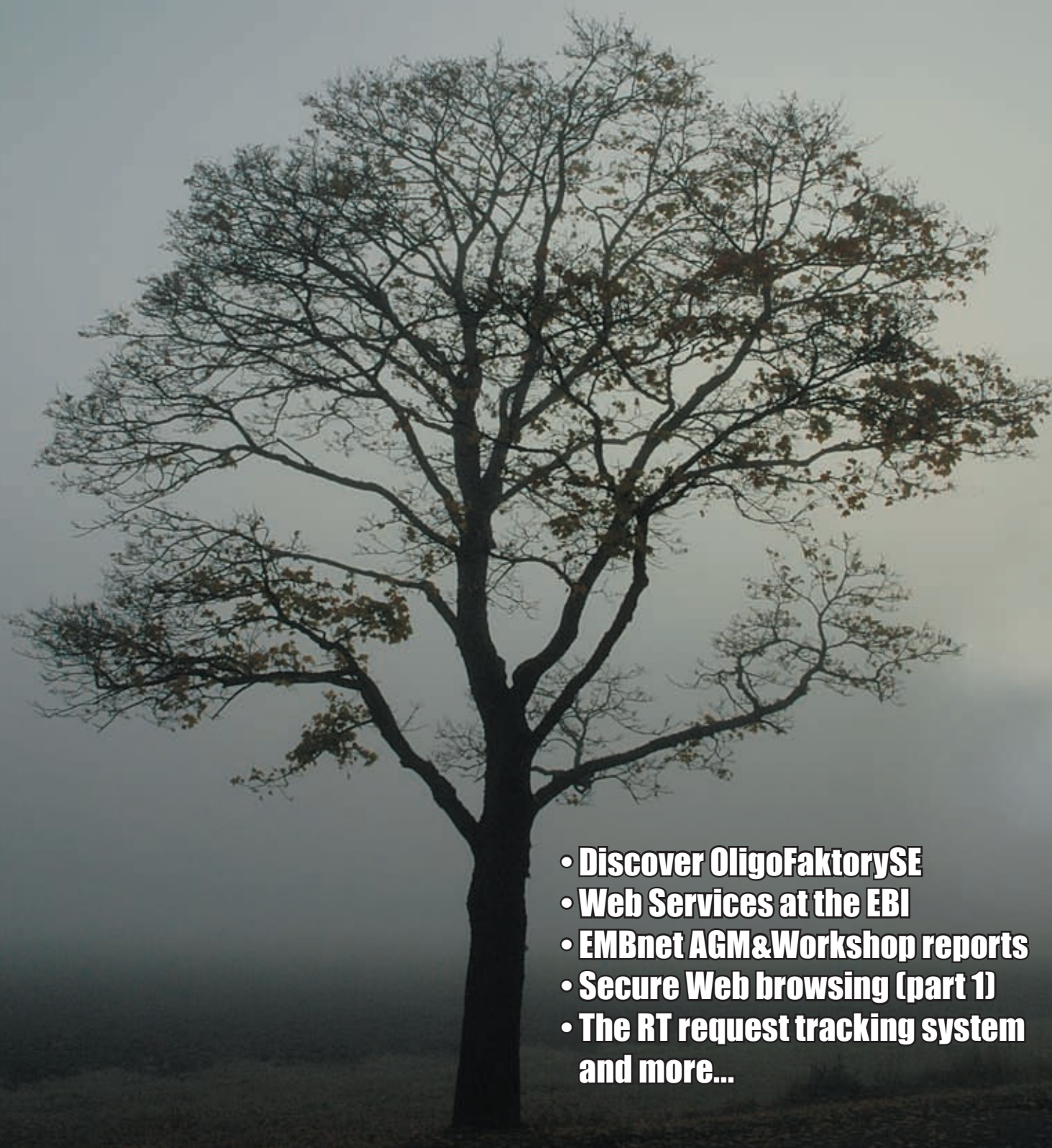


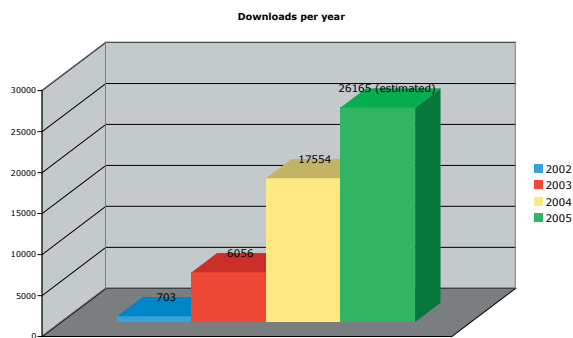
EMBnet.news

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December 2005

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- **Discover OligoFaktorySE**
 - **Web Services at the EBI**
 - **EMBnet AGM&Workshop reports**
 - **Secure Web browsing (part 1)**
 - **The RT request tracking system and more...**

Editorial

At the end of three years of putting together our newsletter EMBnet.news, it is the time for me to make an assessment. Eleven issues, 54 articles, and the number of downloads is expected to exceed 25'000 for 2005 (from 700 in 2002!).



When looking back, it is very satisfactory to see that people like the journal, download it and even read it! I would like to warmly thank all contributors and to Monique Zahn (for proofreading the english) and wish a long life to EMBnet.news and the new editorial board!

Laurent Falquet

The new editorial board: Erik Bongcam-Rudloff, Pedro Fernandes, Kimmo Mattila, Lubos Klucar, and Gonçalo Guimaraes Pereira.



Protein Spotlight (ISSN 1424-4721) is a periodical electronic review from the SWISS-PROT group of the Swiss Institute of Bioinformatics (SIB). It is published on a monthly basis and consists of articles focused on particular proteins of interest. Each issue is available, free of charge, in HTML or PDF format at <http://www.expasy.org/spotlight>

We provide the EMBnet community with a printed version of issue 63. Please let us know if you like this inclusion.

Cover picture: Autumn in Ultuna, Sweden, October 2005. [© Erik Bongcam-Rudloff]

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The RT request tracking system



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Introduction

Most organisations need an efficient user helpdesk. In 2003, three groups of the Swiss Institute of Bioinformatics (<http://www.isb-sib.ch/>), namely the Swiss EMBnet node (<http://www.ch.embnet.org/>), the Swiss-Prot group (<http://www.expasy.org/people/swissprot.html>) and the Proteome Informatics group (<http://www.expasy.org/people/pig/>) decided to join forces to look for a good helpdesk software/ticketing system to track and store user questions. This was prompted by the ever-increasing number of user requests which are directed to several mailing lists (see <http://www.expasy.org/contact.html> and <http://www.ch.embnet.org/pages/contacts.html>). This structure raises several important issues, some of which are listed below:

- mailing list management;
- automatic handling of user requests;
- ability to receive and send attachments;
- check that every request has been answered (in particular when an answer is given by an external expert);
- comprehensible organisation of all the transactions pertaining to users' requests (attachments, various email exchanges, dates, etc.);
- tracking of identical requests sent to different mailing lists (as this may duplicate work or even lead to the loss of the request when sent inappropriately);
- avoiding to answer similar requests over and over again by easily searching questions which have already been resolved;

- staff management (people answering user requests) during holidays, for example, or any kind of other absence;

The candidates

In this context, several free or open-source software were tested, such as :

GNATS

<http://www.gnu.org/software/gnats/>

Jitterbug

<http://samba.anu.edu.au/jitterbug/>

Mantis

<http://www.mantisbt.org/>

phphelpdesk

<http://phphelpdesk.sourceforge.net/>

oneorzero

<http://www.oneorzero.com/>

Request Tracker

<http://www.bestpractical.com/rt/>

The choice

Request Tracker (RT), a ticketing system available under the GNU General Public License, appeared to be the best candidate as it fulfilled most of our specific constraints at the time of testing besides a well thought-out web interface (Figure 2 & 3). A few RT basic requirements, concepts and definitions - which reflect the features of RT that convinced us to use it - will be briefly presented before describing the basics of our installation. Finally, the way we decided to handle spam will be discussed.

Please note that this article is not intended to be an installation guide. It is a brief overview of the ticketing system used currently at the Swiss Institute of Bioinformatics. If you need installation instructions or more details read "RT Essentials" (by Jesse Vincent *et al.*, from O'Reilly Media Inc.) or look at: <http://wiki.bestpractical.com/>.

Request Tracker (RT): the basics

RT can be used to track, manage and archive requests sent by email or via a web interface. Typically, a request is sent to RT by email. RT stores it in a database, replies automatically to the requestor (receipt) and notifies a group of RT staff members of the new ticket creation. One member of the group takes

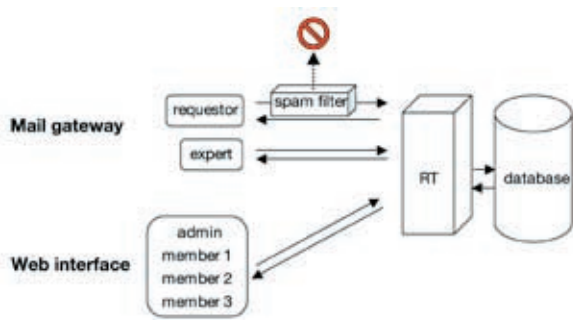


Figure 1. RT typical workflow.

responsibility for the ticket through the web interface (or by email) and resolves it. Some requests may need external expertise before the answer is sent back to the requestor (Figure 1).

A ticket is created by email or by using the web interface and stored in a database. It is assigned a unique identification number that allows a lot of information to be linked such as requestor, status, queue, replies, etc. All correspondence and modifications, called the ticket's history, are also stored in the database. RT staff members can either reply directly to the requestor or ask for an external expertise before an answer is sent back to the requestor. Note that this is only one possible workflow, as RT can be extensively customized.

Requirements

RT is a relatively complex piece of software that can run on most Unix systems (a port on Windows is also available). It needs the following to work:

- Perl. Version 5.8.3 or higher is needed for proper support of languages other than English. Fortunately, RT provides a tool to install the numerous different Perl modules using Perl's CPAN system (<http://www.cpan.org>).
- A database management system (DBMS). RT supports MySQL (<http://www.mysql.com/>), PostgreSQL (<http://www.postgresql.org/>) or Oracle (<http://www.oracle.com/database/>).
- A web server. Apache with mod_perl (<http://perl.apache.org/>) is recommended but any webserver supporting FastCGI (<http://www.fastcgi.com/>) will do.
- A Mail Transfer Agent (MTA). Any standard MTA should work: sendmail, postfix, exim or qmail.

It is important to note that the installation of RT is quite well documented and all necessary

Preferences | Logout
Logged in as Admin_David

RT for test New ticket in external_1 Search

Home **RT at a glance**

Tickets

Configuration

Preferences

Approval

10 highest priority tickets I own...			
#	Subject	Queue	Status
15	What is EMBnet ?	external_3	open

[Update]

Quick search		
Queue	New	Open
external_1	1	1
external_2	1	0
external_3	1	4
internal_1	0	2
internal_2	1	2
spam	0	0

Don't refresh this page. Go!

RT 3.0.11 from Best Practical Solutions, LLC

Figure 2. RT's main window. Menus are listed on the left. A summary view of all mailing lists (queues) and their respective number of requests is shown on the right, together with the identity of the logged-in RT staff member (here: Admin_David). Tickets in progress of the logged-in RT staff member are displayed in the middle (here: ticket #15 sent to external_3 mailing list). Most items are clickable.

BEST PRACTICAL™ Preferences | Logout
Logged in as Admin_David

RT for test New ticket in external_1: Search

Home #15: What is EMBnet ? Reply | Resolve | Comment

Tickets
Search
New Search

#15
Display
History
Basics
Dates
People
Links
Jumbo

Configuration
Preferences
Approval

The Basics
Id: 15
Status: open
Worked: 0 min
Priority: 0/0
Queue: external_3

Dates
Created: Wed Nov 02 17:01:09 2005
Starts: Not set
Started: Not set
Last Contact: Wed Nov 02 17:06:16 2005
Due: Not set
Closed: Not set
Updated: Wed Nov 02 17:22:03 2005 by Jeff.Asks@somewhere.com

People
Owner: Admin_David
Requestors: Jeff.Asks@somewhere.com
Cc:
AdminCc:

Relationships
Depends on:
Depended on by:
Parents:
Children:
Refers to:
Referred to by:

More about Jeff.Asks@somewhere.com
Comments about this user:
Autocreated when added as a watcher
This user's 10 highest priority tickets:
• 15: What is EMBnet ? (open)

History Display mode: [Brief headers] [Full headers]

Wed Nov 02 17:01:10 2005 Jeff.Asks@somewhere.com - Ticket created [Reply] [Comment]
Subject: What is EMBnet ?
Date: Wed, 2 Nov 2005 16:19:14 +0100
To: external_3@somewhere.com
From: Jeff Asks <Jeff.Asks@somewhere.com> Download (untitled) 503b

Sender Name: Jeff Asks
Hello,

I would like to have more information about EMBnet,

Thank you,

Jeff

Wed Nov 02 17:02:28 2005 Admin_David - Taken

Wed Nov 02 17:06:13 2005 Admin_David - Correspondence added [Reply] [Comment]
Download (untitled) 447b

Dear Jeff,

EMBnet is a science-based group of collaborating nodes throughout Europe and a number of nodes outside Europe.
The combined expertise of the nodes allows EMBnet to provide services to the European molecular biology community which encompasses more than can be provided by a single node.

you can find more information at:
<http://www.embnet.org/>

Please do not hesitate to send me an email, should have more questions,

Regards,

David

Wed Nov 02 17:06:14 2005 RT_System - Status changed from new to open

Figure 3. RT's ticket display. Menus are listed on the left. Note the expansion of the "Tickets" menu. Each of the four main categories of the Ticket can be edited by using either the menus on the left or the main display following which the history of the ticket is displayed. The "People" and "Dates" categories show among others whether any RT staff member has taken responsibility for the resolution of a ticket and the time of the last exchange. This prevents RT staff members to take care of the same request and to avoid pending requests. We modified the "More about" category to display all tickets sent by a requestor (status new, open and resolved). This helps in seeing immediately multiple identical queries (same requestor, same subject) or spam emails (not visible here). The "Search" function (left menu) is also an extensively used feature as a help in responding to similar requests available from the database.

parameters are explicitly commented. So there shouldn't be any major problem to install it, at least on a dedicated computer. However, its integration into an existing (and complex) environment may require good knowledge in system administration. Moreover, the web server and the DBMS do not need to be installed on the same computer.

Requests, which can be sent by email or created by using a web interface, are stored in a relational database. An automatic reply containing the ticket identification number used for further correspondence can be optionally sent to the requestor. Request management can then be performed by RT staff members either via CLI (not discussed here), email or by using a web interface (Figures 2 & 3).

A few definitions

Requestor: person submitting a request.

Ticket: all the information pertaining to a request including: status (new, open, resolved, etc.), dates (created, last contact, etc.), watchers (see below), relationships (merge, depends on, parents, children, etc.), replies and comments.

Queue: way to keep tickets organised. It contains all the tickets you wish to keep together (for instance all requests sent to a specific email address).

Watcher: any person interested in a ticket, i.e. requestor, owner (the person who decides to take care of the resolution of the ticket or adminCc (a person that supervises all the ticket transactions)).

Group: set of related users. For instance, one group can be responsible for a specific queue or set of queues.

Rights: way to control all RT features very precisely. Rights can be assigned at three different levels: global (properties and configurations which apply to all queues), queue (properties and configurations which are restricted to a specific queue) and group (properties and configurations which apply to a specific group).

Scripts and Templates: RT so-called "scrips" provide the ability to trigger actions (Autoreply To Requestors, Notify Requestors, Notify Owner, Notify AdminCcs, User Defined, etc.) under specific conditions (On Create, On Transaction, On Correspond, On Comment, On Status Change, On Owner Change, On Queue Change, On Resolve, User Defined). Templates are text forms that can be linked to actions. There are several default global scrips including the automatic reply which contains the ticket identification number used for further correspondence:

Condition: On Create
Action: Autoreply to Requestors
Template: with Global Template: Autoreply.

Naturally, there are many other features, including ticket relationship (depends on, parent, children, refers to, etc.), approvals (an easy way to get someone's approval without creating a new system) or custom fields (data fields that can be created globally or for particular queues with four different types: select one value, select multiple value, enter one value and enter multiple values). But this is beyond the scope of our discussion (for more, read "RT Essentials" by Jesse Vincent *et al.*, published by O'Reilly Media Inc.).

RT: our working structure

During our testing period, we started with a regular RT installation (3.0.0) on a (old) dedicated server, which served both as web server and DBMS (dual Pentium 1GHz, 1 Gb memory and 250 Gb disk storage running Linux. Apache was statically compiled with mod_perl. MySQL 3.23.xx and Sendmail as MTA were also installed).

Each new version of RT has been installed which, as a consequence, corrected a lot of bugs and added some new features, including better reactivity, email encoding and attachment handling as well as improved SQL queries. We kept version 3.0.11, which seemed stable enough to be used in production and installed RT web server (Perl 5.8.3, Apache 1.3.23 and mod_perl 1.2.3 running Solaris on a Sun Sparc 250 with 2 Gb memory and 250 Gb disk storage) separately

from the DBMS server (MySQL 4.1.10a installed on a 2 x Xeon 2.80GHz with 4 Gb memory and 2x36 Gb disk storage running Linux) to fit our current installations. We use Exim 4.30 as MTA. Note that version 3.0.11 is not RT's latest version. In fact, RT development has split into two main branches, 3.2 and 3.4 (more information on the different branches and latest versions are available from: <http://bestpractical.com/rt/download.html>).

When you first install RT, one important parameter is the "rtname". Basically, it is the tag that will be added to the subject line of all emails in addition to the unique identification number, to help RT put emails of existing tickets in the right place. Due to the heterogeneity of our existing mailing lists, we have chosen a generic "help" tag. Thus our RT installation adds [help #X] to the subject line of all outgoing emails, where "X" represents the ticket identification number. This is not trivial, as the help tag cannot be changed once it has been set or incoming emails referring to existing tickets may not be correctly assigned.

There are two major types of users interacting with RT. Those who have been granted rights and who, consequently, are "privileged" (typically RT staff members). And the "unprivileged" users, who are not RT staff members and are usually only allowed to submit requests or to reply to requests when asked for an external expertise. Currently, we have over 30 privileged users. And all of them have been granted the global "modify self" right (i.e. the possibility to modify their name, nickname, password, signature, etc.) and given the following rights "Let this user access RT" and "Let this user be granted rights" to allow them to access the web interface.

We decided to create one queue per email address. The exception is a queue, which collects requests from four administrative email addresses, which are not heavily used. Many queues (let us call them "external") receive requests from worldwide users. However, several "internal" ones have been created for internal use only. We currently have 12 external and 6 internal queues

including one dedicated to spam (see below). To control internal queue usage, only privileged users can send requests and create tickets. This contrasts with external queues where privileged and unprivileged users can create tickets. Therefore, the Autoreply scrips has been disabled on the global level and only a external queues have been assigned a customised automatic reply, which is not used for internal queues.

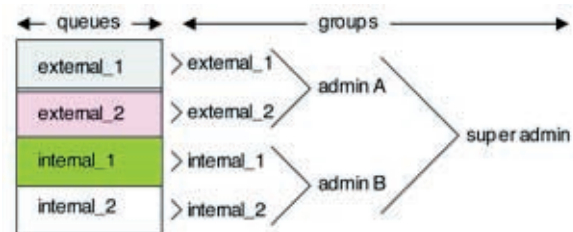


Figure 4. Management of queue rights. Every queue is managed by a group (set of privileged users). These groups are granted limited rights. Some groups with more rights have been created to administrate a given set of queues and groups, but only one group has been granted all available rights.

Due to the number of privileged users, we decided to define all rights related to the queues at the group level (Figure 4). In short, almost every queue is managed by a group of several RT staff members (we usually kept the same name to facilitate the management), which has been granted the following extended rights:

- CommentOnTicket (allow comments to tickets. Comments are not sent to the requestor)
- CreateTicket (allow the creation of a ticket)
- ModifyTicket (allow modification of subject, status, watchers, relationships, etc.)
- OwnTicket (allow ownership on tickets)
- ReplyToTicket (allow replies to tickets. Requestor receives replies)
- SeeQueue (render the queue visible in the lists)
- ShowTicket (see tickets)
- ShowTicketComments (see the comments attached to tickets)
- TakeTicket (assign the ticket to the Taker. Only possible if no other RT staff member is in charge of the ticket.)

As rights are granted at the group level, it is very easy and more efficient to add or

The screenshot shows the RT interface for a user named Anne. The top navigation bar includes 'Home', 'Tickets', 'Configuration', 'Preferences', and 'Approval'. The main content area is titled 'RT at a glance' and is divided into two sections: '10 highest priority tickets I own...' and '10 highest priority tickets I requested...'. The 'Quick search' table shows the following data:

Queue	New	Open
external_1	1	1
external_2	1	0
external_3	1	3
spam	0	0

Figure 5. Selective display using rights. RT staff member called Anne belongs to group "external_1" with extended modification rights for that queue (CommentOnTicket, CreateTicket, ModifyTicket, OwnTicket, ReplyToTicket, SeeQueue, ShowTicket, ShowTicketComments, TakeTicket) and limited display rights for the queues "external_2", "external_3" and "spam" (CreateTicket, SeeQueue, ShowTicket, ShowTicketComments).

remove a group member, during any kind of absence for instance, without modifying existing group rights, rather than adding or removing a member's rights (see list above) specific for a queue.

For most external queues, the groups (other than the one managing the queue) are given the following limited rights:

- CreateTicket
- SeeQueue
- ShowTicket
- ShowTicketComments

This is very convenient as it allows easy ticket transfer from one queue to another, if it was sent to the wrong mailing list or to move spam tickets into the spam queue. Moreover, this helps to reveal when a requestor submits the same request to different queues. In such a case, one can use RT's merge feature.

In addition to groups managing their corresponding queue, we created some administrative groups (see Figure 4) that manage several queues and have two additional rights:

- DeleteTicket (Ticket is not visible anymore, but still physically in the database)
- StealTicket (re-assign an already owned ticket. Useful in the owner's absence)

There is also one administrative group that has all possible rights.

It is worth outlining the fact that the different groups are not granted the same rights. It is therefore very easy to restrict access to

certain queues or to hide some of these from some RT staff members. One group, for instance, has been granted all rights. Thus, all of its members have unlimited access to all queues with all modification rights (Figure 2, six visible queues). In contrast, another group called "external_1" has been granted limited rights (Figure 5, four visible queues).

Handling of spam

As stated above, whenever a request is sent to RT, it creates a ticket and stores all its information in the database - including the attachments - and (at least for our external queues) a reply is sent back to the requestor with the ticket identification number. This is a great feature that many users appreciate as it certifies that the correspondence has been received. However, this is also true for spammers... Thus, during preliminary tests, our database was populated with spam (which frequently contains huge attachments !) and most of the time was spent discarding unwanted emails. Moreover, our email addresses were recycled by spammers.

For all these reasons and after trying several different configurations, we decided to use an anti-spam filter, namely Mailcleaner from Fastnet (<http://www.fastnet.ch/>) to prevent spam entering RT. In short, this filter adds a tag in the subject line of suspect emails, which are then redirected by the exim intermediate MTA (<http://www.exim.org/>) in an external mailbox not related to RT. This prevents over 90% of spam from entering RT. The remaining 10% is transferred from the

different queues to the internal queue spam, which is visible to all privileged users, where it is subsequently deleted by an administrative group. The external mailbox is checked regularly for false positives. However, only very few have been found so far.

There are numerous other features, most of which we do not use. These include ticket priority, ticket approval, ticket relationship, etc. However, we plan to update RT to the latest version (version 3.4.4 at the time of writing) before the end of the year. Indeed, we would like to use additional new features such as, for instance, improved usage of custom fields or a brand new search tool. In addition, we are investigating another software, namely the RT FAQ manager - RTFM - which is said to integrate seamlessly into RT (<http://bestpractical.com/rtfm/>). But this is another topic.

Conclusion

One has to consider what is really expected from a helpdesk software. In many instances, more basic programs could suit perfectly so it is always worth looking around to see what is available.

We encountered several problems upon installations and configurations of early versions of RT but RT mailing lists (<http://bestpractical.com/rt/lists.html>) and later RT's support web site (<http://wiki.bestpractical.com/>) were of great help to solve most of them before corrective updates (including the addition of new features) were distributed. RT installation into our complex environment has not been trivial; however, the RT ticketing system proved to be a good choice because of its many functionalities and its quality, besides a very active user community and regular updates.

Acknowledgements

Many thanks to all the people involved in having RT up and running. In particular, Christian, Dmitry, Giovanna, Ivan, Karin, and Volker. In addition I thank Monique and Vivienne for reviewing the manuscript.

Secure Web browsing: How to safely surf the web? (part 1)



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Introduction

Every biologist today interacts with some sort of web application. Whether you read your favourite blog, wish to shop something or launch your SRS session, you will certainly find yourself involved with your web browser. No doubt your computer has become such an essential tool that you (or your IT support folks) also make sure you have installed an anti-virus with up-to-date signatures and keep up with application and Operating System updates (also known as 'patches'). If you don't, be very worried. On the other hand, if you do keep up with all the hard work of updating your system, you must have done everything you could to prevent malicious code from harming your computer, right? Well, as far as the web is concerned, not really. No, I am not trying to make you paranoid and I am neither suggesting that you should unplug your machine from the net. You just have to be aware of the basics of security threats that emerge from the World Wide Web and then read on how you could stop most of them by means of configuration options supported by your web browser, which is really what this article is all about.

What is presented here is true more or less for every Operating System (O/S) platform. O/S specific comments will clearly be mentioned in the text. However, the discussion will be limited to the two most commonly employed web browser applications: Microsoft Internet Explorer (IE) and Mozilla Firefox.

Please be aware of two things. First, the suggested techniques of this article are not a panacea. They should never be used as a substitute of up-to-date patches and essential security systems that your sysadmin dictates, but you should rather treat them as a complement. Secondly, the configuration options suggested here might break the functionality of some web applications. We will indicate these 'problematic' techniques throughout the article. Security always comes at the expense of functionality and flexibility. So, make a note of the browser options you change and then if you encounter the problem, switch back to the original configuration. In that case, if you have to switch back to a 'not-so-secure' configuration option, the fact that you are aware of the issue and some additional steps we are going to suggest will at least improve your data security awareness.

World Wide Web security threats

Back in 1990, when Tim Berners Lee wrote the first browser-editor 'Nexus' and started the World Wide Web era [1], it is unclear whether he had foreseen all the 'surfing' threats we face today. Whilst he certainly thinks about them now directing the W3C folks, today the average web user exposes himself in various categories of information security threats. It is good to examine the most important of them, prior describing how certain web browser settings can aid in their mitigation.

Breach of your personal privacy/confidentiality

Whilst you would like to think of the Web as a way for you to obtain information, you should take into account that in the process of obtaining the information, you provide also various levels of data back to the information provider. Most of the time, this two-way transaction is harmless for you. For example, when you fill in a series of web forms trying to purchase something in an 'honest' web site, the provider will take your personal data and store them securely for the purposes of the transaction only and/or for allowing easier access to the site for future purchases. This is achieved by using the 'cookies' mechanism.

'Cookies' are files placed in your hard disk by a web site. These files contain specially encoded state information that enables your web browser to auto-complete web forms (useful if you visit the site often to complete the same form time after time), count correctly what you have in your shopping basket, etc. Unfortunately, not all web site providers are honest and they misuse cookies in concerted efforts to record your web visits in detail and send this data to marketing-driven companies that re-sell the information to third-party providers. There are other unlawful uses of your data, but the point is that information about you is suddenly in the hands of individuals without your permission.

The whole story does not stop here. An entire category of programs can be more sophisticated than cookies and you could end up having files of your hard disk and even your password transmitted to a third party without your knowledge, adverts suddenly popping up from nowhere ('adware') and a system that is slow and unstable. These programs are known as 'spyware', they currently devastate mainly Microsoft Windows systems and they are a serious threat to the health of your system.

However, in contrast to cookies, sophisticated 'spyware' has to be installed explicitly in the system by a separate process, not by just visiting a web page. In fact, most (not all) spyware code is installed by the users themselves. Spyware writers often offer 'eye-candy' utilities (internet 'optimizers', 'cool' web search tools) and underneath the surface they insert code they don't tell you (or don't tell you clearly) about. 'CoolWebSearch' [2] and '180solutions' [3] are some of the widespread examples of spyware/adware programs in distribution. Most of these programs work in synergy with other technologies described in the next section.

Breach of System Integrity

The pervasive nature of Web applications has dictated greater integration of the web browser with other desktop applications and their respective data formats. Have you ever wondered what goes on behind the scenes, when you open a PDF document inside Firefox, or when you are able to perform a virus

scan of your hard drive from a web page link in IE? The answer is that a number of software technologies bridge the gap between Web protocols and local application interfaces or enhance your web browsing experience.

ActiveX [4] is one of the aforementioned bridging technologies that exists in the Microsoft world and enables IE to integrate all sorts of fancy applications. Whilst it is out of the scope of this article to describe how ActiveX achieves integration, the bottom line is that it allows execution of code that someone else has written to execute locally in your machine. This entails danger, because if you do not know exactly what is in the code you are about to execute, you could be heading for an unpleasant surprise. This is the reason ActiveX has been a very nice 'backdoor' to infect your computer with all sorts of 'virus', 'trojan' and 'spyware' infections.

'Virus', 'trojan' and 'spyware' are what people call collectively as 'malware', programs that tend to harm you by either causing your computer to malfunction ('virus' and 'trojan') or steal personal information ('spyware'), as described in the previous section. As mentioned in the earlier section, some spyware utilities require the user to explicitly install software. However, 'Gator'-based spyware [5] uses extensively ActiveX to achieve its goal and complete the installation.

For all these reasons, ActiveX is one of the greatest security holes. Although its concept is interesting, the way it is implemented is not at all security-orientated and it can only cause trouble.

Whilst ActiveX focuses on web-desktop integration, Javascript [6] is another technology embedded widely in many web browsers designed to enhance the web browsing experience. Whilst the language itself is not responsible for security bugs, its implementation engine on different browsers does occasionally contain security faults that facilitate arbitrary code execution. The Mozilla Firefox 1.0.3 Javascript arbitrary code execution fault [7] and a similar IE 6 Javascript-driven 'Ghost' Security Flaw [8] are two examples of critical implementation faults that could affect fully patched machines on different Operating Systems and browsers.

Exploring the security settings of Internet Explorer 6

IE6 is at the moment the most widely deployed web browsing software. Microsoft is finalizing version 7, but in the meantime, let's have a look at what's on offer in IE6 with regards to security settings. Please note that all settings are with reference to a Windows XP Service Pack 2 machine. If you don't have SP2 installed, you should not really have your machine in the Internet!

First of all, let's see how we get to these settings. The normal way is to launch IE and from the top toolbar 'Tools' menu, go to 'Internet Options'. Another way to launch these settings is to go to 'Control Panel' -> 'Security Center' -> 'Internet Options'. Either way, you will get to a menu like the one shown in Figure 1.

The 'Internet Options' window contains several tabs ('General', 'Security', 'Privacy'...) and when first launched, it switches to the 'General' tab. Here you can set the default home page and you can also regulate what is stored on the 'Temporary Internet' files area as well as the 'History' of all your web site visits. The last two settings relate to privacy. Firstly, both the 'Temporary Internet files' area and the URL 'History' are targets for malicious spyware programs. The role of the Temporary Internet files' area is to act as a storage for content that you visit often, so that you do not have to download it repeatedly. If you have a fast Internet connection, there is not a point caching (storing locally) web content. If you are using a public machine that might be infected with spyware or is mis-configured so that other users can get into these files, your best bet is to click on the 'Temporary Internet files' area 'Settings' button. On the 'Settings' window that will pop up, choose the option 'Never', reduce the amount of disk space to use for storage to say 10 Megabytes for storage of cookies and click OK. Then 'Apply' the settings. Now, you:

- i) Consume less valuable disk space for temporary web content that you might not need.
- ii) Increase the speed of IE.

Note the button option of deleting cookies. If you do, beware that you will lose automatic login to certain web sites. This might be a problem for some people that login to various web sites and they forget their password for manual entry! So, make sure you get all your passwords before you do delete your cookies.



Figure 1: IE Internet Options Menu - General tab.

The 'History' area keeps a file that contains all your web page visits for a number of days. Again, if you have privacy issues and do not wish to leave a footprint of your web site visits on a system, you can clear your website history. On the downside, if you clear the web history IE will lose the ability to auto-complete the URLs as you type them in the Address bar. This comes handy for long URLs, so do what's best for you.

We now move to the 'Security' tab area of the 'Internet Options' menu (Figure 2). IE offers compartmentalized security based on the type of web content you are visiting. There are four content zones, illustrated graphically with different symbols that you can click on. Each of these zones has its own pre-defined security settings ('Default Level' button) or it could be tailored to your needs ('Custom Level' button). Starting from the left, the

'Internet' zone concerns general access to non-local web sites, with a medium level of security restrictions by default. The 'Local Intranet' zone contains by default less rigid restrictions and allows you to enter the URL of your locally administered web site(s) (Intranet). This is because (in theory) intranet applications should be more trustworthy than applications on remote web servers that your organization does not control. 'Trusted sites' (remote or local) have the least restrictive access regulations. Finally, the 'Restricted sites' zone defaults to the highest possible level of restrictions, for web servers that you have to visit that you do not trust at all. Let's see how this works and how you can customize the defaults for each zone.

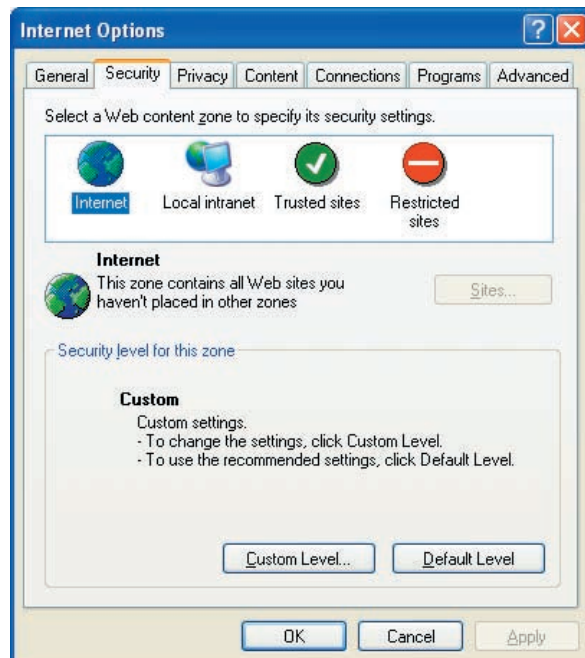


Figure 2: IE Security Internet options.

Click on the leftmost 'Internet' zone and then click on the 'Default Level' button. You will see that it contains a 'Medium' level and you will get a quick text description of what the Medium level means. Let's now assume that you do not wish to execute 'ActiveX' controls at all. The default level says that unsigned ActiveX will not be downloaded, but digitally signing a control does not really safeguard you against harm, does it? So, let's disable it. Click on the 'Custom Level' button. You will

see a detailed menu with various radio-button options like the one in Figure 3.

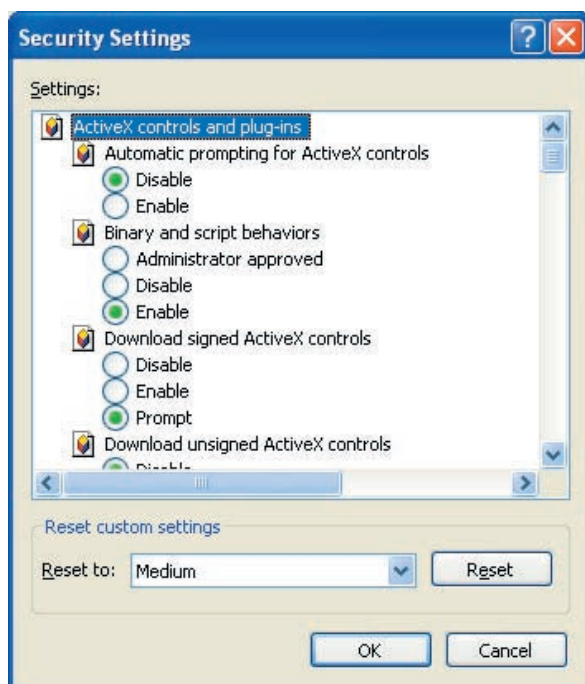


Figure 3: Customizing IE security settings.

Make sure that you disable all ActiveX manually. The alternative to going down the custom level route is to choose the default zone security level to be 'High'. However, the first method (disabling all ActiveX controls manually) is preferred, as the 'High' security level might disable non ActiveX features you might like to enable. Make sure that you cautiously play around with the rest of the zones and the security controls. The menus for adjusting the security settings for every zone are the same. If something does not work after the changes, revert back to your old settings. You will discover that IE contains a comprehensive array of security options. Whilst some people have criticized that the number of security options can make things worst for the web user, I find the safety of its ActiveX controls to be a more controversial point. My choice is to disallow anything that has to do with ActiveX controls on every Internet web site. The only exception is windowsupdate.microsoft.com, a site used by Microsoft to distribute necessary updates. For that you will need ActiveX controls enabled, so I suggest that you place this URL in the 'Trusted Sites'

zone, in order to ensure that your Windows machine gets the necessary updates.

The part 2 in the next issue of EMBnet.news will describe the security settings of Firefox.

References

- [1] <http://www.w3.org/People/Berners-Lee/WorldWideWeb.html>
- [2] http://spywareguide.com/product_show.php?id=599
- [3] <http://www.benedelman.org/news/111804-1.html>
- [4] <http://www.microsoft.com/com/default.aspx>
- [5] <http://www.pcpitstop.com/gator/Confused.asp>
- [6] <http://developer.mozilla.org/en/docs/JavaScript>
- [7] <http://www.mozilla.org/security/announce/mfsa2005-42.html>
- [8] <http://www.enterpriseitplanet.com/security/news/article.php/3511241>

Announcement



In-Silico Analysis of Proteins
Celebrating the 20th Anniversary of Swiss-Prot
July 30 - August 04 2006 / Fortaleza - Brazil

Topics covered

- Knowledgebases, databases and other information resources for proteins
- Sequence searches and alignments
- Protein sequence analysis
- Protein structure prediction, analysis and visualization
- Proteomics data analysis

This meeting will take place in the week before ISMB 2006 and participants to both meetings will be entitled to reduced registration fees. More information soon here:

<http://www.swissprot20.org/>

EMBnet Stichting Annual General Meeting 2005

The 19th EMBnet AGM was held in Smolenice Castle (Slovakia) on September 16-17, 2005.

New specialist node member

The Institute for Health and Consumer Protection (IHCP), division Biotechnology and GMOs of the European Union, represented by Dr. William Moens was accepted as a new specialist node.

Short description

The IHCP is one of the seven scientific institutes of the Joint Research Centre (JRC) of the European Commission. It is located in Ispra, Northern Italy and has a staff drawn from the Member States of the European Union and associated countries.

The Institute activities are related to genetically modified organisms, biotechnology, chemicals and risk assessment, nano-biotechnology, exposure, to environmental stressors, food contact materials and consumer products, and alternative methods to animal testing.

New types of node!

In order to facilitate access to EMBnet membership for new countries or industries and institutes from already member countries, new EMBnet **associate academic** and **associate industrial** node memberships were discussed and accepted.

Definition

Associate academic/industrial node

Any academic/industrial group looking to serve, or already serving its regional community or institute with tools and databanks in bioinformatics, or is proficient in the development of such tools or databanks, can apply for the status of associate academic/industrial node.

Rights

An associate academic/industrial node has all rights of a national/industrial node, except for the following issues:

1. it has no voting rights at the Annual General Meeting (AGM)

2. it is not entitled to become member of the Executive Board
3. it is not entitled to reimbursement of the expenditures incurred when attending the EMBnet meetings, unless when elected member of a committee

Duties

An associate academic/industrial node must produce a yearly activity report to the AGM. It pays a yearly fee amounting to 25% of the fee of a national/industrial node. Failure of payment of the yearly fee exposes the node to discharging by the AGM.

Renewal of membership

The status of associate academic/industrial node is to be renewed every year by the AGM

More details are available on our web site:

<http://www.embnet.org/members/description.html>

Nominations

The round of nominations to the committees for next year produced the following:

- EB** Erik Bongcam-Rudloff (SE) chairman
Oscar Grau (AR) treasurer
Robert Herzog (BE) secretary
Laurent Falquet (CH) member
- E&T** Isabel Marques (PT) chairwoman
Lisa Mullan (UK) treasurer
Vassilios Ioannidis (CH) secretary
Valérie Ledent (BE) member
- P&PR** Pedro Fernandes (PT) chairman
Kimmo Mattila (FI) treasurer
Lubos Klucar (SK) secretary
Gonçalo Guimarães (BR) member
- TM&RD** Nils-Einar Eriksson (SE) chairman
Kristian Vlahovicek (ICGEB) treasurer
George Magklaras (NO) secretary
José R. Valverde (ES) member

The 20th AGM will be held in June 2006 organized jointly by Sweden and Finland!

EMBnet collaborative workshop Smolenice, September 15, 2005

The Universal Protein Resource (UniProt)

Anne Estreicher, Swiss-Prot group

Established in 2003, the Universal Protein Resource¹ (UniProt) (<http://www.uniprot.org/>) provides the scientific community with a single, centralized, authoritative resource for protein sequences and functional information. It is produced by the UniProt Consortium, a collaboration between the Swiss Institute of Bioinformatics, the European Bioinformatics Institute and the Protein Information Resource.

UniProt is made of three components: the UniProt Knowledgebase (UniProtKB), the UniProt Reference Clusters databases (UniRef) and the UniProt Archive (UniParc).

UniProtKB, the centrepiece, consists of two sections: manually annotated UniProtKB/Swiss-Prot² and computer-annotated UniProtKB/TrEMBL.

UniProtKB/Swiss-Prot manual annotation includes analysis, comparison and merging of all available sequences for a given protein from a given organism, as well as a critical review of associated experimental and predicted data, mostly based on the scientific literature. Information about recent and forthcoming format changes can be retrieved from <http://www.expasy.org/sprot/sp-docu.html>.

UniRef provides sequence clusters in order to furnish complete coverage of sequence space while hiding redundant sequences from view and thus permitting faster similarity searches.

UniParc is a comprehensive repository, reflecting the history of all protein sequences submitted to the main publicly available protein-sequence databases, not only UniProtKB, but also EMBL, Ensembl, VEGA, RefSeq, etc.

UniProt is updated biweekly. Questions, requests, suggestions? Please contact us at help@uniprot.org

¹Bairoch A., Apweiler R., Wu C.H., Barker W.C., Boeckmann B., Ferro S., Gasteiger E., Huang H., Lopez R., Magrane M., Martin M.J., Natale D.A., O'Donovan C., Redaschi N., Yeh L.S.

The Universal Protein Resource (UniProt). *Nucleic Acids Res.* 33:D154-159(2005). PUBMED: 15608167

²Boeckmann B., Blatter M.-C., Famiglietti L., Hinz U., Lane L., Roechert B., Bairoch A.

Protein variety and functional diversity: Swiss-Prot annotation in its biological context. *C.R. Biologies*, in press.

SRS Federation

Robert Herzog, Belgian EMBnet node

The project to build a collaborative infrastructure of SRS servers was started in September 2004. The basic idea was to share the work of databank indexing among several nodes, each of them giving other partners the access to the sets of ready to use indexed data. Lion Bioscience provides the members with the last version of the software (SRS 8.1), as well as the Prisma databank maintenance tools and a very significant support from their staff, under a specific licensing agreement. Three EMBnet nodes (Sweden, Slovakia and Belgium) started as "master nodes". They were joined around the turn of the year by partners from Brazil, Colombia and Poland, acting initially as "slave nodes", i.e. essentially assembling the data produced by the masters.

The goal set up for the first phase of the project, namely having six nodes well synchronised for the EMBL, PDB, OMIM, UNIPROT, KEGG and PROSITE datasets was reached by 2005's summer.

The second phase of the project has now started; it consists in improving overall robustness and QoS of the system, by including "secondary master nodes" that will provide some level of redundancy. The SRS federation is looking for more partners to join, with the hope that some of them will be in the position to offer additional datasets to the community. The next goals are to allow SRS queries to be federated, in order not to impose the presence of the complete datasets on all nodes.

The SRS Federation technology is put in use within the SIMDAT EU Grid project where five "Pharma" partners build a secured infrastructure for bioinformatics workflows.

The SRS Federation website is at

<http://www.srsfed.org>

Virtual bioinformatics seminary series

Erik Bongcam-Rudloff, Swedish EMBnet node

This presentation discussed the idea to form a "Virtual Bioinformatics Academy". To be able to accomplish this goal we need to create:

- Web-based courses
- Organize Marratech live sessions
- Create a Library of movie tutorials

Web based courses

We will create a single entry page from the main EMBnet homepage. This page will inform about coming events: e.g., Marratech based tutorials, lectures, etc. Other pages will offer video based tutorials and demos.

Marratech event

The video sessions (teachers and students) will be divided in sessions for people with accounts (more advanced contents) and with users connected to EMBnet nodes.

Free lecture sessions will be announced in advance on the "Virtual Bioinformatics Academy" web pages.

Movie tutorials

The video events will also offer free tutorials on basic use of bioinformatics tools. Prerequisites for EMBnet Education and Training (E&T) PC to start this project are:

- recruitment of interested teachers,
- selection of interesting topics and discussion about suitable subscription models.

The E&T PC needs also to discuss administrative issues concerning the project management.

Demonstration

During the collaborative workshop the author demonstrated the use of the videoconferencing system Marratech, the video streaming server system "Broadcast Machine" from participatoryculture.org and "Snapz Pro" a utility for creating movies from computer screens (<http://www.ambrosiasw.com/utilities/snapzprox/>).

AR.EMBnet Live CD

Diego Bellante and **Martín Sarachu**, AR.EMBnet, Instituto de Bioquímica y Biología Molecular, Facultad de Ciencias Exactas, UNLP, Argentina

"AR.EMBnet Live CD" is a customized distribution of "Knoppix" (a live-cd version of Debian GNU/Linux). It was designed specifically for the needs of the molecular biology user community, that does not have a fast internet connection. It offers the whole functionality of a bioinformatics server.

As it is Knoppix-based, this live CD provides an excellent hardware detection (through Kudzu, the Red Hat Linux hardware probing library) and does not install anything on the user's hard disk. Due to its compressed filesystem, this live CD can hold up to two gigabytes of software and databases. During Knoppix remasterization, many applications that are not useful for the biologist were removed.

"AR.EMBnet Live CD" provides a graphic interface through the "X Window System". "iceWM" (a lightweight window manager for Linux) was chosen to control the appearance of windows because of its reasonable performance even on slow machines.

Bioinformatics Tools in the AR.EMBnet Live CD

- **EMBOSS**: Free Open Source software analysis package containing a range of bioinformatics tools.
- **wrappers4EMBOSS**: These wrappers are an EMBOSS interface to many widely used sequence analysis software: CLUSTAL, BLAST, fastA, ps_scan, pf_make, bscan.
- **wEMBOSS**: Web environment from which the user can access EMBOSS. It also supplies users with space and tools to organize and review their work. As this "Live CD" uses RAM memory for user space, files should be saved in non-volatile memory before shutting down the computer).

Local Databases

- **nucDB**: EMBL Subset
- **protDB**: Uniprot Subset
- **dinoDB**: "Dinosaur" Sequences

Remote Databases (at EBI)

- **embl**: EMBL nucleotide sequence database
- **emblsva**: EMBL sequence version archive. (Repository of all entries which have ever appeared in EMBL)
- **embicds**: Nucleotide sequences of the CDS (coding

sequence) features, as annotated in EMBL database plus accompanying annotation

- **emblcon**: The CON database division of EMBL (represents complete genomes and other long sequences constructed from segmented entries)
- **uniprot**: Universal Protein Resource

This live CD can be downloaded from
<http://www.ar.embnet.org/livedvd.html>

Supported by ANPCyT, CONICET and CIC BA.

PairsDB protein sequence database

Kimmo Mattila, CSC - Scientific Computing Ltd.

PairsDB is a database of protein families and protein pairwise comparisons. It is based on nonredundant set of protein sequences, collected from the public protein databases. Clustering is used to find families that contain more than 90 % or 40 % identical sequences. For each cluster, a representative sequence is selected. This produces two smaller sets, where the difference between the sequences is more than 90% or 40%. For these two sets, all-against-all sequence comparisons are done using PSI-BLAST (for the 40% set) or BLAST (for the 90 % set).

The information about the pairwise similarities and the cluster members are all stored to a database together with information from protein domain analysis (InterPro, Adda, SCOP, Cath). The resulting database contains pre-calculated information about protein families and similarities for all the known protein sequences. This allows very fast access to the most essential protein sequence analysis results and studies that utilize the similarity information of large protein sets.

The PairsDB database is developed by the group of Liisa Holm (University of Helsinki). CSC has been developing a web interface and maintenance for this database in collaboration with prof. Holm. CSC plans to provide open www access to the PairsDB database in the end of year 2005.

EMBnet LiveDVD - EMBnet resources and bioinformatics applications at your fingertips

Martin Grabner, Max F. Perutz Laboratories
 Center for Integrative Bioinformatics Vienna,
 EMBnet Austria

The basic idea for developing a livesystem was to produce a valuable auxiliary for education in applied bioinformatics. To make the LiveDVD even more useful the original concept to produce:

A uniform and mobile small budget working environment was refined and extended by adding the following tasks:

- put together a complete package for basic office work and protocolling tasks in the laboratory
- standardize and internationalize the environment
- preconfigure the system for easy installation
- configure the bioinformatics tools
- produce an educational tool with presentation programs
- include manuals and educational materials
- include e-learning tools
- include groupware tools for members
- include powerful communication tools
- use LiveDVD to present new applications developed within EMBnet

In February 2005 Release 0.19.5 was offered for download at the Austrian EMBnet server. The release, which was put together and mastered at the Austrian EMBnet node, was tested in several courses within EMBnet. The experience showed that it was not only valuable as livesystem but also as installation media for a preconfigured system, taking away a burden of course room administrators.

In the workshop it was demonstrated how to install a complete livesystem with office, graphics and bioinformatics application to the harddisk in just 30 min.

<http://www.at.embnet.org/discussion-fori/embnet-livedvd/>

<http://www.at.embnet.org/toolbox/embnet-livedvd/> (member link)

Web Services at the EBI



**A. Labarga, S. Pilai, F. Valentin,
M. Anderson and R. Lopez**

External Services Group EMBL Outstation-
Hinxton, European Bioinformatics Institute,
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Cambridge, CB10 1SD, United Kingdom

SOAP (Simple Object Access Protocol) based Web Services technology has gained much attention as an open standard enabling interoperability among applications across heterogeneous architectures and different networks. The European Bioinformatics Institute (EBI) is using this technology to provide information retrieval and data analysis tools to the scientific community in order to enhance and ease the use of the bioinformatic resources it already provides.

Introduction

Today, biological databases comprise large collections of data that are relatively difficult to maintain outside the centres and institutions that produce them. The European Bioinformatics Institute provides access to more than 200 such databases and to about 150 bioinformatic applications.

These data and tools are mainly accessed using browser-based World Wide Web interfaces. When large amounts of data need to be retrieved and analysed, this often proves to be tedious and impractical. EBI also provides other mechanisms such as email batch job submissions, but this method lacks the interactivity of the web interfaces.

Moreover, research is rarely completed just by retrieving or analyzing a particular nucleotide or protein sequence. Database information retrieval and analysis services have to be linked, so that, for example, search results from one database can be used as the base of a search in another, the results of which are then analyzed. When performing these operations using a Web browser, researchers are forced to repeat the troublesome tasks of searching, copying the results for subsequent searches to other databases, and again copy the results for analysis.

Creating a local bioinformatics work environment is possible by downloading and installing the necessary database content and services (such as retrieval and analysis programs). This has the advantage that processes that otherwise require manual operations can be automated. However, the amount of disk space required to store biological sequence databases can be huge, often exceeding several terabytes, requiring several hours, if not days, to complete analysis, even when using a supercomputer. For this reason, creation of a local system is not a suitable option for most individual researchers or institutions.

On the basis of these observations, the EBI has chosen to use the Web Services technology to expose its services [1] in a programmatically accessible manner [2].

Web Services technology enables scientists to access EBI data and analysis applications as if they were installed on their laboratory computers. Similarly, it enables programmers to build complex applications without the need to install and maintain the databases and analysis tools and without having to take on the financial overheads that accompany these. Moreover, Web Services provide easier integration and interoperability between bioinformatics applications and the data they require.

All that is required at the user side is a lightweight program that communicates with the servers running at the EBI. These services have several advantages. As traditional web browsers cannot be used programmatically, these services provide an easy and flexible way to deal with repetitive tasks such as bulk

submission with minimal intervention from the user.

Web Services clients allow the programmer as well as the service provider to integrate and build more complex analysis workflows using existing EBI services.

Web Services technologies

Web Services (<http://www.w3.org/ws>) is an integration technology. According to the W3C a Web service is defined as a software system designed to support interoperable machine-to-machine interaction over a network.

To ensure software from various sources work well together, this technology is built on open standards such as Simple Object Access Protocol (**SOAP**), a messaging protocol for transporting information; Web Services Description Language (**WSDL**), a standard method of describing Web Services and their capabilities, and Universal Description, Discovery, and Integration (**UDDI**), a platform-independent, XML-based registry for services. For the transport layer itself, Web Services can use most of the commonly available network protocols, especially Hypertext Transfer Protocol (**HTTP**).

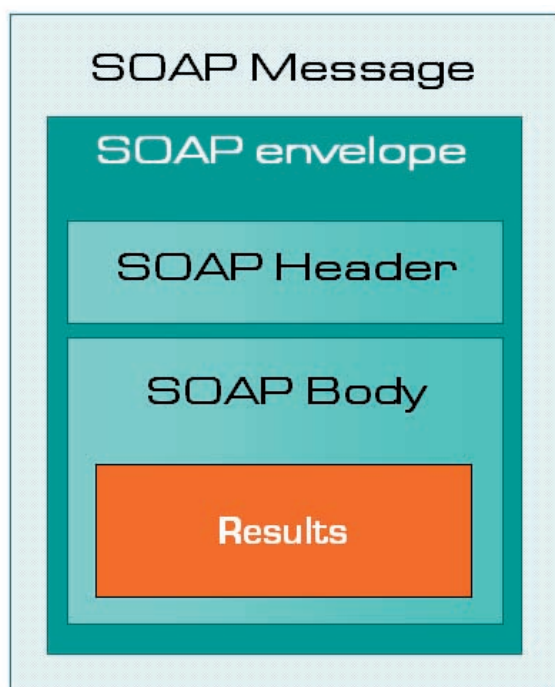


Figure 1. SOAP message structure.

SOAP: Simple Object Access Protocol

SOAP (<http://www.w3.org/TR/soap>), is a protocol for exchanging XML-based messages over a computer network, normally using HTTP. SOAP forms the foundation layer of the web services stack, providing a basic messaging framework that more abstract layers can build on.

A SOAP message (Figure 1) is contained in an envelope. Within this envelope are two additional sections: the header and the body of the message. SOAP messages use XML namespaces.

The header contains relevant information about the message. For example, a header can contain the date the message is sent, or authentication information.

Code 1 is an example of how a client might format a SOAP message requesting a database entry from EBI WSDbfetch web service. The user wants to retrieve the EMBL entry for the ID J00021 in XML:

```
<soap:Envelope xmlns:soap="http://schemas.xmlsoap.org/soap/envelope/">
  <soap:Body>
    <fetchData xmlns="http://www.ebi.ac.uk/webservices">
      <query>embl:J00021</query>
      <format>embl</format>
      <style>xml</style>
    </fetchData>
  </soap:Body>
</soap:Envelope>
```

Code 1. SOAP message example.

WSDL: Web Services Description Language

The Web Services Description Language (WSDL) is an XML format published for describing Web services.

WSDL describes the public interface to the web service; namely the protocol bindings and message formats required to interact with the web services listed in its directory. The supported operations and messages are described abstractly, and then bound to a concrete network protocol and message format.

A client (program) connecting to a web service can read the WSDL to determine what functions are available on the server. Any special datatypes used are embedded

in the WSDL file in the form of an XML Schema. The client can then use SOAP to actually call one of the functions listed in the WSDL.

For more information on WSDL, please refer to the W3C WSDL v1.1 Document (<http://www.w3.org/TR/wsdl>).

Table 1 contains a list of WSDL URLs that describe the WebServices available at the EBI:

EBI Web services descriptor files
http://www.ebi.ac.uk/tools/webservices/wsdl/WSDbfetch.wsdl
http://www.ebi.ac.uk/tools/webservices/wsdl/WSInterProScan.wsdl
http://www.ebi.ac.uk/tools/webservices/wsdl/WSEmboss.wsdl
http://www.ebi.ac.uk/tools/webservices/wsdl/WSClustalw.wsdl
http://www.ebi.ac.uk/tools/webservices/wsdl/WSTCoffee.wsdl
http://www.ebi.ac.uk/tools/webservices/wsdl/WSFasta.wsdl
http://www.ebi.ac.uk/tools/webservices/wsdl/WSWUBlast.wsdl
http://www.ebi.ac.uk/tools/webservices/wsdl/WSMPsrch.wsdl
http://www.ebi.ac.uk/tools/webservices/wsdl/WSScanPS.wsdl

Table 1. WSDL files for EBI web services.

UDDI: Universal Description, Discovery, and Integration

The Universal Description, Discovery, and Integration is a platform-independent, XML-based registry for services worldwide to list themselves on the Internet. It is designed to be interrogated by SOAP messages and to provide access to WSDL documents describing the protocol bindings and message formats required to interact with the web services listed in its directory.

The figure 2 represents how this set of protocols are designed to work together

Our implementation

We have implemented our services using SOAP and HTTP using Apache Axis (<http://ws.apache.org/axis/>) for Java based development and SOAP::Lite (<http://www.soaplite.com>) for Perl based development.



Figure 2. SOAP, WSDL and UDDI interaction scheme.

Services available

Currently, we support SOAP services for both database information retrieval and sequence analysis.

Sequence and Literature data retrieval:

WSDbfetch provides programmatic access to the popular sequence and literature data retrieval tool dbfetch (<http://www.ebi.ac.uk/cgi-bin/dbfetch>). The databases currently available for data retrieval using this service include EMBL, EMBL-SVA, MEDLINE, UniProt, InterPro, PDB, RefSeq and HGVBBase [2]. The data backends currently used are SRS, Sequence Version Archive (SVA) and the UniProt consortium server at the EBI (<http://www.ebi.uniprot.org>), but the service can be easily modified to use other data retrieval systems. It is implemented on Apache Axis. Users can call the WSDbfetch service from an application written in any programming language that supports SOAP.

Programming Perl SOAP clients

1. Download and install SOAP::Lite latest version from www.soaplite.com
2. Import the SOAP::Lite module into your program (use SOAP::Lite;)
3. Create a new stub from a WSDL file

Example: `$dbfetch = new SOAP::Lite->service(http://www.ebi.ac.uk/tools/webservices/wsdl/WSDbfetch.wsdl);`

4. Use the created object to access the server methods

Example: `$result = $dbfetch->fetchData($query, $format, $style);`

```

use SOAP::Lite;

$wsdl="http://www.ebi.ac.uk/tools/
webservices/wsdl/WSDbfetch.wsdl";

$dbfetch = new SOAP::Lite->service($wsdl);

$query="uniprot:wap_rat";
$format="default";
$style="raw";

$result = $dbfetch->fetchData($query,
$format, $style);

```

Code 2. Perl client example for the EBI Dbfetch web service.

Data can be retrieved from a database using either a primary or secondary identifier. Each database supports various formats and styles, of which one is set as a default. The results can be obtained as pure ASCII text, HTML with hyperlinks or XML, where available. A sample client in Perl is shown in code sample 2.

Sequence analysis

The EBI provides Web Services for sequence similarity tools (Fasta, WUBlast, NCBIblast, MPsrch and ScanPS); protein analysis (InterProScan); multiple alignment (ClustalW and Tcoffee); and the European Molecular Biology Open Source Software Suite (EMBOSS). These are Web Services servers that provide the same or even more advanced functionality than the traditional browser-based services found at <http://www.ebi.ac.uk/services>.

These services are implemented on a Perl-based, SOAP::Lite (<http://www.soaplite.com>) server and are tightly integrated with EBI hardware and middleware infrastructure. All web services have been developed using a common framework, and offer a similar interface to the user. They provide three basic methods: runApp, checkStatus, and getResult.

The runApp method (where App is the name of the application, i.e. runFasta, runClustalW etc) is used to submit a job to the EBI job dispatcher. This method accepts two inputs: an InputParams structure with the options to be passed to the application, and a string array with the sequences. The job can be submitted in two modes: synchronous and asynchronous. In both cases, the server returns a job identifier which can be used to retrieve the results (see Figure 3).

Synchronous mode

This mode is equivalent to a user running a command on a console or terminal and waiting for it to complete. This requires the client to be constantly connected to the server. This mode is suitable for database searches that can be executed in up to 5 min (e.g. protein versus protein searches).

Asynchronous mode

In this mode, the user submits a job and receives a job identifier in return. This is the same as running a UNIX command in the background and obtaining a job id. The user

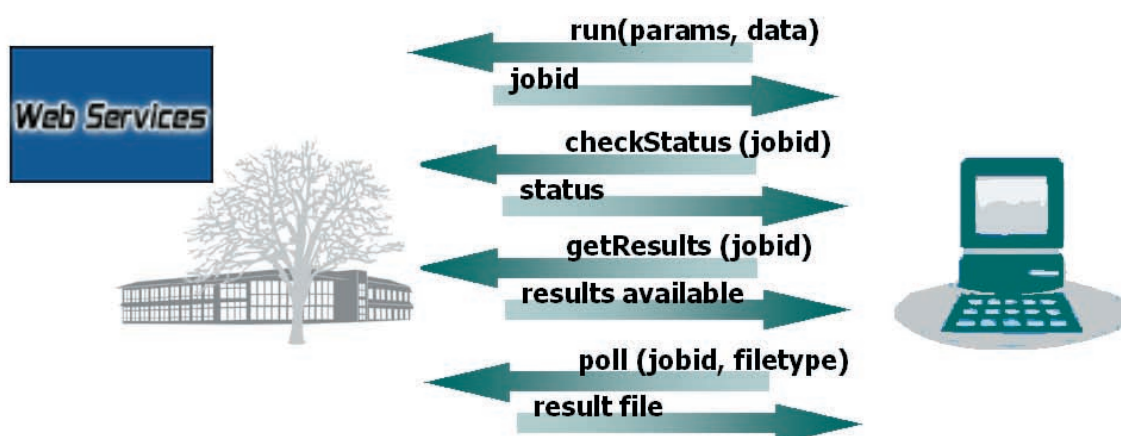


Figure 3. Message flow diagram for EBI web services.

Programming Java Axis clients

1. Download and install Axis latest version from <http://ws.apache.org/axis/>
2. Use wsdl2java tool to generate stub classes from a wsdl file
Example: `java org.apache.axis.wsdl.WSDL2Java http://www.ebi.ac.uk/tools/webservices/wsdl/WSEmboss.wsdl`
3. Import the generated classes (`import uk.ac.ebi.www.*;`)
4. Use the service implementation (WSEmbossServiceLocator) to create an instance of the service interface (WSEmbossService), and then create an instance of the service (WSEmboss).
5. Use the created object to access the server methods
Example: `WSEmbossService service = new WSEmbossServiceLocator();
WSEmboss emboss = service.getWSEmboss();
String jobid = emboss.run(params,inputs);`

can query the status (using the checkStatus method) of an asynchronous mode job and receive the following four states in response: JOB RUNNING (i.e. the job is currently being processed), JOB PENDING (i.e. the job is in a queue waiting processing), JOB NOT FOUND (i.e. the job id is no longer available; job results are deleted after 24 h) and JOB FAILED (i.e. the job failed or no results were found). Typically, the asynchronous submission mode is recommended when users are submitting batch jobs (e.g. many protein sequences to analyse using InterProScan) or large database searches (e.g. searching the whole of the

EMBL nucleotide sequence database). One advantage of this mode is that it is impervious to system or network failure. The results of jobs are stored at the EBI for 24 h after the job has completed.

Once the job has been completed, the user can retrieve a list of the produced results using the getResults method. This generates a list of results identifiers and the type of file (text, image, etc). The method poll is then used to retrieve the desired result. Sample code 3 presents a simple Java client for the Emboss *water* application.

```
import uk.ac.ebi.www.*;
public class water {
    public static void main (String[] args) {
        InputParams params = new InputParams();
        Data inputs[] = null;
        params.setTool("water");
        params.setAsequence("uniprot:alk1_mouse");
        params.setBsequence("uniprot:alk1_human");
        try {
            WSEmbossService service = new WSEmbossServiceLocator();
            WSEmboss emboss = service.getWSEmboss();
            String jobid = emboss.run(params,inputs);
            byte[] resultbytes = emboss.poll(jobid,"tooloutput");
            String result = new String(resultbytes);
            System.out.println(result);
        }
        catch (Exception e) {
            System.out.println("ERROR:\n" + e.toString());
            e.printStackTrace();
        }
    }
}
```

Code 3. Java client example for EMBOSS water program.



Figure 4. EBI web services are accessible from <http://www.ebi.ac.uk/tools/webservices>.

Using EBI webservices

All available information about EB web services can be accessed from the web page <http://www.ebi.ac.uk/tools/webservices>. There you can find a tutorial on how to build a web services client using Perl, Java and .Net technologies together with off-the-self clients using these technologies, the WSDL file descriptors for all web services, and more useful information on EBI web services and SOAP technology in general (Figure 4).

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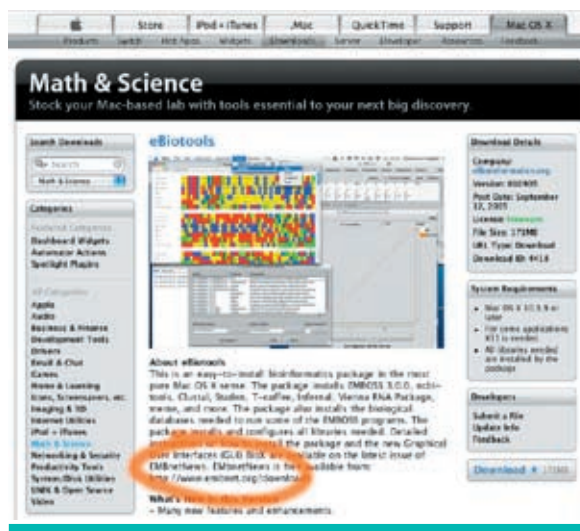
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Introduction

The OligoFakto Standalone Edition is an integrated suite of bioinformatics tools for the design of long oligonucleotides for microarray, of primer pairs for PCR, of siRNA and more...

A unified presentation of results provides overviews with distribution charts and relative location bar graphs, as well as detailed features for each oligonucleotide. Furthermore, the design pipeline can use BLAST servers to evaluate the specificity of selected oligonucleotides.

Each oligonucleotide design application has been implemented using a common mul-

tilevel optimization pipeline [Schretter and Milinkovitch, 2005]. However, the design of siRNA is based on the method described in Reynolds et al., 2004.

Features

Many features are described in details on the next page.

Acknowledgements

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Also available from apple.com

http://www.apple.com/downloads/macosx/math_science/oligofactorystandaloneedition.html



Figure 1. The main screen of OligoFakto Standalone Edition. The toolbar allows one-click access to any functionality and provides controls to choose the presentation of results. Colored bar-graphs show the position of amplicons and oligonucleotides relative to their query sequence.

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About OligoFakto Standalone Edition

An integrated suite of bioinformatics tools for the design of long oligonucleotides for microarray, of primer pairs for PCR, of siRNA and more.

The user interface emphasizes usability and is aimed at assisting researchers for a painless, rapid, automated and reliable design.

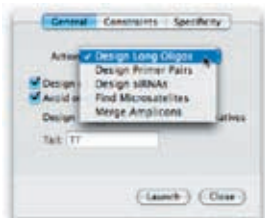
This free software was hand-crafted by Colas Schretter in 2005.

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Encoder for query sequences

A master-detail interface allowing users to enter their query sequences and related amplicons ranges. Users can cut-and-paste query DNA into the Editor view, or they can use the File Import menu item to import FASTA files.



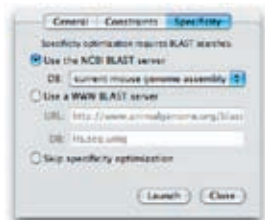
Five complementary actions

Several design iterations can be applied on an arbitrary number of target sequences, using five complementary actions that allow for the automated design of specific long oligonucleotides, of optimal 19 bp siRNA and of specific PCR primer pairs.



Design constraints

For design actions, the user has the possibility to control various constraints such as the range of oligonucleotide length, the range of product length for PCR, the range of melting temperatures, the preferred location of the oligonucleotides and the presence of a 5'-end tail.



Specificity evaluation

If needed, the user can choose a species against which oligonucleotide specificity will be tested. When choosing that option, the software will check whether any oligonucleotide exhibits a significant match with other targets in the database. The user can choose a database hosted on the NCBI server. The user can also use his/her own WWW BLAST server and custom databases.



Three different views of results

The results can be visualized with different views. A complete listing shows the relative location bargraphs of queries and results. The results can be summarized with charts showing the distribution of main features.



Details available in one click

The output includes the list of oligo sequences together with their corresponding locations on the query sequences, their lengths, and their melting temperatures. Easy-to-spot warning flags are shown in case of problems with secondary structures and/or with specificity. Detailed information can be obtained by clicking on the oligonucleotide sequence.



Export to various file formats

The user can export results to FASTA or a comma delimited file (CSV), readable by most spreadsheet programs (such as Microsoft Excel). The user can also export the current view to a web archive compatible with Safari.



Advanced controls

Shared parameters and advanced controls are available in the preferences panel. The user can define, among other things, the sampling of the candidate oligonucleotide space and the sensitivity of warning flags raised in the listings.

The color of the rose

Vivienne Baillie Gerritsen

One of the beauties of autumn is the firework of orange, yellow and red hues it displays. Anthocyanin is a plant pigment involved in this colorful palette. And not only is it at the heart of the autumnal shades but also the reds, blues and purples of petals and fruit all year round. The array of colors offered to us by Nature has always fascinated scientists who have put a great deal of effort into understanding both the structure of the various pigments but also the pathway leading to their synthesis. The last steps leading to anthocyanin are performed by an enzyme known as an anthocyanidin glucosyltransferase. Interestingly, in roses, this particular enzyme seems to catalyze not only one reaction – as is the case in the production of other flower anthocyanins known to date – but two reactions ultimately leading to rose anthocyanin.

Roses have been exhibiting their bright colors in gardens for thousands of years – the first rose gardens seem to have been Sumerian – and incessant crossbreeding has produced the many tints we know today. In 1840, the horticultural societies of Britain and Belgium offered a 500'000 franc prize to those who could produce a blue flower. Why blue? Simply because blue roses do not exist, yet they seem to have all the necessary ingredients to conjure up such a color. It was perhaps an event like this which first sparked numerous scientists' desire to know what pigments are on a more intimate level.

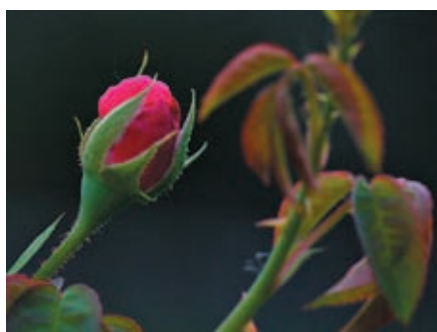


Fig.1 A rose bud in dusk.
Courtesy of Bruce M. Burton.

It was the German chemist Richard Willstätter (1872-1942) who made the first breakthrough. Not towards the growth of blue roses but

towards a greater understanding of the chemical structure of plant pigments and how colors could vary from plant to plant. As a result, he was rewarded the 1915 Nobel Prize in Chemistry. He demonstrated that anthocyanins are glucosides that can be split up into glucose – mainly – and a color component, cyanidin. He also showed that the color of a plant is not only dependent on the pigment's structure but also the plant's sap – or to be more precise its physiological pH – and, naturally, the concentration of the pigments themselves.

Surprisingly though, despite Willstätter's clear sightedness on the various pigments, he – amongst others – did not believe that enzymes were biological entities but 'merely' chemical substances. And it was only in the 1930s that the notion of an enzyme as something truly biological was agreed upon universally. Willstätter's work was interrupted by World War I when he was asked to turn his attention to the making of a gas mask... After the war, he pursued his research but it was interrupted a second time by World War II. Furthermore, being a Jew, he decided to leave Germany in 1939 for Switzerland where he died only three years later. In the decades that followed, the different enzymes and chemical entities which are part of anthocyanin biosynthesis were revealed and today the pathway is known in its molecular detail and entirety.

Anthocyanin glucosyltransferase is present in all plants. However, it seems that roses have their very particular transferase: an anthocyanidin 5,3-O-glucosyltransferase, which catalyzes not only one glycosylation reaction as in other plants but two succeeding ones. The enzyme's first substrate is anthocyanidin. Anthocyanidins are low molecular weight phenylbenzopyrones – or flavonoids – of which there are over 4000 compounds. Unglycosylated anthocyanidins are unstable and they are the first substrate to which the rose glucosyltransferase adds a glucoside. Only it adds it in such a way that the novel glucoside is unstable and the glucosyltransferase adds a further glucoside – thus creating a diglucoside which, in roses, is a stable anthocyanin and in turn gives a rose its color. Why there is a glucosyltransferase specific to roses remains a mystery. Why is it that glycosylation in roses does not proceed in the same way as in other plants?

The intricateness of color – as of smell – evolved in plants for the purpose of pollination.

Plants fast needed the aid of insects to survive and spread and it is no surprise that the two genders have been evolving in unison for millions of years now. Besides their role in pollination, anthocyanins also protect plant cells from harmful UV rays thanks to their antioxidative properties. Both these properties – coloration and protection – are of great practical interest. Anthocyanins can replace harmful dyes which have been banned and their anti-oxidant properties – revealed by the apparent lower risk of chronic diseases such as cancer and cardiovascular disease associated with the consumption of fruit and vegetables – have been proved. In July 2005, a first account of anthocyanin synthesis via recombinant *Escherichia coli* was reported. Such an adventure should permit the synthesis of anthocyanin compounds on an industrial scale but also the creation of fresh ones with novel catalytic activities, singular structures and – who knows – perhaps the color blue?

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