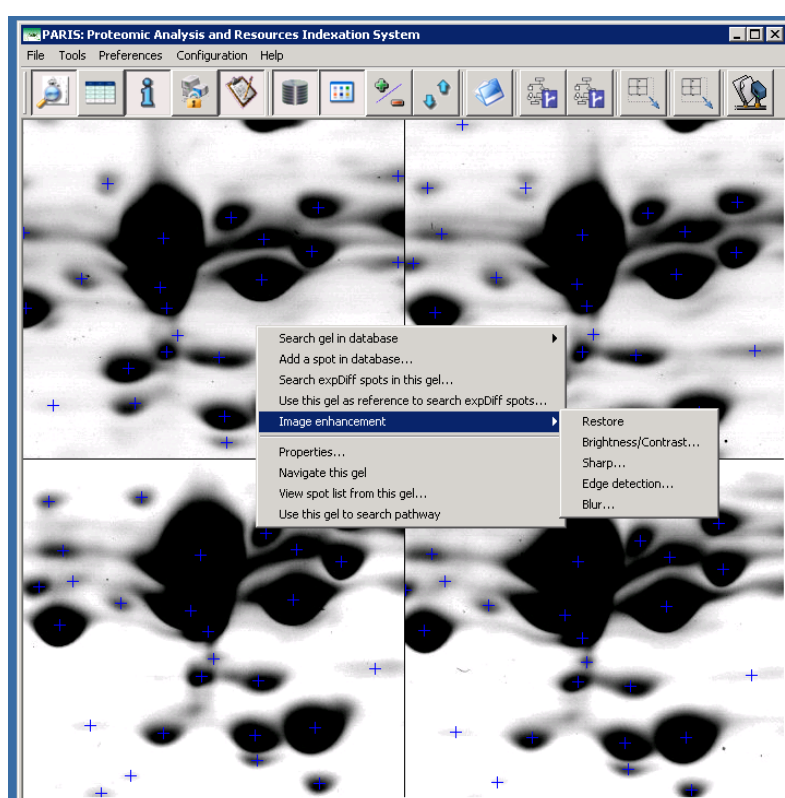


Fig. 20 – the image enhancement tools implemented in **PARIS**.

7.3 Spot Proprieties Panel

The **Spot Proprieties Panel** is a tool that gives you the possibility to visualise detailed information about a spot. To accede to this panel, just click on the **Properties Icon** of the **Tool Bar** of the **Main Window**, the **Spot Proprieties Panel** will be popped up on the screen. Move the cursor on the image, the detailed information about the spot under the cursor will be displayed in the **Spot Proprieties Panel**. These include the spot ID, the associated gene name, the experimental M_w and pI , the spot area, the relative volume (the volume of the spot normalized with the total volume of the spots contained in the gel), the annotation mode

(obtained with mass spectrometry experiment or computationally deduced from image pattern matching), and the relationships with other spots.



Fig. 21 - Spot Properties Icon on the Tool Bar of the Main Window.

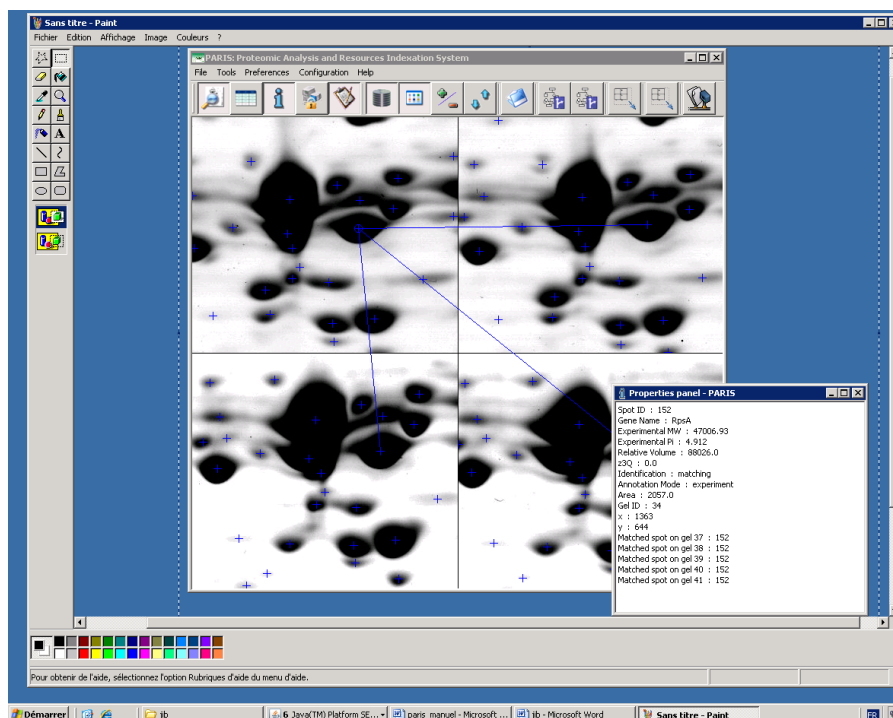


Fig. 22 - Spot Properties Panel

8. VISUAL DATA CORRECTION AND GEL ANNOTATION

It's well known that image analysis software for two-dimensional electrophoresis gel is not mature enough to be considered stable and reliable. Automatically obtained results need to be checked and validated by the biologists. **PARIS** provides the possibilities to visually check and validate data obtained with high throughput instruments. By example, you can add and remove spots, add and remove relations between spots, define and add new type of relations between spots or gels, etc.

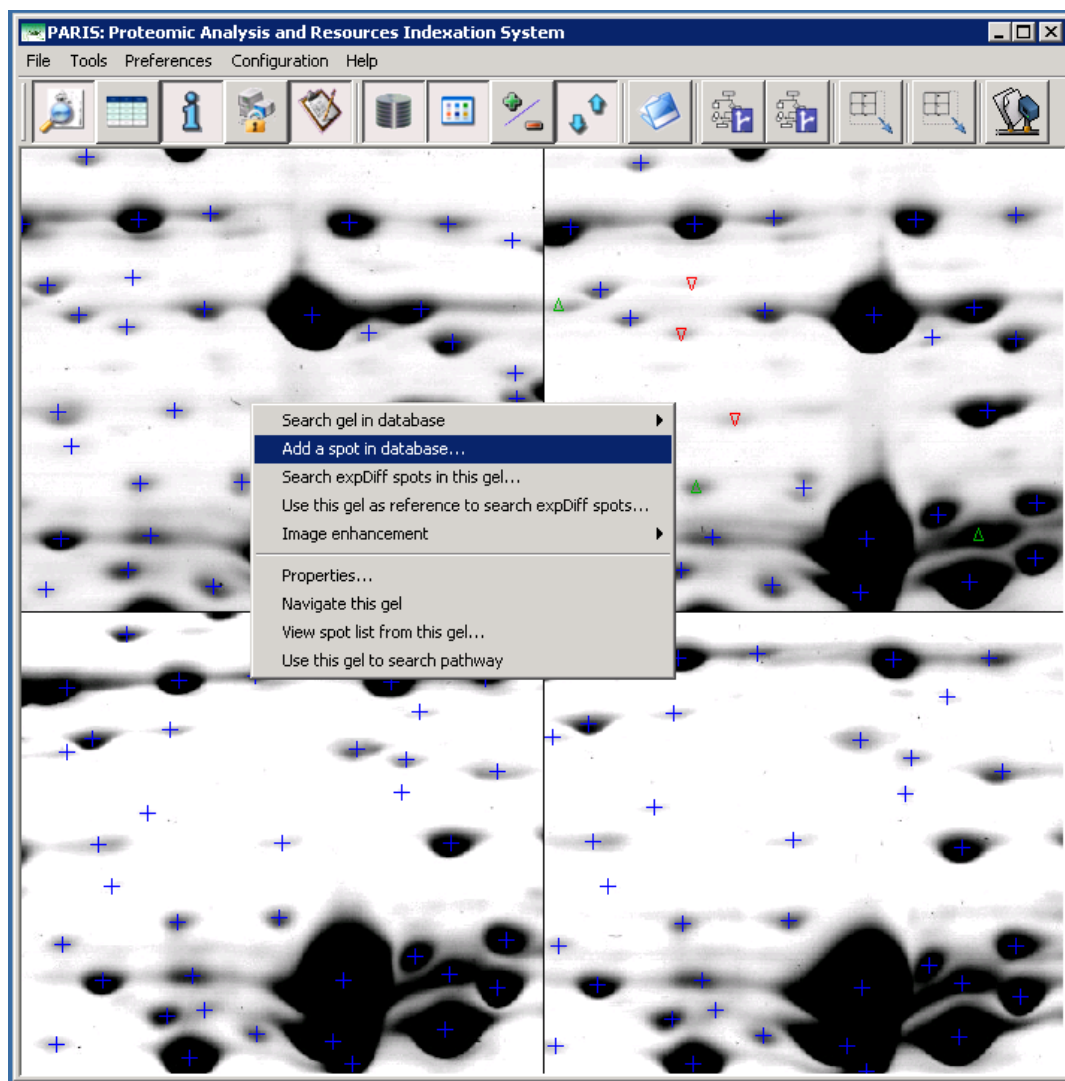


Fig. 23 - Spot addition. To add a spot, click a point on an image with the right button of the mouse and select the item “*add a spot in database*” of the pop-up list.

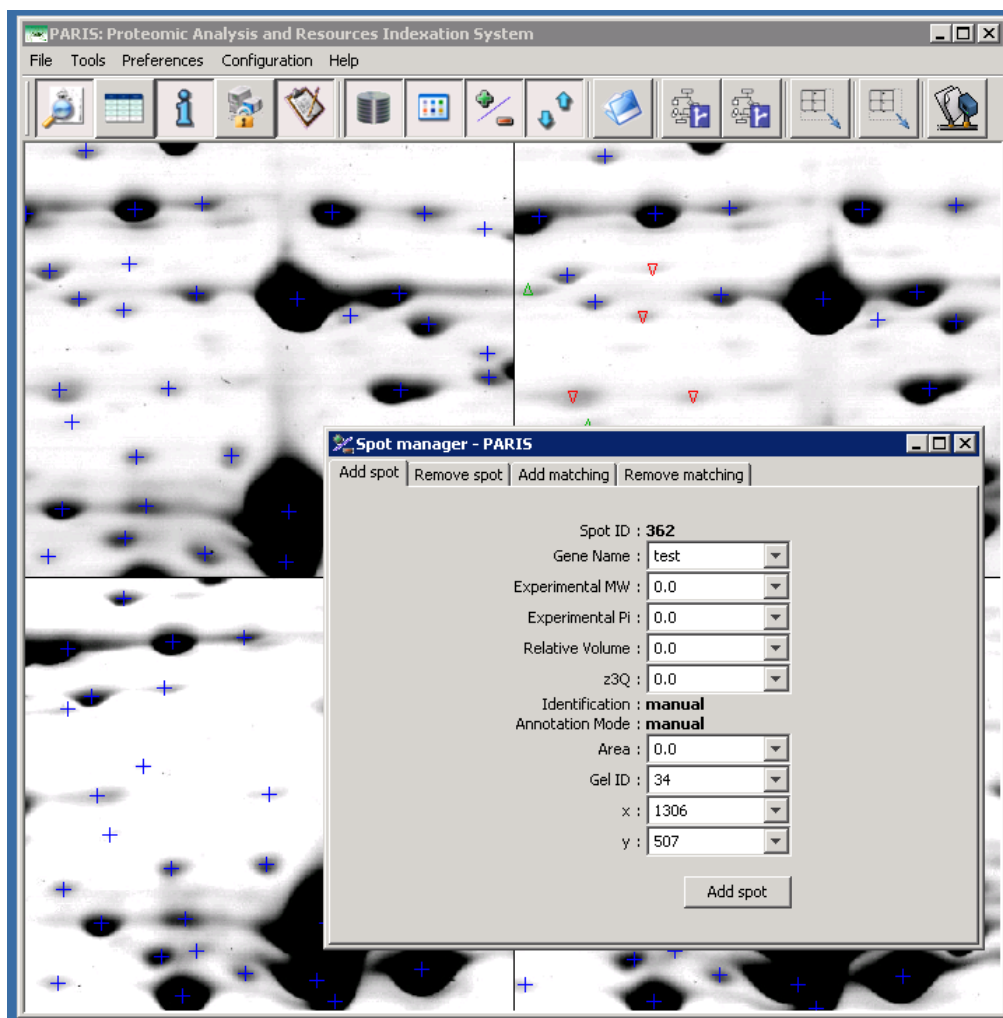
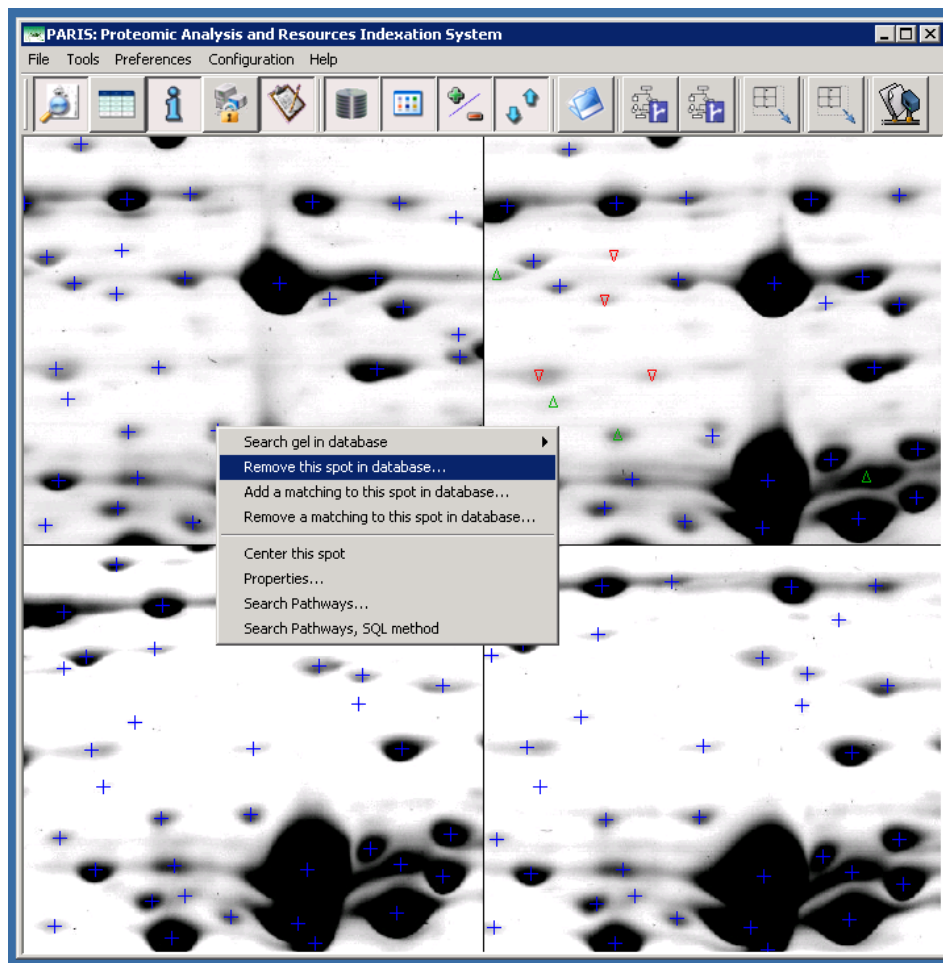
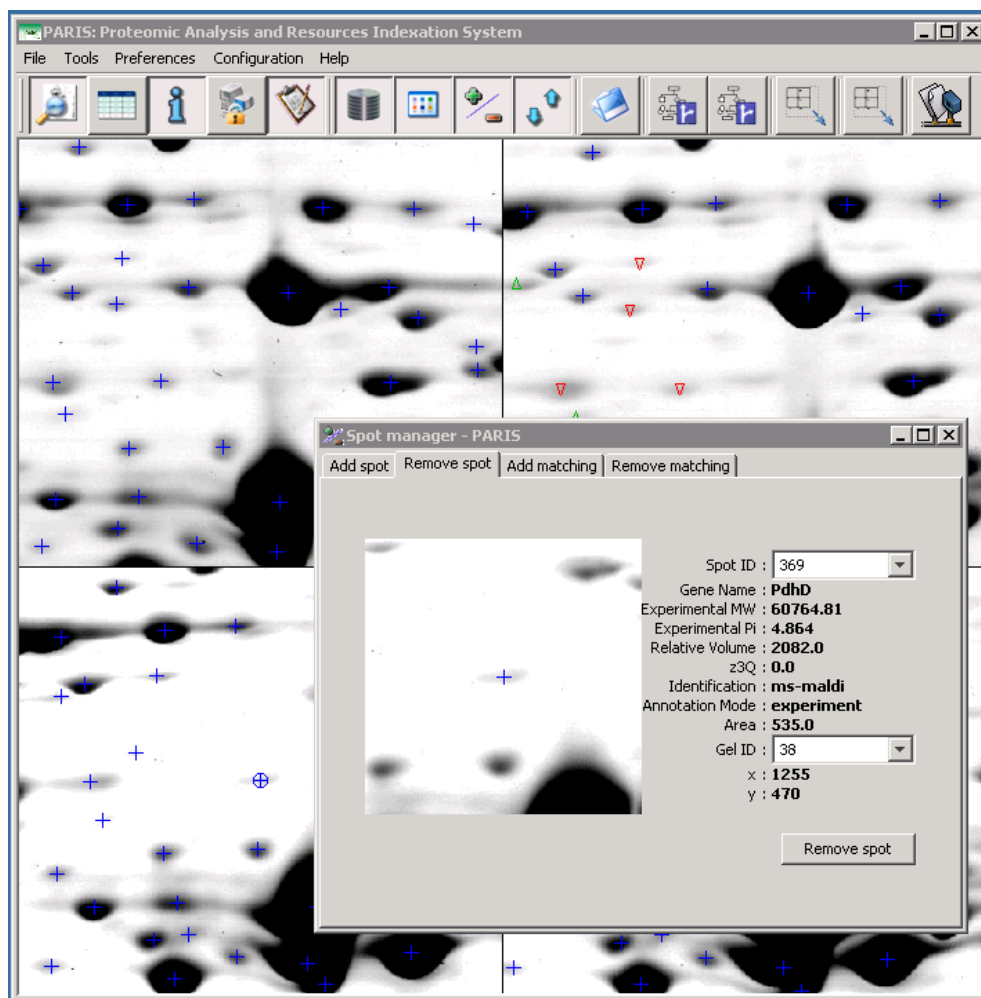


Fig. 24 - Add a new spot and store the information associated with the new spot. The manually added spot is distinguished by marking the “Annotation Mode” attribute as “manual” in the database.

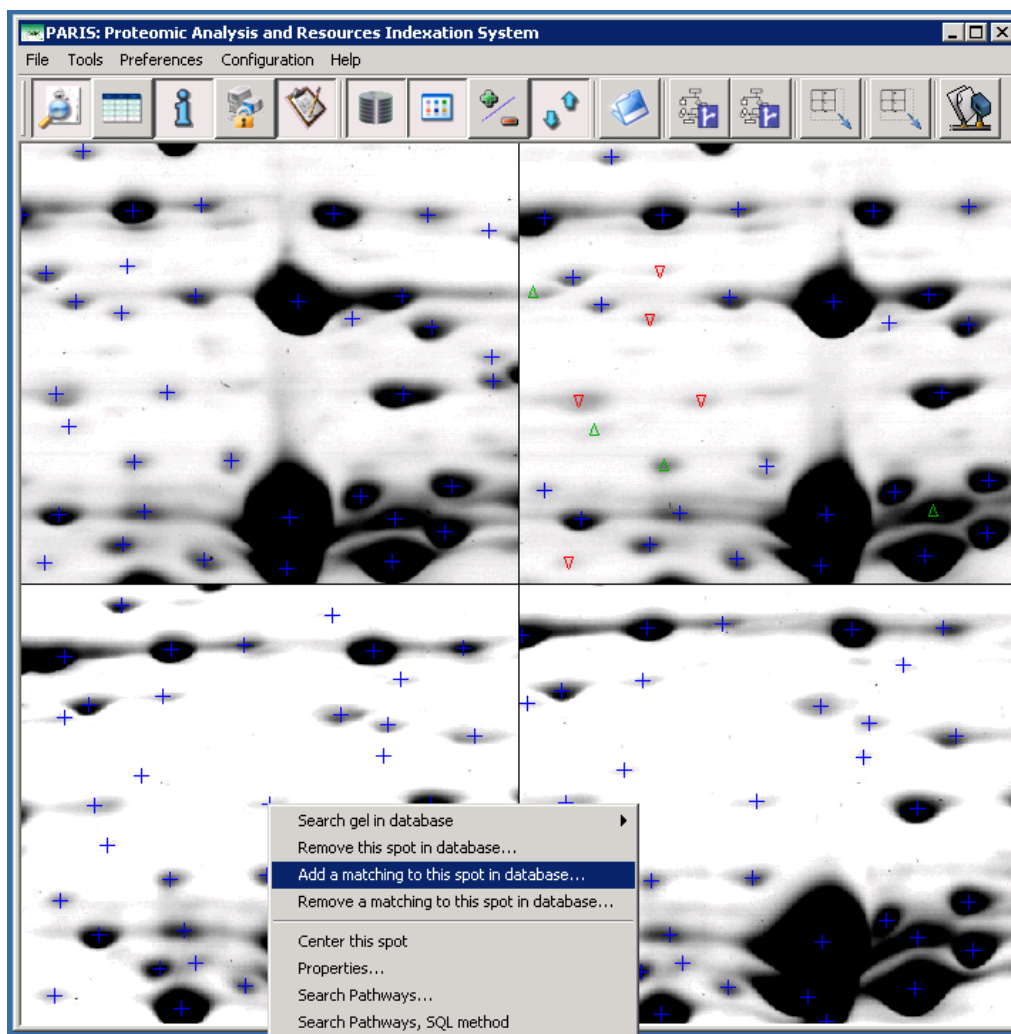


(a)

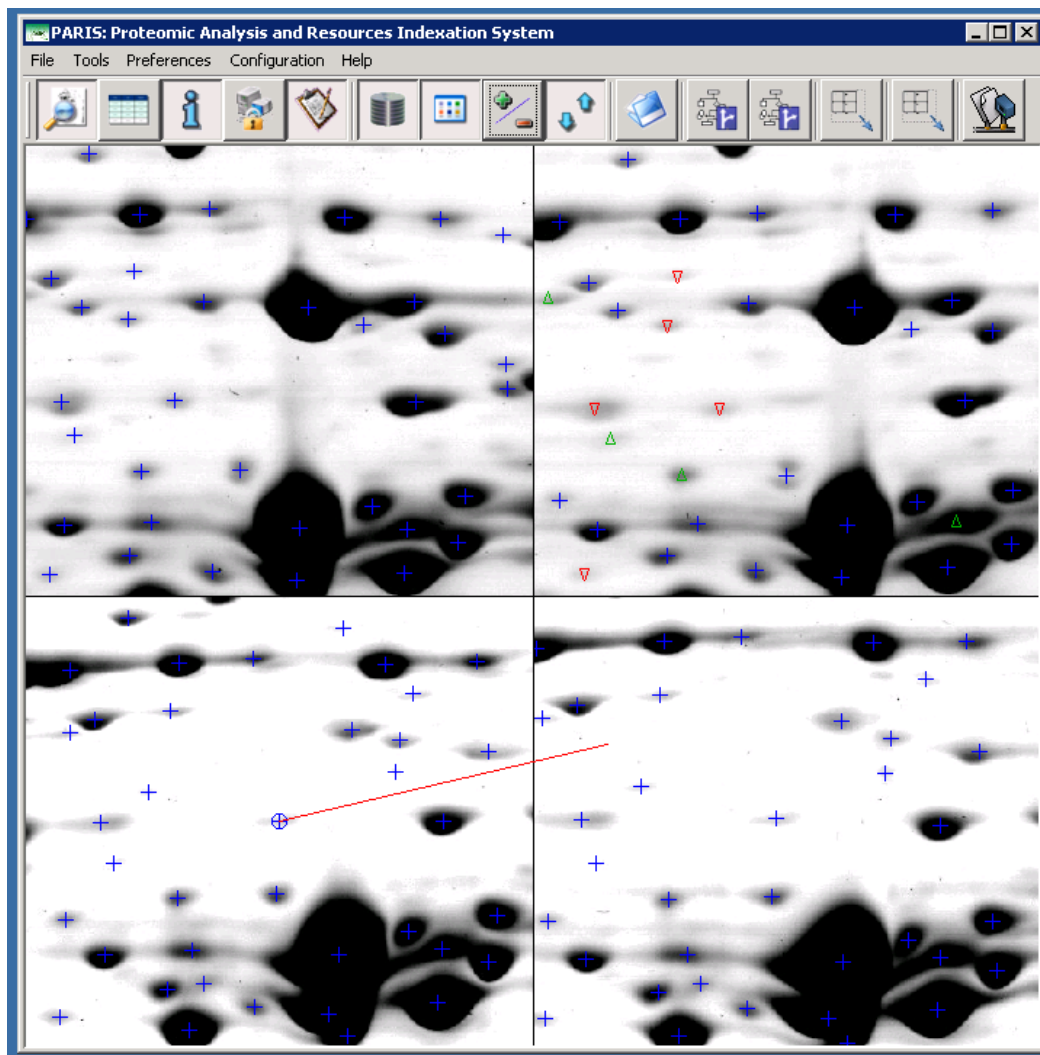


(b)

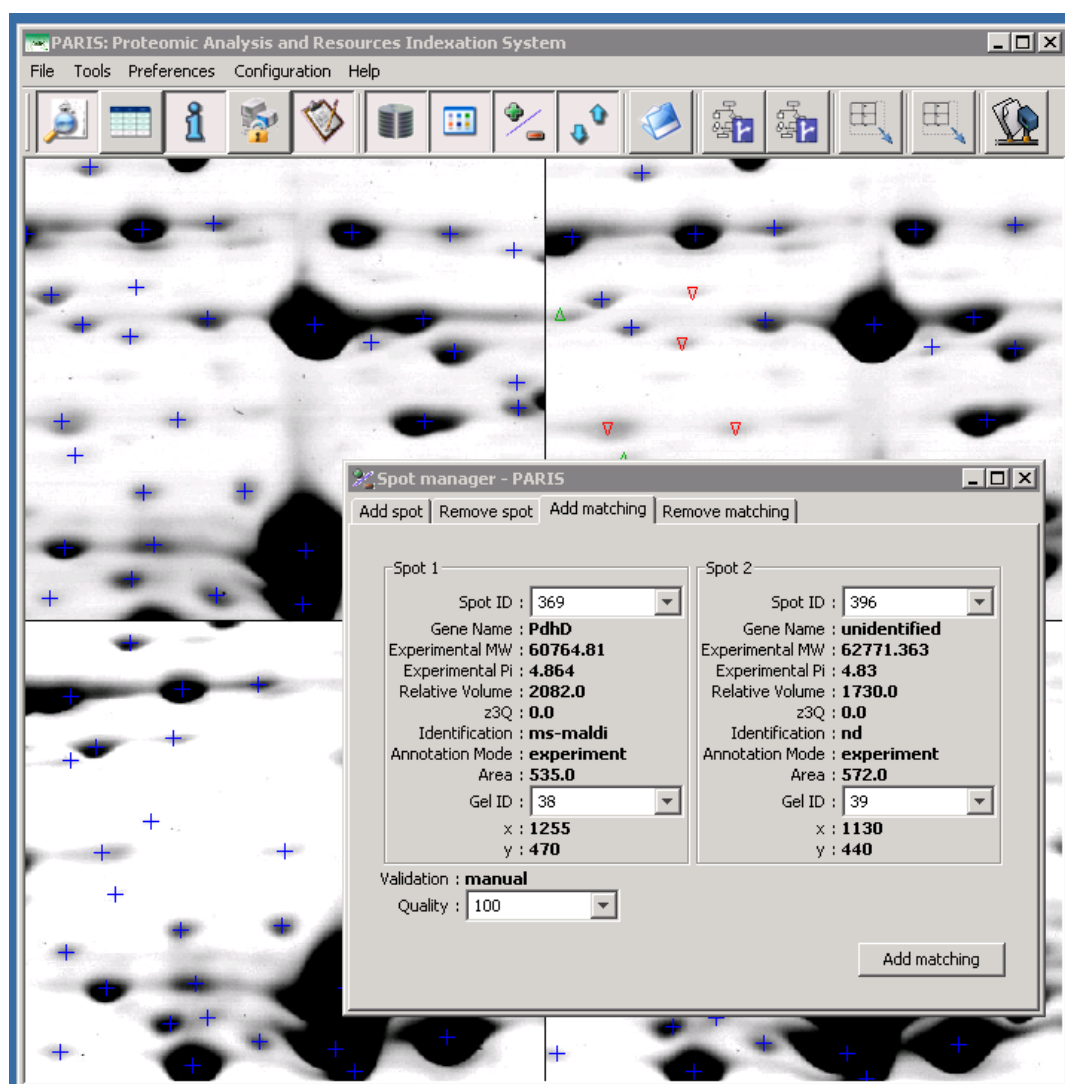
Fig. 25 - Spot removing. To remove a spot from the gel and the database, just click a spot with the right button of the mouse, and select the item of “*remove this spot from the database*” (a). A pop-up window allows you to confirm the operation (b).



(a)

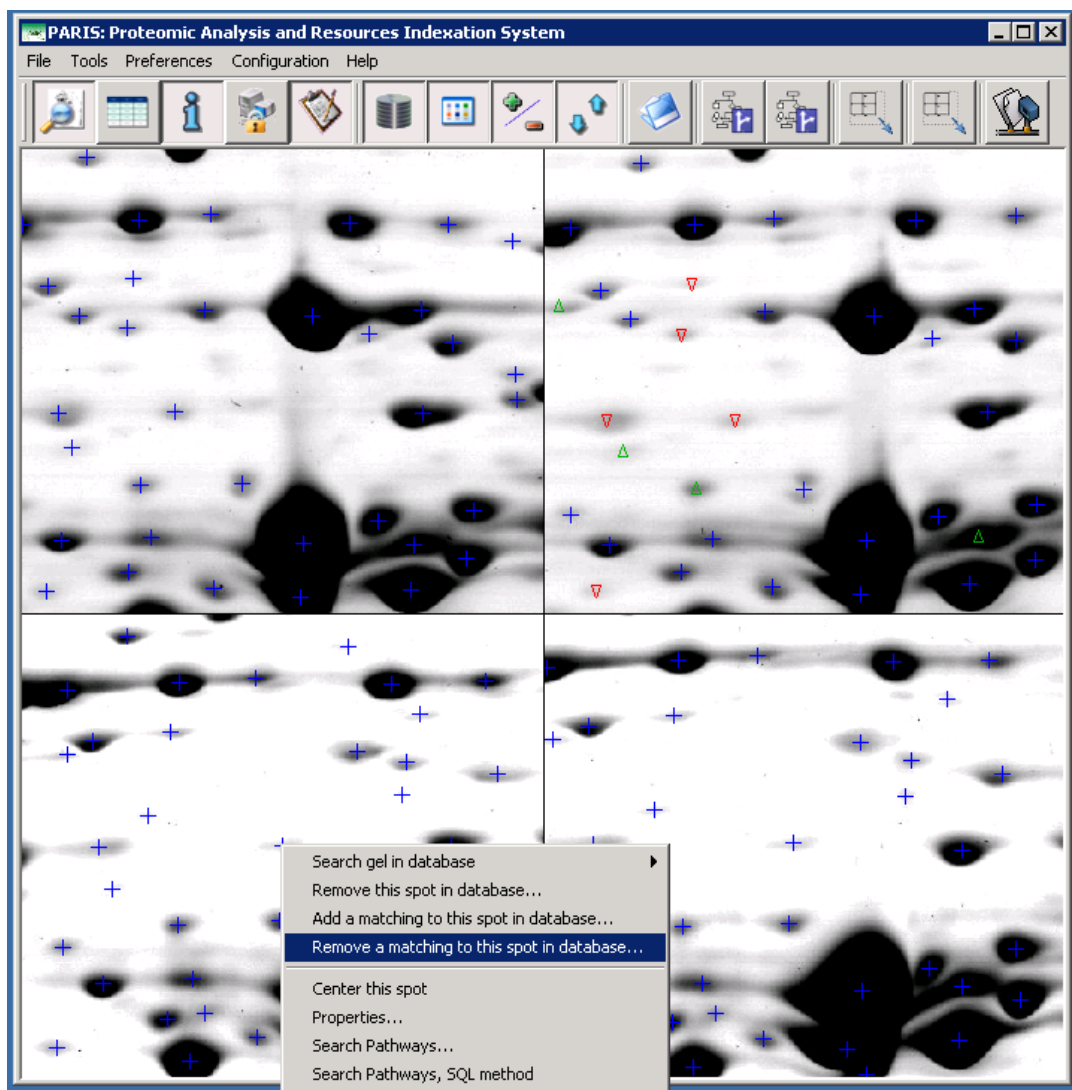


(b)

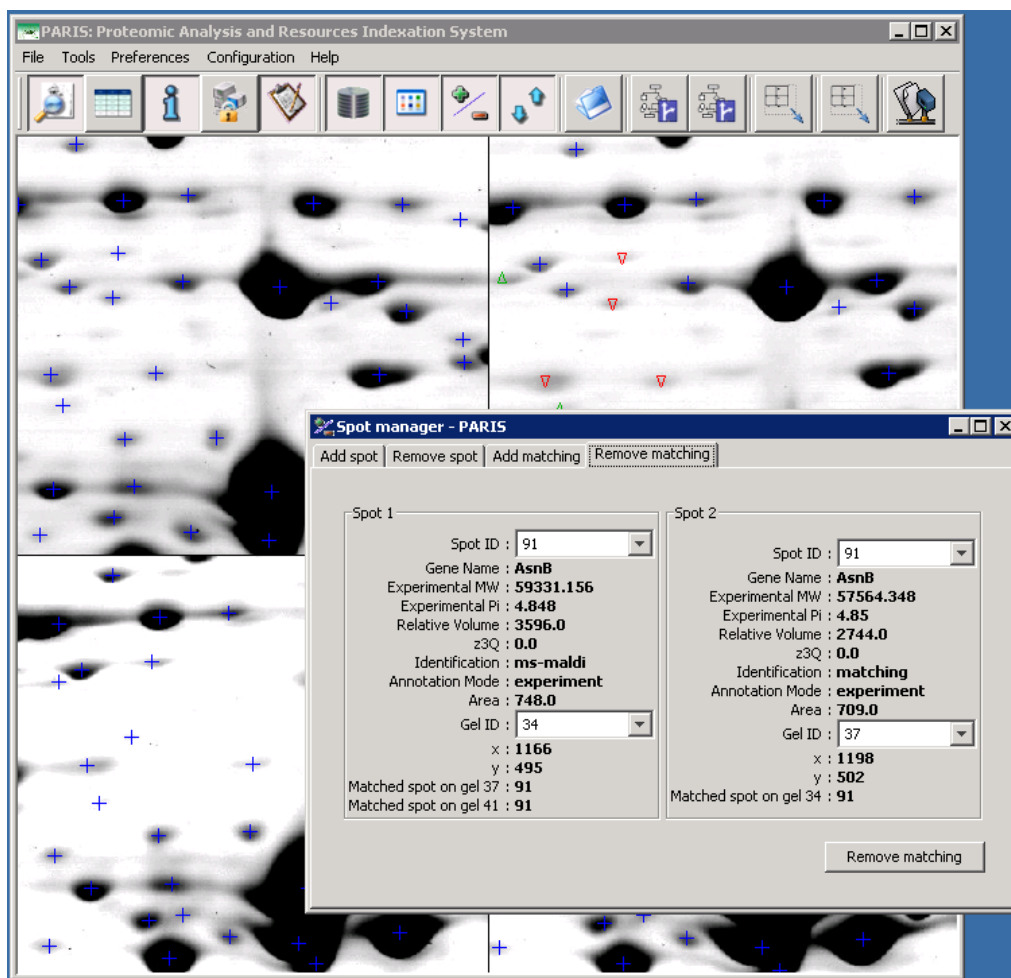


(c)

Fig. 26 - Spot relation addition. To add a new relation between two spots, click a spot with the right button of the mouse and select the item of “*add a matching to this spot*” (a). Guide the automatically drawn line to reach the destination spot (b). When arriving at the destination spot, click the right button of your mouse. A pop-up window will allow you to confirm the operation (c).



(a)



(b)

Fig. 27 - Spot relation removing. To remove a relation between two spots, click a spot with the right button, select the item of “*remove a matching of this spot from the database*” of the pop-up list, and move the cursor to follow the link to remove (a). When arriving at the destination spot, click the left button of the mouse. A pop-up window will allow you to confirm the operation (b).

9. GEL-WIDE PROTEIN DIFFERENTIAL EXPRESSION ANALYSIS

PARIS allows us to compare the protein expression levels between two gels. The comparison results can be displayed both on the image and from a list. On the image, over-expressed proteins are marked with a up-pointed green triangle and under-expressed proteins are displayed with a down-pointed red triangle.



Fig. 28 - Icon to accede the gel-wide protein differential expression analysis from the **Tool Bar** attached to the **Main Window**.

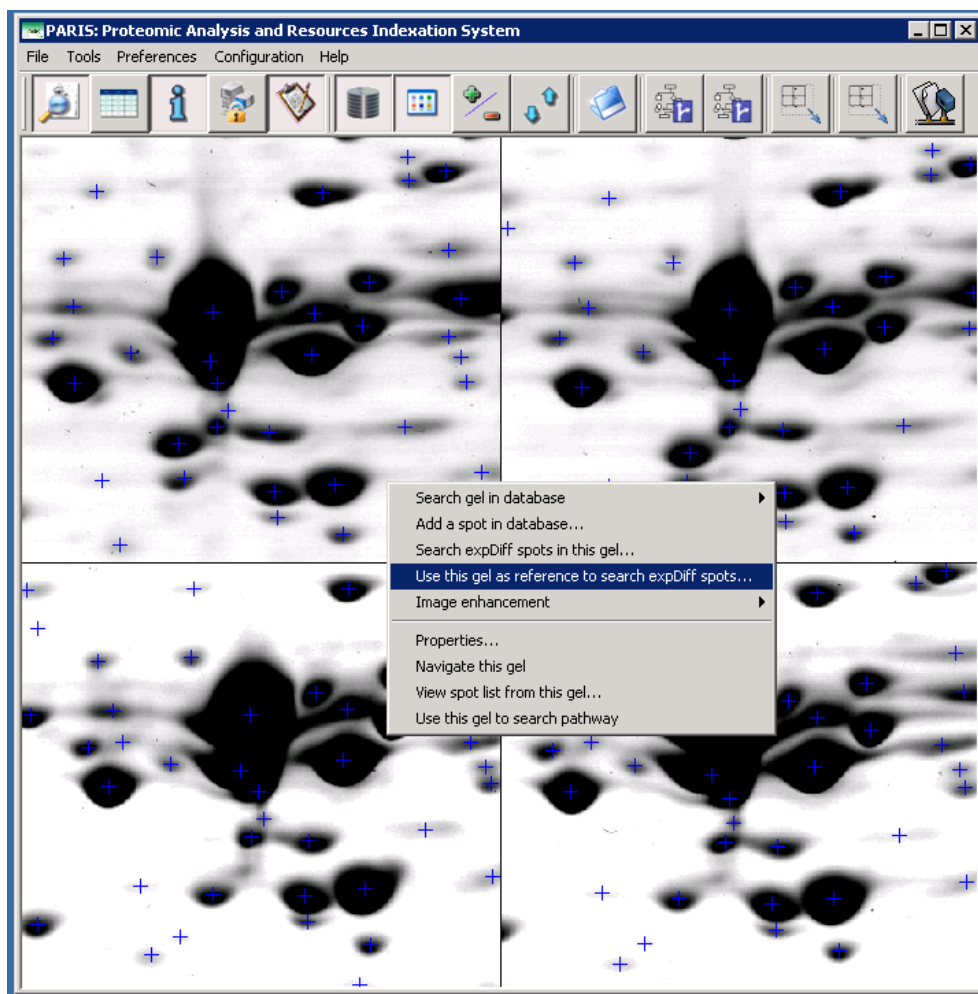


Fig. 29 - Reference gel setting for inter-gel comparison.

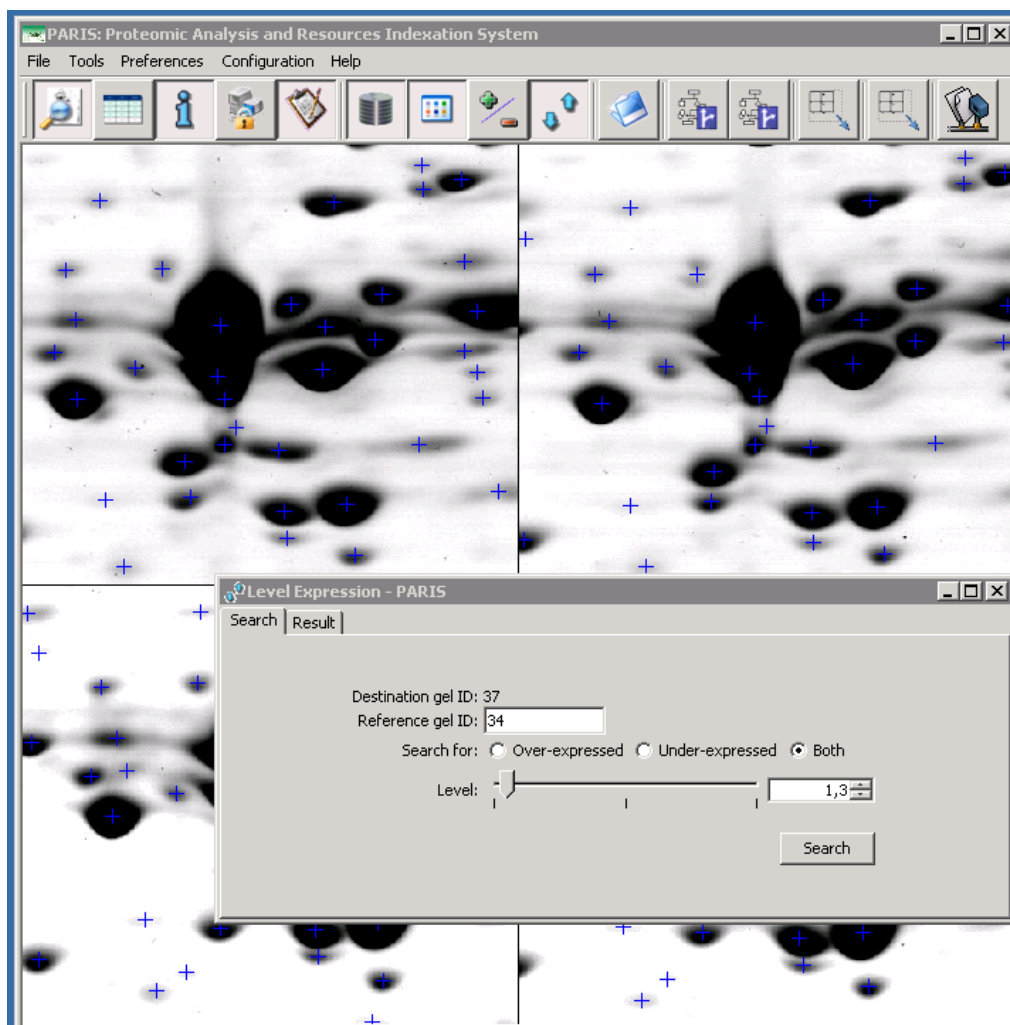


Fig. 30 - Parameter setting for gel-wide protein differential expression analysis. In this example, we can visualize the proteins 1.3 fold over-expressed, or 1.3 fold under-expressed proteins, or both between gels 37 and 34. The results will be superposed on the destination image which is the image 37 and located at the top-right frame.

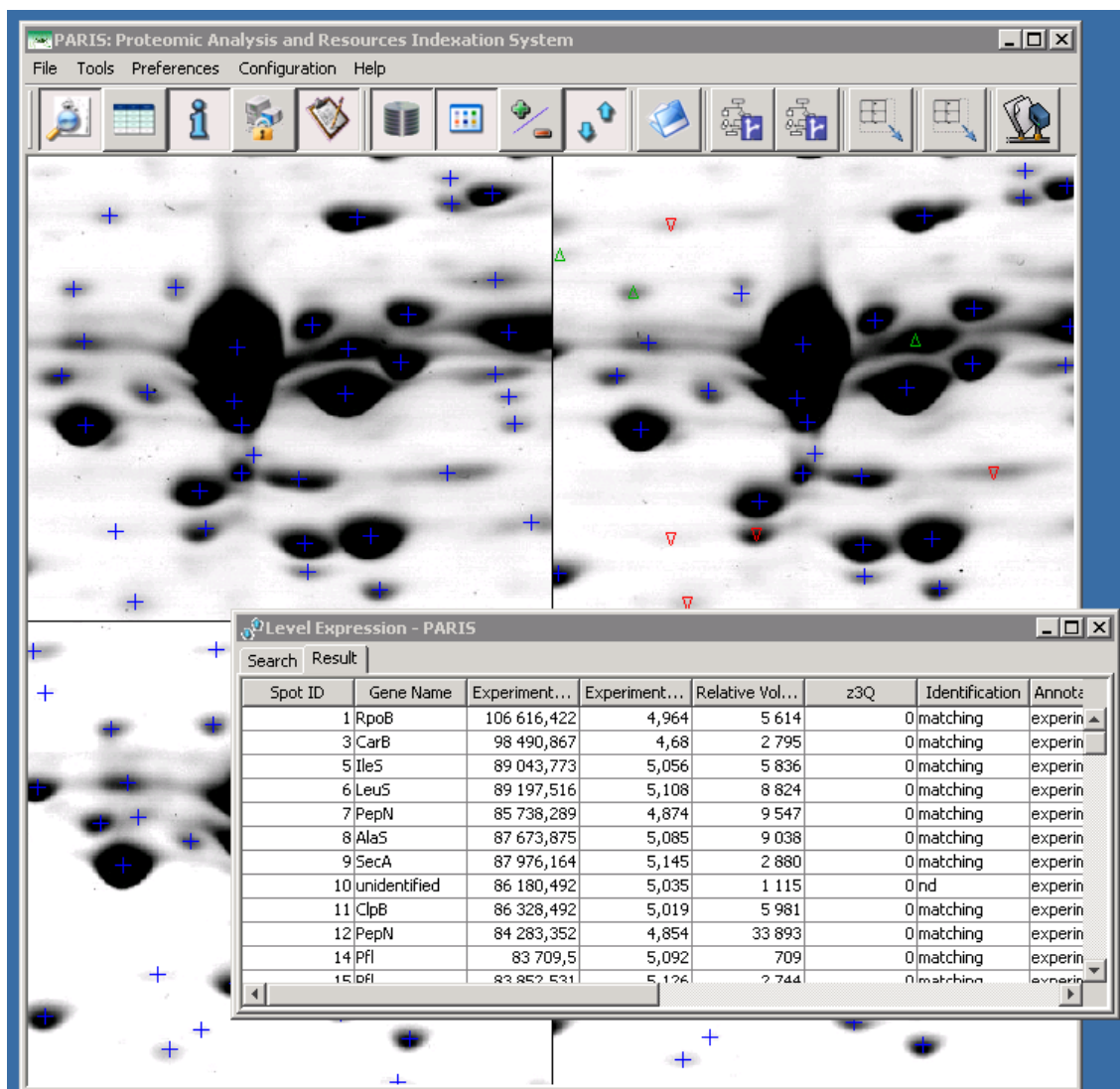


Fig. 31 - Results of gel-wide differential protein expression analysis. The results are shown on the image and as a list. On the image, over-expressed proteins are marked with an up-pointed green triangle, and the under-expressed proteins with a down-pointed red triangle.

10. INTRA/INTER GEL RELATION EXPLORATION

This set of functionalities constitutes the most important feature of **PARIS**. It provides our system with the capability to analyze data in an integrated and post-planned manner. From a set of new data, we can query the data servers for particular findings (genomic information, experimental conditions, etc.) and compare the findings with the new data. We can also annotate and analyze together the archived and new data. This helps us to confirm or on the contrary, cancel conclusions obtained previously. By grouping results from different investigations, we can expect to generate new findings.

There is no doubt that even the state-of-the-art technology in data exploration couldn't make the task automatic. Although the biologist is still the actor of this kind of exploration, we should be able to provide some computer assisted tools to ease those jobs.

PARIS allows you to visualize different relations existing among your data: both the intra and the inter-gel relations. From the menu item “*Preference*” of the **Main Window**, you can choose to display different type of relations among the spots such as: the spots matched manually by the biologist or detected automatically by the image analysis software, the spots marked with the same gene (in the biology term, this kind relation is called phosphorylation isoform since they usually correspond to different possibilities of the protein phosphorylation), etc. Notes that some terms (such as “undefined”, “unidentified”, etc.) usually used to flag the non processed spots by biologists might result in nonsense relations. **PARIS** is provided with a simple tool to prevent from this perturbation. You can specify a list of terms to prevent **PARIS** from processing the spots implied in these terms. This list can be acceded and modified from the menu “*Configuration*” of the **Main Window**.

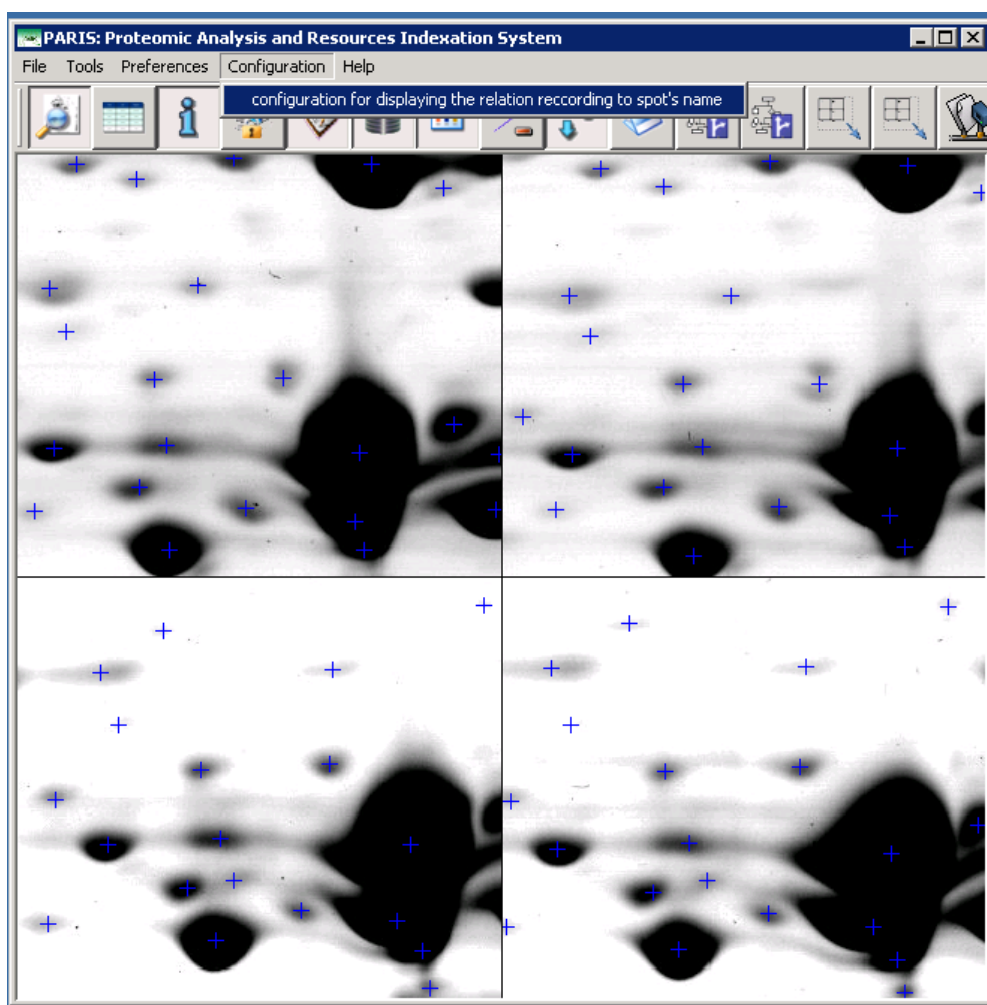


Fig. 32 - Access to the editor to specify the “non-sense” terms.

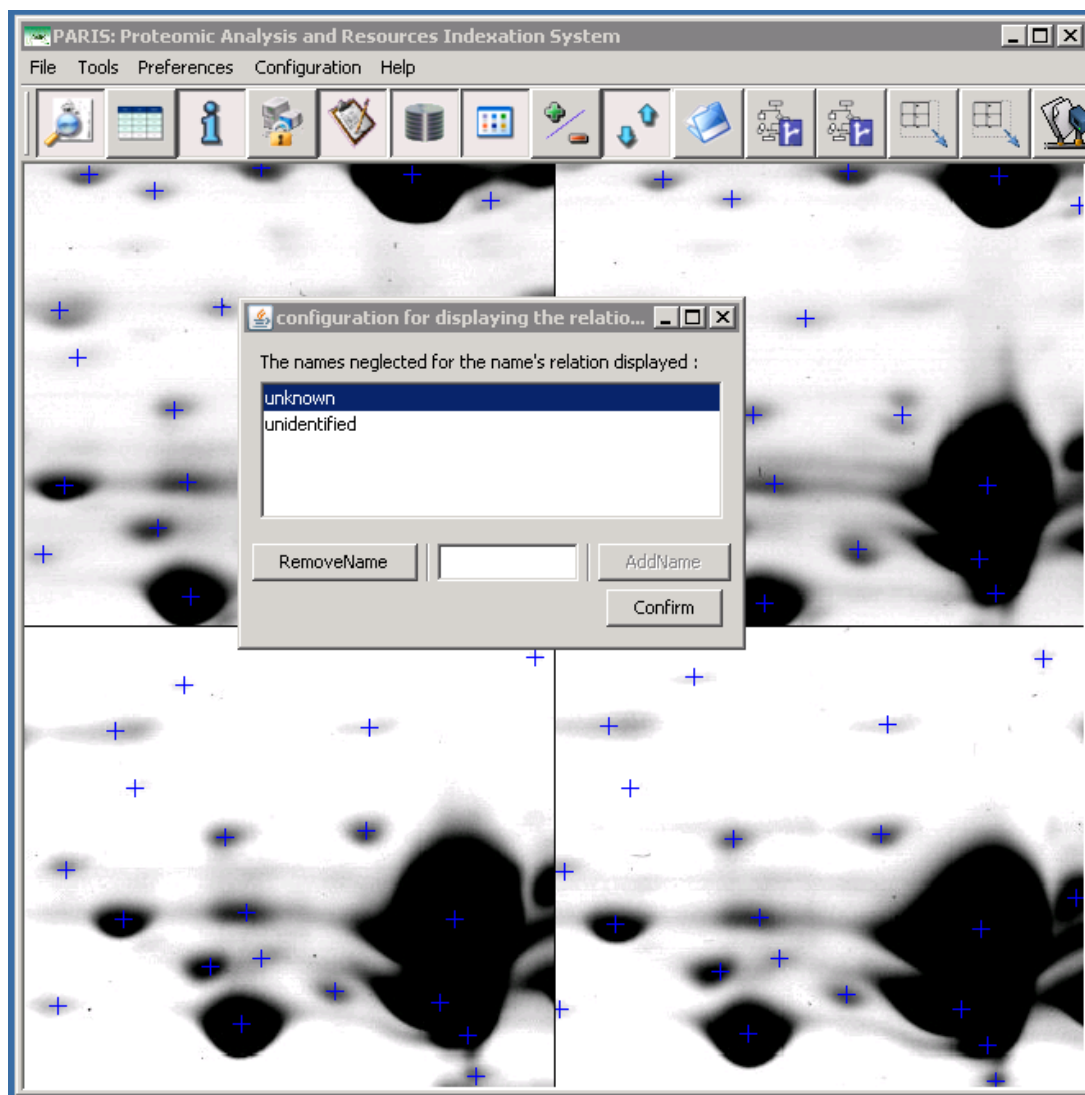


Fig. 33 - Editor for adding and removing “non-sense” terms.

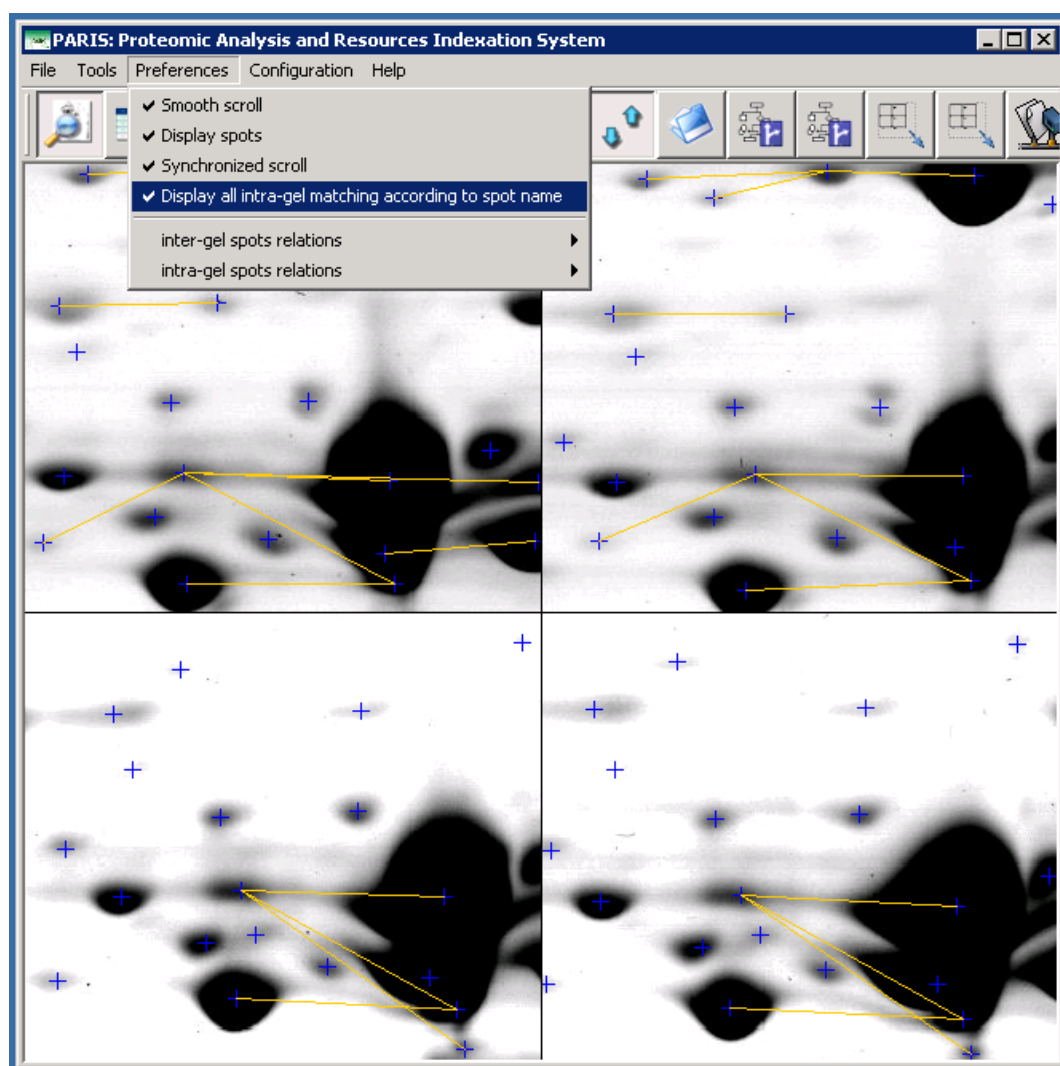


Fig. 34 - Parameter setting to visualize the protein isoforms.

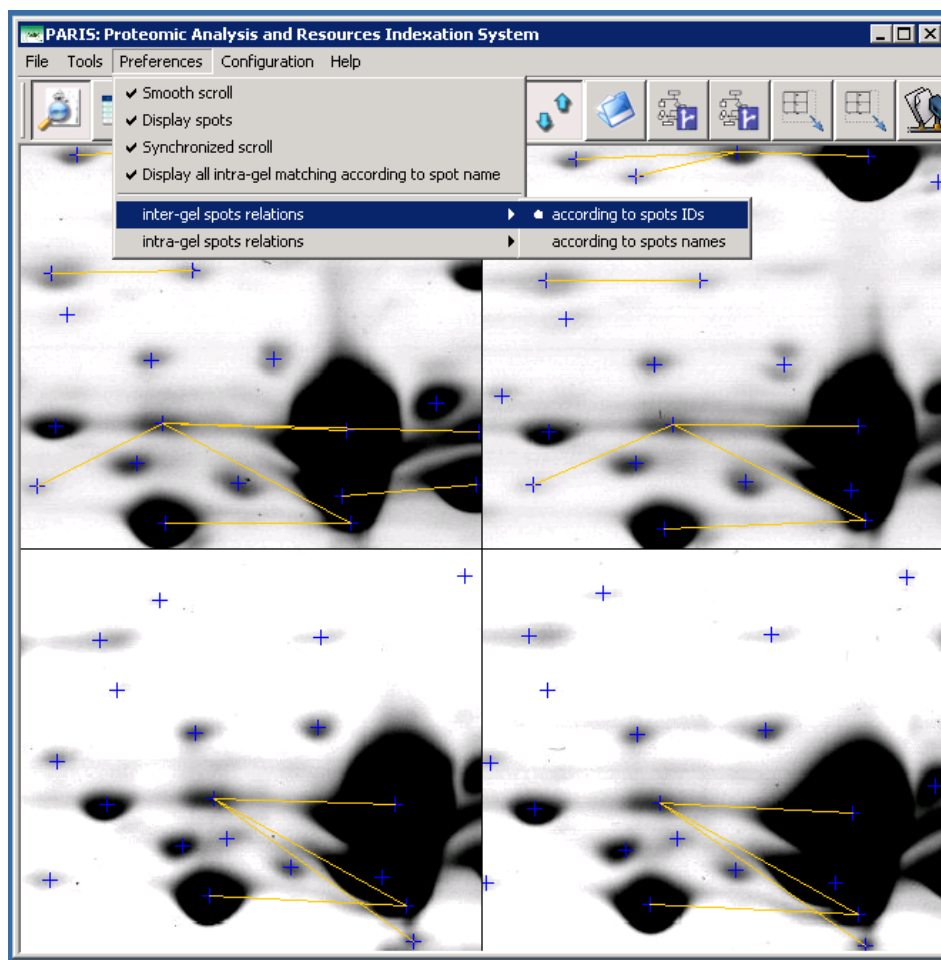


Fig. 35 - Parameter setting to visualize the spots matched among different gels. Once the option has been turned on, we can visualize the matching relations among spots as shown in the **Fig. 36**.

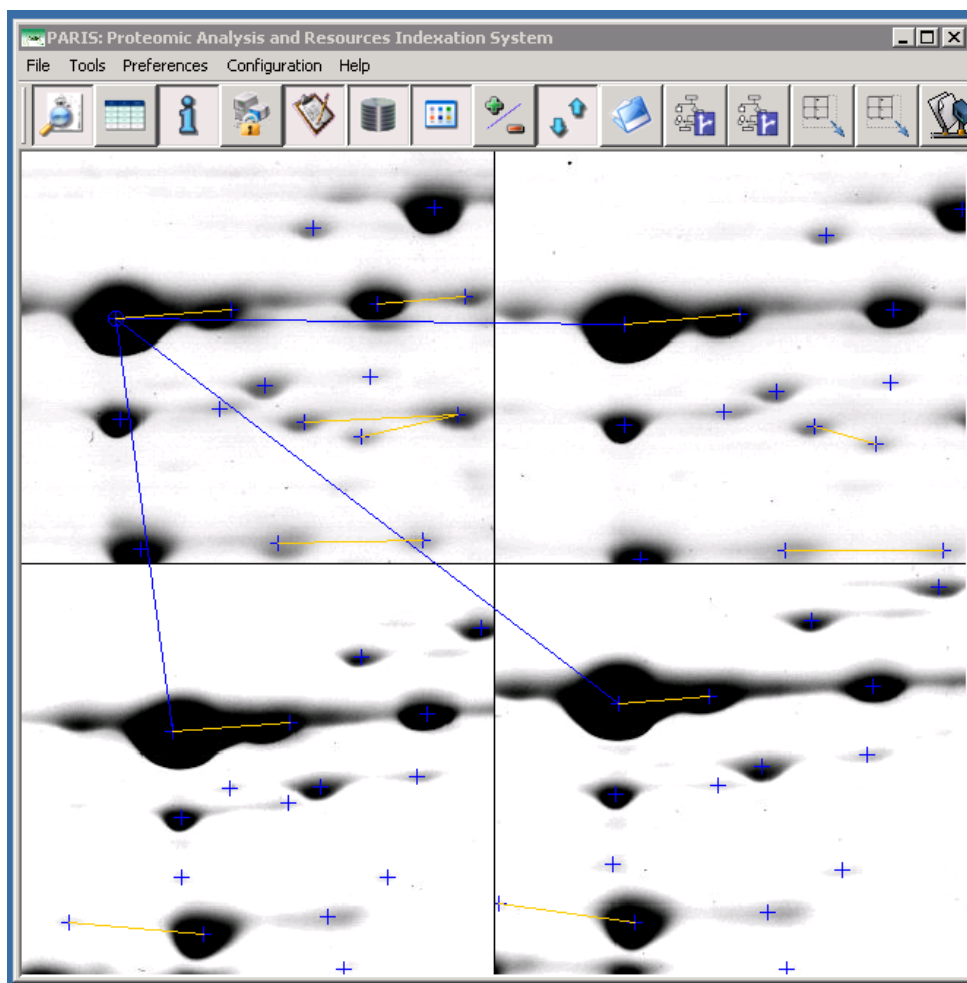


Fig. 36 - Visualization of the inter-gel matching relations between spots. Yellow links indicate protein isoform relationships, and blue links indicate the matching relations among spots either manually annotated by the biologist or automatically detected with image analysis software.

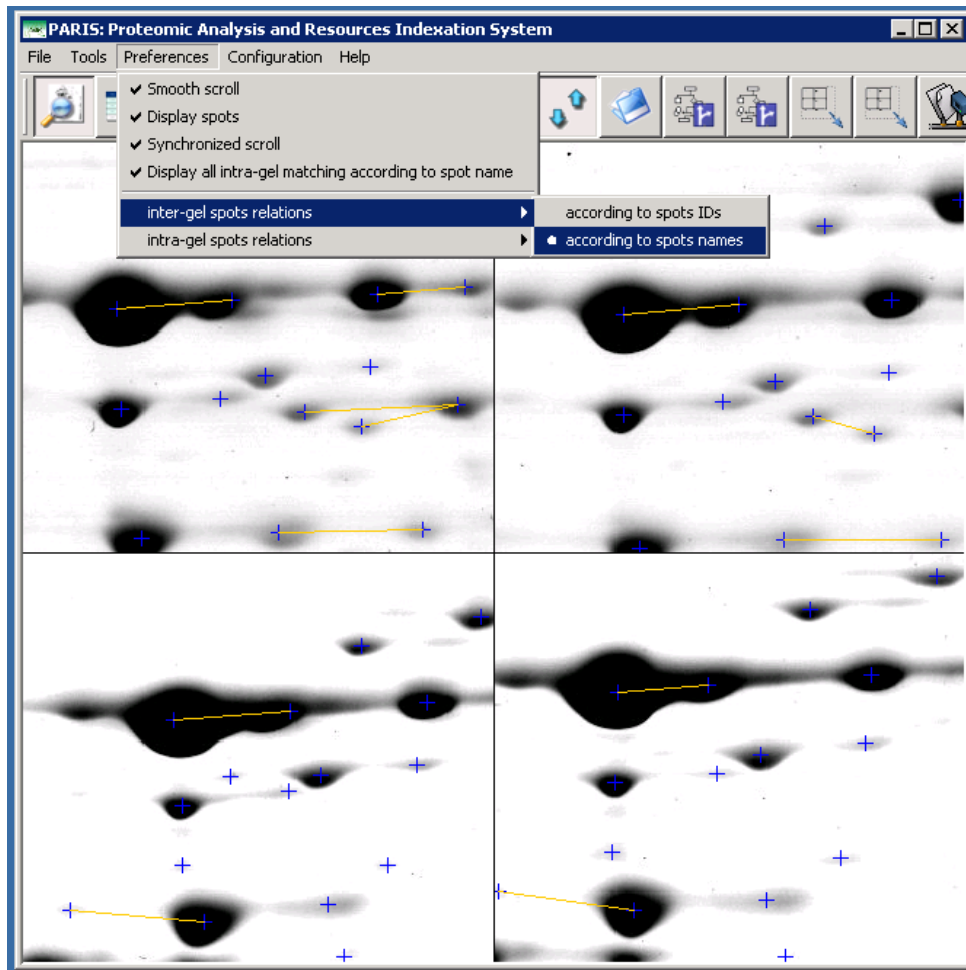


Fig. 37 - Parameter setting for visualizing the inter-gel gene name relationships among spots. Once this option has been turned on, we can visualize the matching between protein isoform patterns observed in different gels as shown in **Fig. 38**. This also gives us a tool to link data produced by different experimenters or obtained in different biological contexts.

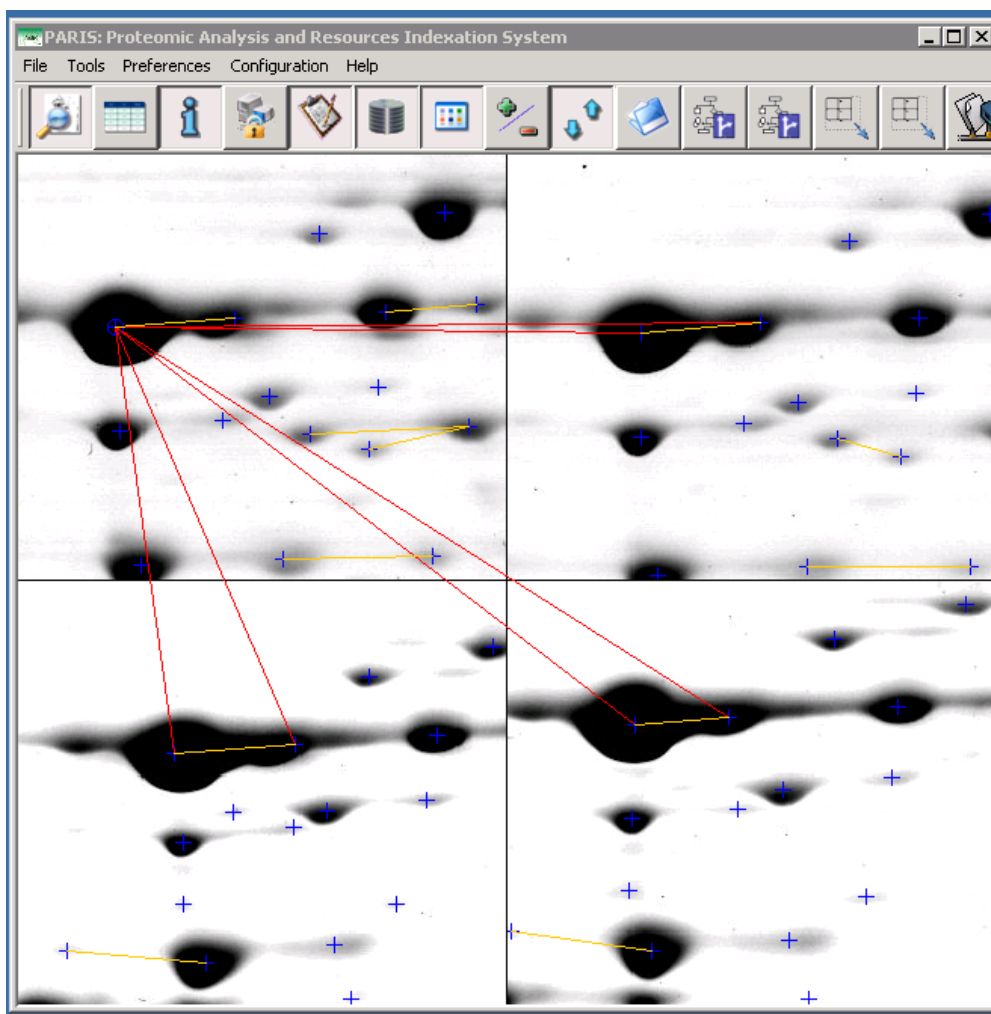


Fig. 38 - Visualization of the relations among patterns formed by different protein isoforms and observed in different gels.

11. GEL ANALYSIS IN THE CONTEXT OF THE METABOLIC PATHWAY

This function consists in exploring features which can be useful, and does not have real existence in the database, but they can be derived in association with other publically available proteomics resources such as **KEGG**, **SWISS-PROT**, etc. It is about suggestions made from configurations or relationships discovered by synthesizing different types of information found in private and public resources. Herein, we illustrate a situation of pathway integration in which, given a protein and a gel, we synthesize an image to compare the *in silico* calculated and experimentally found positions of the co-regulated proteins implicated in a metabolic pathway. This gives us a way to control our experimental data with some theoretical ones, if bias found, to make deeper investigation on where and why the *in silico* and experimental data are not consistent, and therefore to make benefit from other proteomics data for our own experiment design.

This function is achieved by a series of basic database queries. Given a protein, we first search from **KEGG** all pathways containing the protein. For each found pathway, we then

identify the co-regulated proteins, and calculate their theoretical pI and Mw values, and finally project these values on to the original gel image. The achievement of this process requires to explore data contained in several public data resources such as **GENBANK**, **UniPROT** and **trEMBL**.

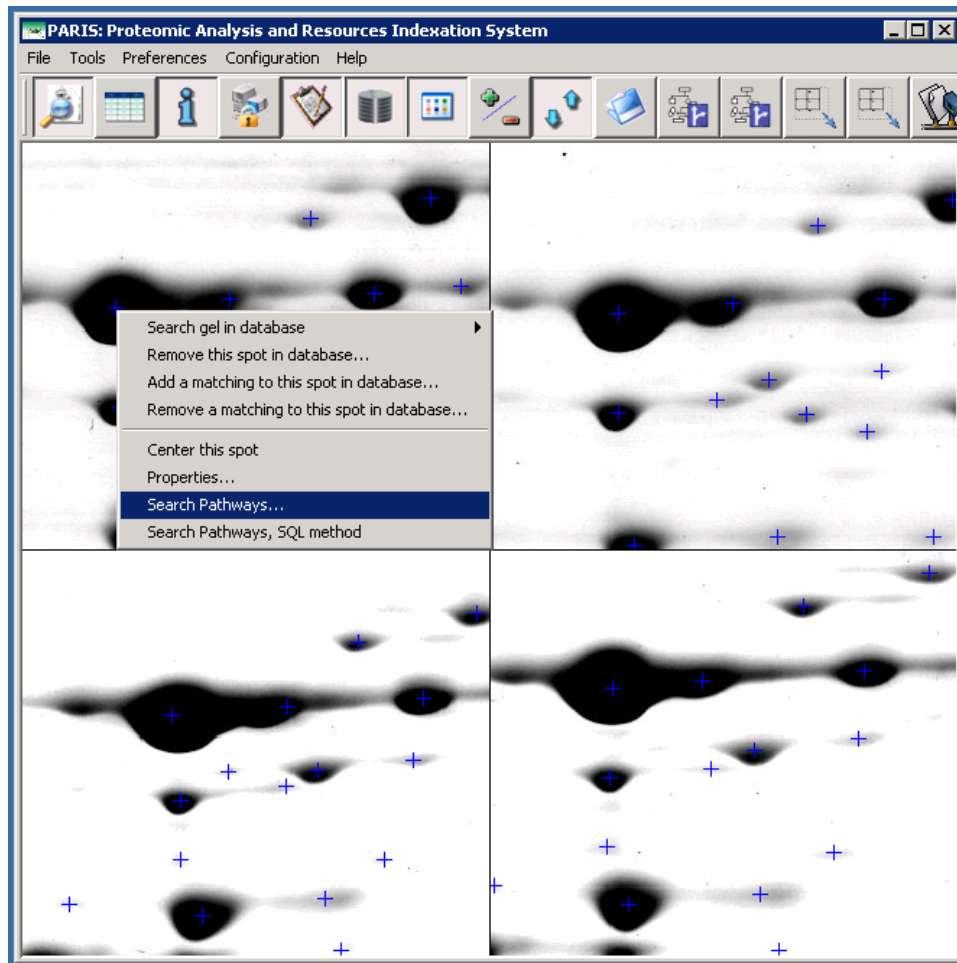


Fig. 39 - To analyse a protein in its metabolic pathway context, just click on a spot with the right button of your mouse and select the item “*Search pathways*” from the pop-up list.

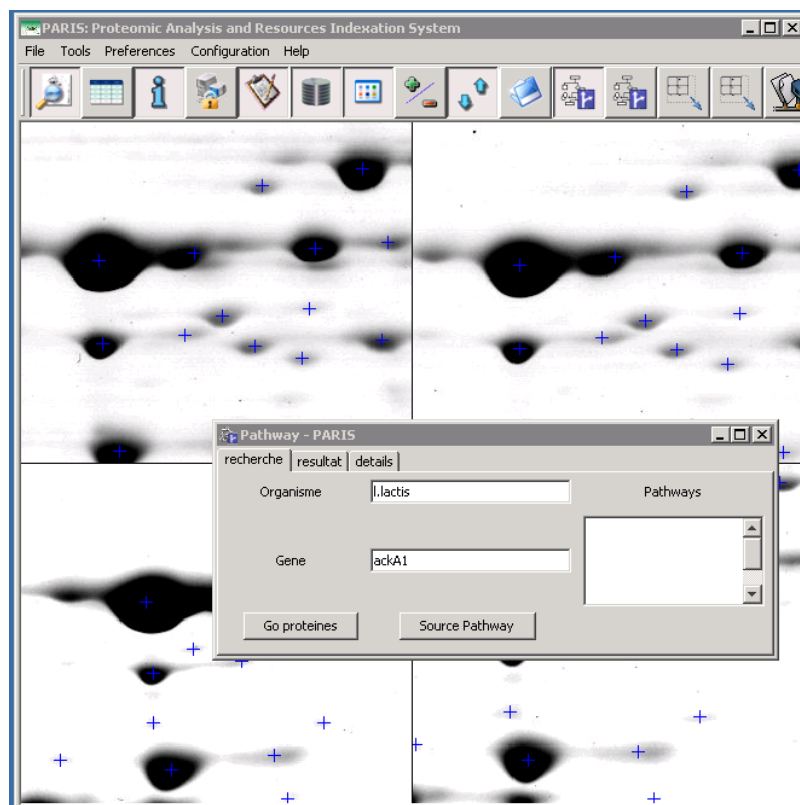


Fig. 40 - Integration of the pathway information about a gene from KEGG.

12. DATA ENTRY

The process to upload gel based experimental data into the server works in three stages. The first is preparing the data to upload. In the second stage users fill interactively some forms to complete the data with non-structured information. In the third stage information will be sent to the server by batch.

```

Terminal - Bananier
Session  Édition  Affichage  Signets  Configuration  Aide

-bash-3.00$ ls -l
total 74557
-rwxrwxrwx 1 6364 bmjj 13655 nov 12 2006 match.csv*
-rwxrwxrwx 1 6364 bmjj 28169 nov 12 2006 p2_ante_081204_1a_23kiaf2.csv*
-rw-r--r-- 1 6364 bmjj 1987490 nov 14 2006 p2_ante_081204_1a_23kiaf2.jpeg
-rwxrwxrwx 1 6364 bmjj 10937348 nov 12 2006 p2_ante_081204_1a_23kiaf2.tif*
-rw-r--r-- 1 6364 bmjj 29987 nov 12 2006 p2_ante_171104_1a_23kiaf2.csv
-rw-r--r-- 1 6364 bmjj 1983642 nov 14 2006 p2_ante_171104_1a_23kiaf2.jpeg
-rw-r--r-- 1 6364 bmjj 10920716 nov 12 2006 p2_ante_171104_1a_23kiaf2.tif
-rw-r--r-- 1 6364 bmjj 34127 nov 12 2006 p2_ante_171104_1b_rv4049af2.csv
-rw-r--r-- 1 6364 bmjj 2039341 nov 14 2006 p2_ante_171104_1b_rv4049af2.jpeg
-rw-r--r-- 1 6364 bmjj 11038530 nov 12 2006 p2_ante_171104_1b_rv4049af2.tif
-rw-r--r-- 1 6364 bmjj 30379 nov 12 2006 p2_ante_171104_2b_rv4049af1.csv
-rw-r--r-- 1 6364 bmjj 2000747 nov 14 2006 p2_ante_171104_2b_rv4049af1.jpeg
-rw-r--r-- 1 6364 bmjj 10840064 nov 12 2006 p2_ante_171104_2b_rv4049af1.tif
-rw-r--r-- 1 6364 bmjj 38549 nov 12 2006 p2_ante_200105_1a_23kiaf1.csv
-rw-r--r-- 1 6364 bmjj 1320095 nov 14 2006 p2_ante_200105_1a_23kiaf1.jpeg
-rw-r--r-- 1 6364 bmjj 10840238 nov 12 2006 p2_ante_200105_1a_23kiaf1.tif
-rw-r--r-- 1 6364 bmjj 35781 nov 12 2006 p2_ante_200105_1b_rv4049af1.csv
-rw-r--r-- 1 6364 bmjj 1274672 nov 14 2006 p2_ante_200105_1b_rv4049af1.jpeg
-rw-r--r-- 1 6364 bmjj 10840238 nov 12 2006 p2_ante_200105_1b_rv4049af1.tif
-bash-3.00$

```

Fig. 41 - Directory containing data to upload.

All data generated by the image analysis software should be put in a unique directory, and this directory should never contain any other kind of user data. **Fig. 41** illustrates an example of the directory used to upload the data which contains 6 gels. Each gel is concerned with three files: the original tiff image, the jpeg thumbnail obtained by reducing the original tiff image in size, and the list of spots detected on the gel. The file containing the list of detected spots should be in CSV format which can be generated from any form processing software such as Microsoft Excel. It should be composed of six columns: the spot id; the x coordinate of the spot; the y coordinate of the spot; the experimental *M_w*; the experimental *pI*; the normalized spot volume; the name of the gene identified from the spot; other genes eventually associated with the spot (we can specify up to three genes for each spot); the method used for the gene identification; the spot area. The inter gel spot matching should be defined in a file named “*match*” which is composed of as many columns as the number of gels to upload. The first line specifies the name of the corresponding gel image, and each of the following line contains the spot matching correspondence detected from the gels. A missing value means that there is no spot matching for the corresponding gel. By example, a matching among the spot number 4 of gel p2_ante_200105_1a_23kiaf1.tif, the spot number 8 of gel p2_ante_081204_1a_23kiaf2.tif, the spot number 422 of gel p2_ante_171104_1a_23kiaf2.tif, the spot number 14 of gel p2_ante_171104_2b_rv4049af1.tif, the spot number 23 of gel p2_ante_171104_1b_rv4049af2.tif and the spot number 7 of gel p2_ante_200105_1b_rv4049af1.tif, should be specified as follows: “4; 8; 422; 14; 23; 7” with the first line of the file defined as p2_ante_200105_1a_23kiaf1.tif;

p2_ante_081204_1a_23kiaf2.tif;	p2_ante_171104_1a_23kiaf2.tif;
p2_ante_171104_2b_rv4049af1.tif;	p2_ante_171104_1b_rv4049af2.tif;
p2_ante_200105_1b_rv4049af1.tif;	

A matching among the spot number 4 of gel p2_ante_200105_1a_23kiaf1.tif and the spot number 422 of gel p2_ante_171104_1a_23kiaf2.tif should be specified as follows: “4; ; 422; ; ;” with the first line unchanged.

The user interface for data uploading is divided into two panels, as indicated in Fig. 42. The **Working Panel** allows you to input unstructured data of the experiment and check and modify the input data. The **Work Flow Panel** allows you to open pages in the **Working Panel** and to process different jobs.

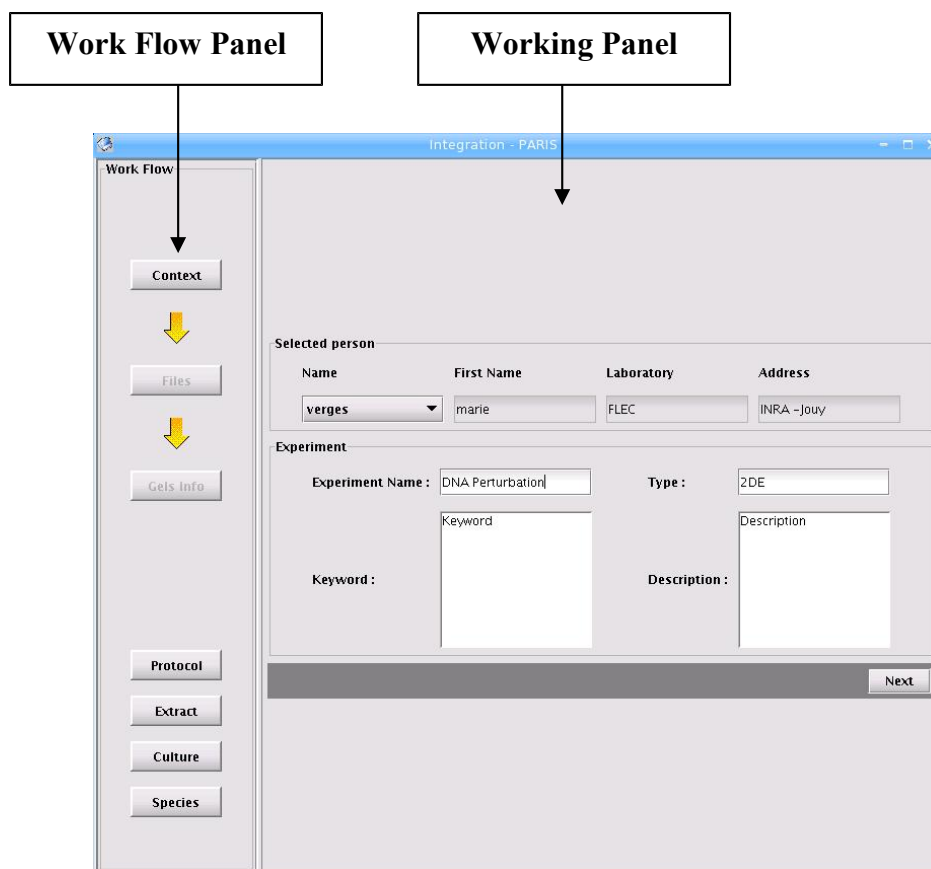


Fig. 42 - User interface to upload the experimental data to the data server.

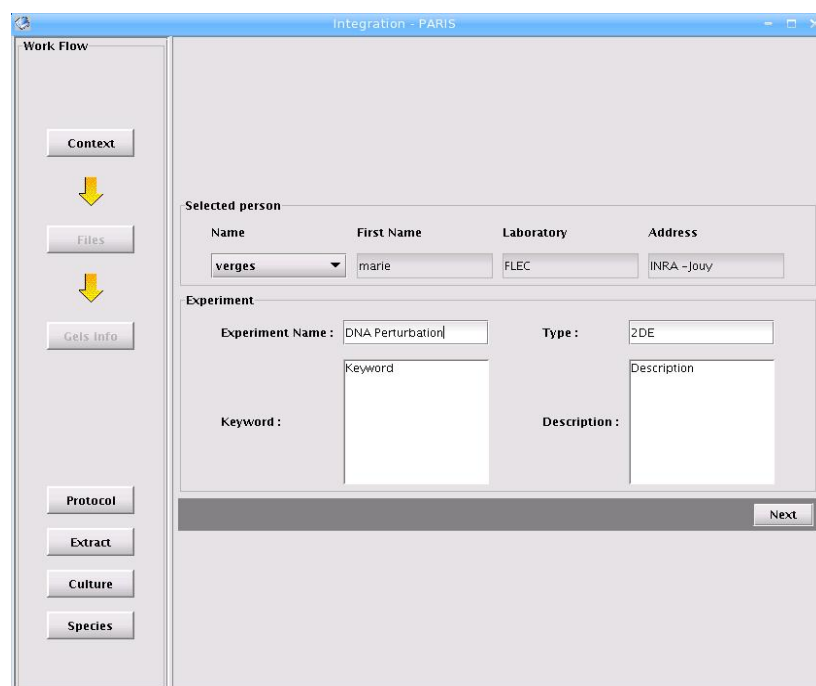


Fig. 43 - Interface used to input information related to the biological context of the experiment.

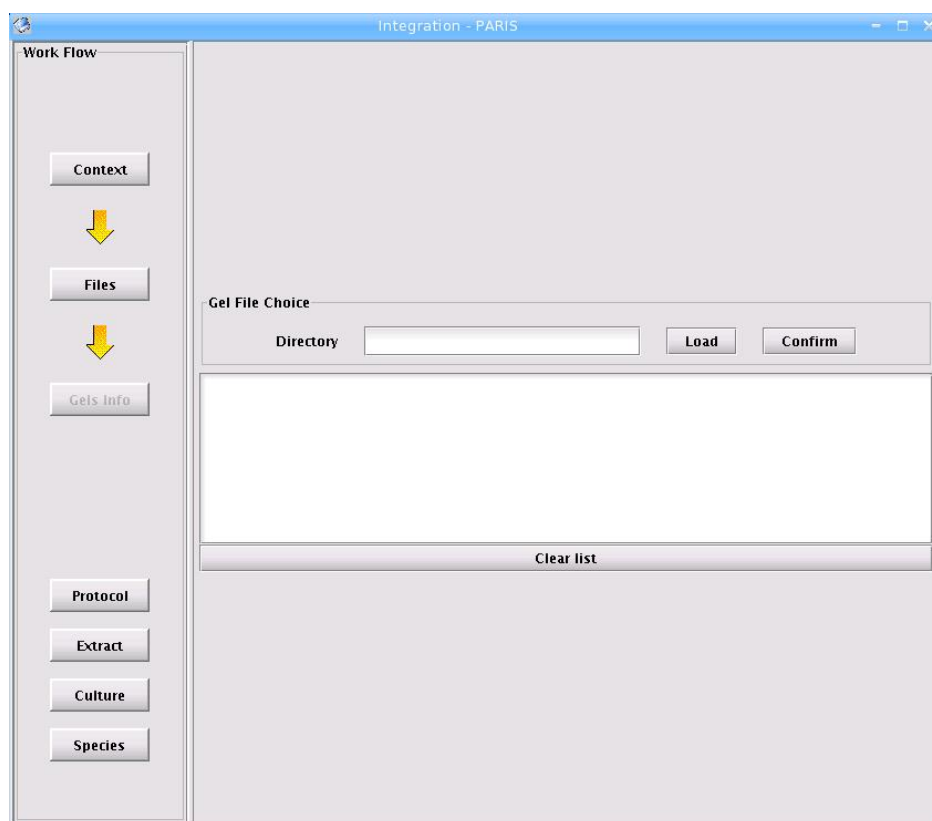


Fig. 44 - Interface used to search the directory containing the data to upload.

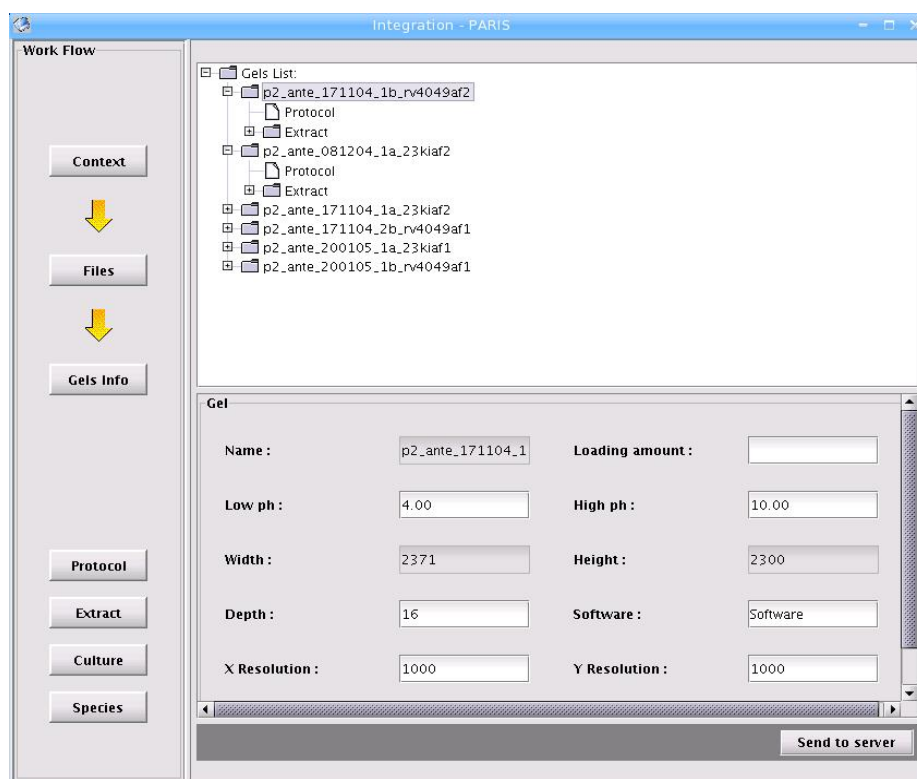


Fig. 45 - Interface used to check and modify the loaded data.

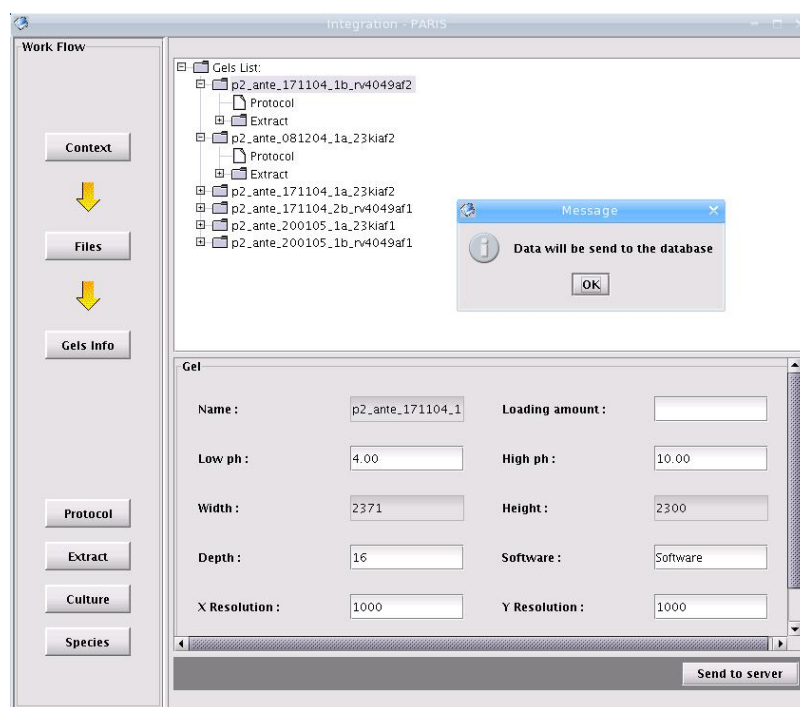


Fig. 46 - Click on the “send to server” button allows you to load the data into the data server.

13. **Acknowledgement**

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1. "Collaborative analysis of electrophoresis gels", inter-EPST Program on bioinformatics, CNRS, INSERM, INRA, INRIA, Ministry of Research; 2001.
2. "Statistical methods for genome profiling from electrophoresis gel", inter-EPST Program on bioinformatics, CNRS, INSERM, INRA, INRIA, Ministry of Research, 2002.
3. "ProteHome", Program of the RNG (Réseau National des Génopôles), 2006.
4. "MIGADI", Projet ANR, 2008-2012.

14. **Publications**

Examples of applications and technical information about the architecture and the design of system PARIS can be found in the publications about PARIS.

1. Juhui Wang, Christophe Caron, Xuefeng He, Audrey Carpentier, Michel-Yves Mistou, Alain Trubuil, Christophe Gitton, Céline Henry, and Alain Guillot. *A system for integrative and post-planned analysis of 2DE-MS centred proteomics data*, «2005 Year-Book of Integrative Bioinformatics», Editor, Dr. Ralf Hofestädt, Publisher Shaker Verlag, April 2006.

2. Christophe Gitton, Mickael Meyrand, Juhui Wang, Christophe Caron, Alain Trubuil, Alain Guillot, and Michel-Yves Mistou. Proteomic signature of *Lactococcus lactis* ncd0763 cultivated in milk. *Applied and Environmental Microbiology*, November 2005, pages 7152-7163, Vol. 71. No. 11.
3. Juhui Wang, Christophe Caron, Xuefeng He, Audrey Carpentier, Michel-Yves Mistou, Alain Trubuil, Christophe Gitton, Céline Henry, and Alain Guillot. *A system for integrative and post-planned analysis of 2DE-MS centred proteomics data*, *Journal of Integrative Bioinformatics*, November, 2005.
4. Juhui Wang, Christophe Caron, Michel-Yves Mistou, Christophe Gitton, and Alain Trubuil. PARIS : a Proteomic Analysis and Resources Indexation System. *Journal of Bioinformatics*, 20(1):133-135, January 2004.
5. Juhui Wang, Christophe Caron, Michel-Yves Mistou, Christophe Gitton. Integrative and post-planned analysis of proteomics data. In *International Workshop on Integrative Bioinformatics : Complex Metabolic Networks*, pages 17-20, Bielefeld, Germany, July 2005, (Oral Presentation).
6. Juhui Wang, Christophe Caron, Michel-Yves Mistou, Christophe Gitton, and Alain Trubuil. PARIS : a system for 2-DE based proteomic data management, *ECCB'2003*, Paris, France (Oral Presentation).
7. Juhui Wang, Christophe Caron, Michel-Yves Mistou, Christophe Gitton, and Alain Trubuil. A System for Proteomic Data Management and Post-Planned Analysis, *HUPO Third World Congress*, 2004, Beijing, China.