Prologue: plan for today

- General overview of CCP4 (~40-50 minutes)

Then (for those who are interested):

- More technical overview/demo of using the software (open-ended):
    - tutorial presentation
    - demo of the software

An Overview of the CCP4 Project

More than just a software suite?

Peter Briggs
CCP4, CCLRC Daresbury Laboratory

About myself

- Based at Daresbury Laboratory
- CCP4 programmer since 1998
  - Maintain & develop core suite
  - Coordinate developments with CCP4 graphical user interface
  - Coordinate CCP4 involvement in BIOXHIT project
  - Manage three staff members
  - Organise workshops & exhibition booths
  - Various other odd-jobs
- In the past I've also
  - Edited CCP4 newsletter
  - Liaised with industrial customers
  - Managed several software releases (4.1, 4.2 and 5.0)

Outline of the presentation

- Description of the CCP4 Project
  - Structure/organisation, role of Daresbury group
- Core Activities
  - Website, resources, conferences, associated projects
- Overview of the CCP4 software suite
  - Philosophy, components, activities
- Software Releases
  - Next release 6.0
- Issues and Challenges

What is a CCP?

CCP's = Collaborative Computational Projects

- First established in late 1970s/early 1980s by UK research councils

- Aim to provide infrastructure for "large-scale" computational projects in different areas of science

- 15 established – currently 12 are active

- **Typical remit:**
  - Implement flagship code development projects
  - Maintain and distribute code libraries
  - Organise training in use of codes
  - Hold meetings and workshops
  - Invite overseas researchers for lecture tours and collaborative visits
  - Issue regular newsletters

Collaborative Computational Project 4

- Established in 1979 by SERC
- Software for protein X-ray crystallography
- Aims:
  - *"Support collaboration between researchers working on PX software in the UK"*
  - *"Assemble comprehensive collection of software to satisfy the computational requirements of the relevant UK groups"*
- Gave rise to the CCP4 Program Suite
- Focus on collating, standardising, maintaining and distributing existing code
  - Some code developed "in-house"
  - Majority contributed by benevolent programmers

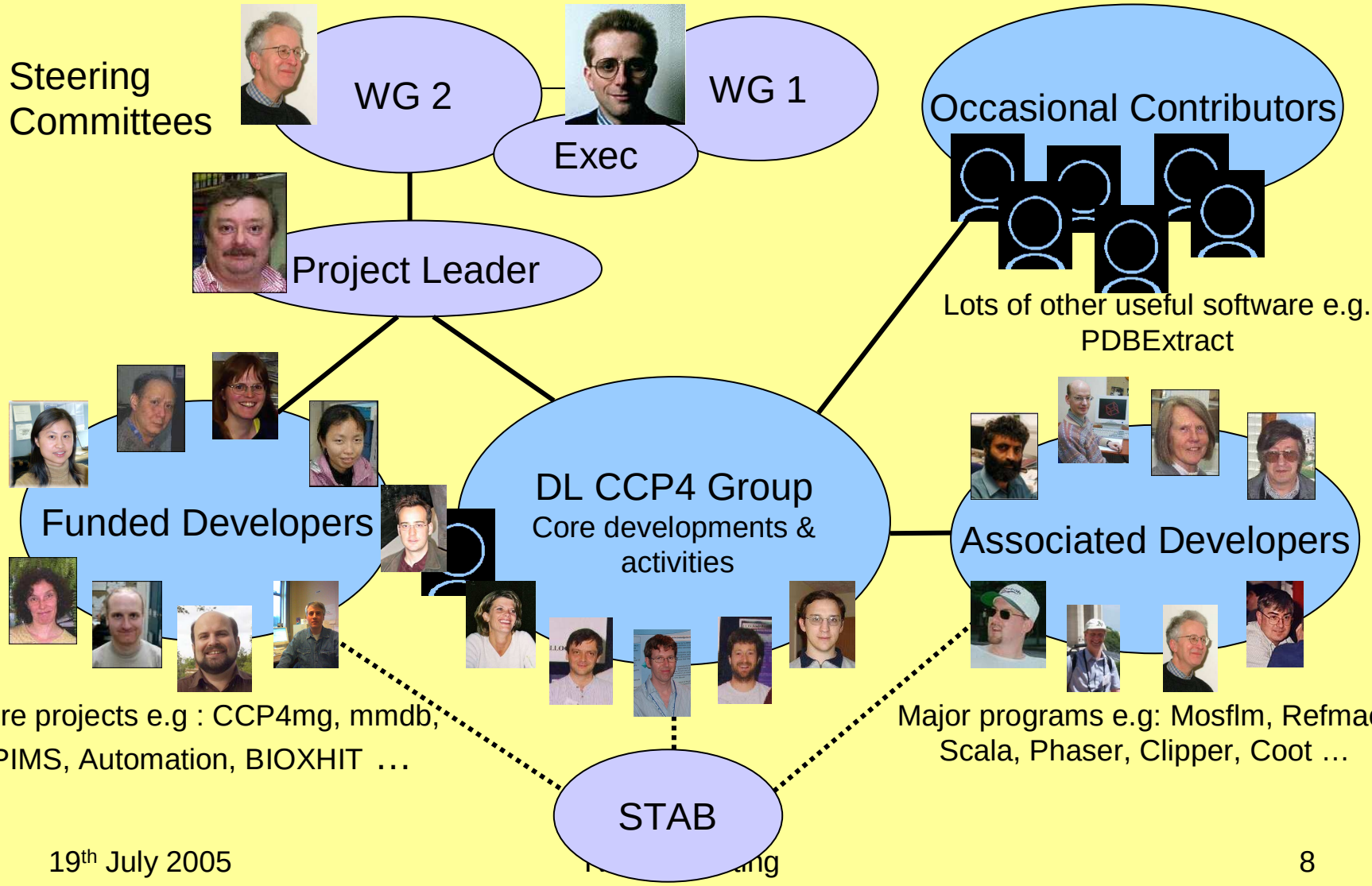
Current Status

- Core funding from BBSRC (5 year peer-reviewed grant)
  - Funds a small number of positions

- Software provided free of charge to academic/non-profit users

- Charge is made for commercial use
  - Provides funds for majority of staff/projects

CCP4 Organisational Structure



Some observations …

- **Organisation is very fragmented**
  - Diverse geographical locations, multiple projects involving contributions from different groups & different aims
  - Very difficult to manage
  - *but it seems to work … most of the time*

- **Daresbury CCP4 group acts as a central focus for the project**
  - make new programs available to general community
  - facilitate the development of new software
  - facilitate the general running of the project

- **Much of software development takes place outside "core" group**
  - *Project couldn't exist without the (often unfunded) contributions from many different developers*

- **No single contribution can be said to be more important than any other**

The Daresbury CCP4 Group

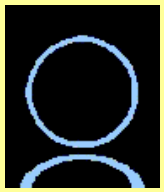
- **Based at CCLRC Daresbury Laboratory in UK**
  - currently home of the UK synchrotron source
  - also HPC centre
  - neutral location

- **Group consists of:**
  - four core programmers (Martyn Winn, Charles Ballard, Francois Remacle, Peter Briggs)
  - two programmers working part-time on core (Norman Stein, Daniel Rolfe)
  - executive assistant (Maeri Howard)

- **Core activities split between these staff**







Core CCP4 Activities

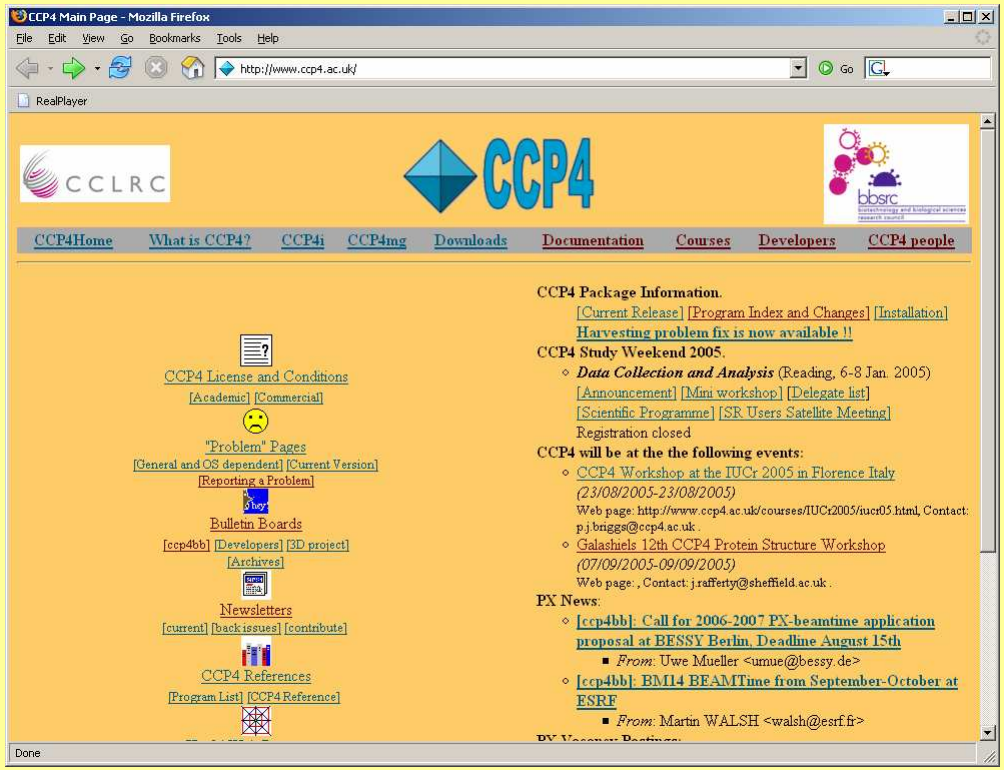
- **Maintenance and development of the core suite**
  - development of software libraries and infrastructure
  - graphical interface CCP4i
  - integrate in new software
  - bug fixing & technical support
- **Software releases**
- **Project administration**
  - commercial liaison
  - newsletters
  - maintain website and electronic mailing lists e.g. ccp4bb
- **Coordinate annual CCP4 Study Weekend**
  - also workshops and conference presence
- **Contributions to external projects**

CCP4 Website and Resources

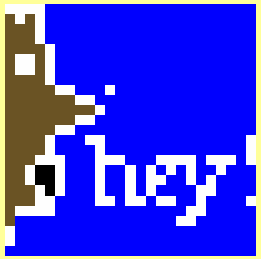
http://www.ccp4.ac.uk

Links to useful information:

- News
- Downloads
- Documentation
- Courses
- Problems Pages
- Developer's Resources
- Bulletin Boards
- Newsletters
- …



E-mail distribution lists



CCP4 Bulletin Board `ccp4bb`

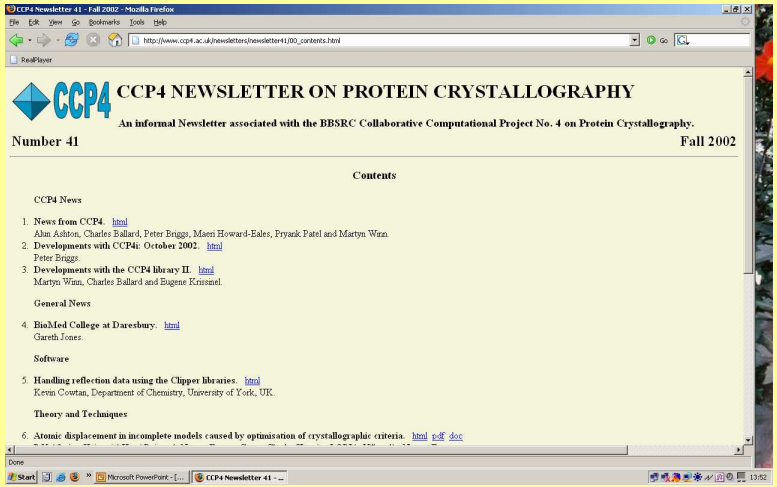
- Members from all over the world
- Fast expert help from colleagues
- Lively forum for discussing all aspects of PX
- "Sorry about the non-CCP4 posting …"
- Moderated list
- Online form for postings:
  `http://www.ccp4.ac.uk/reportaprob.php`

Other lists:

- Developers List **`ccp4-dev`**
- Also project-specific lists

CCP4 Newsletter on Protein Crystallography

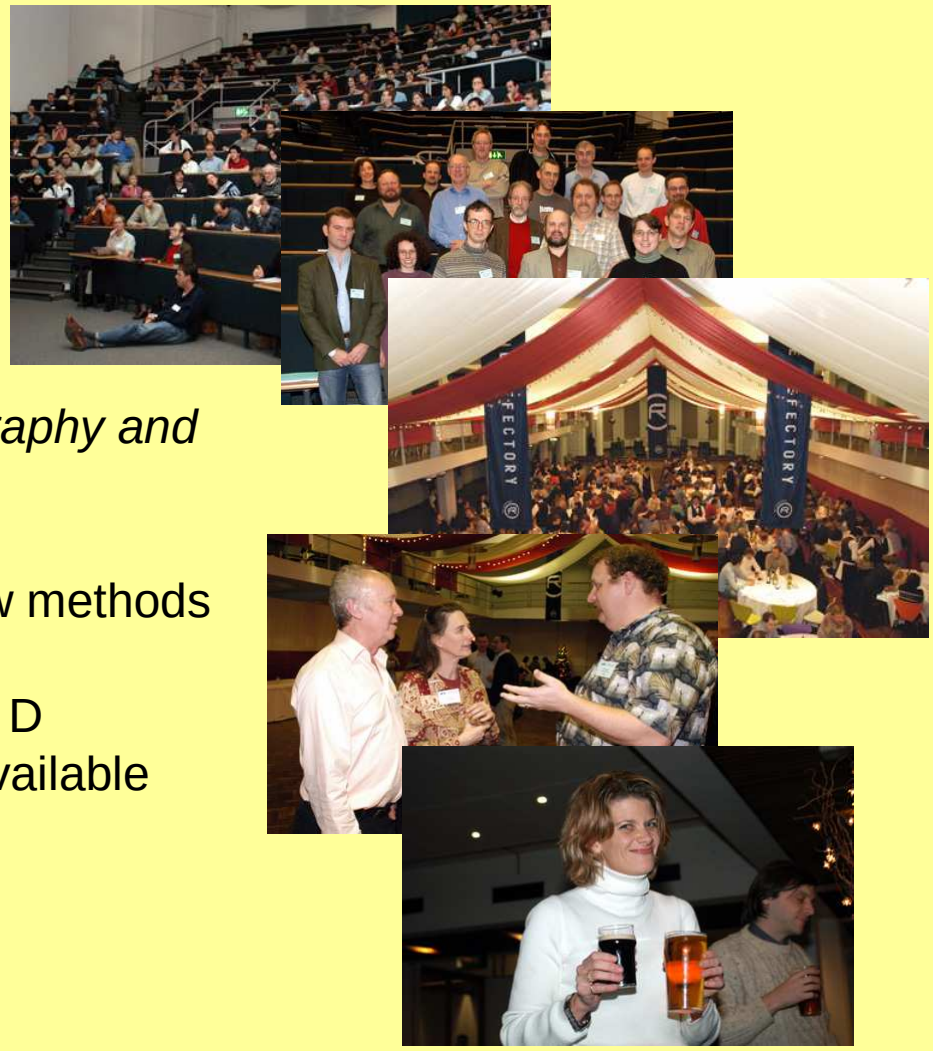
- News items
- Reports on new software and algorithms
  - CCP4 and non-CCP4
- Web-based publication since 2001
  - Back issues available on-line
  - Next issue due this summer



- **`http://www.ccp4.ac.uk/newsletters.php`**
  - or go via the CCP4 website

CCP4 Study Weekend

- CCP4's flagship event
- Held first weekend of each year
- Focus on particular aspect of PX
  - Next year: *"Complex Crystallography and Crystallography that is Complex"*
- Mixture of teaching material with new methods
- Proceedings published in Acta Cryst D
  - Older proceedings (pre 1998) available from Daresbury Library



Other Outreach Activities

- **Exhibition booths at major conferences**
  - ACA, IUCr, ECM, AsCA
  - Software demos and Q&A
- **One-day satellite workshops**
  - Focus on using the software
  - Last year: joint with CCP4-PDB (again this year)
- **Longer one-off workshops**
  - less frequent (< once a year)
  - e.g. one-week workshop in Bangalore, March 2005
- **Travel Scholarships**
  - 2-3 students from India & China
  - Visit UK labs for 2 weeks and attend Study Weekend

e-HTPX, DNA and Automation

e-HTPX – E-science Resource for High Throughput Crystallography

- BBSCR e-science initiative
- aim to provide a single interface to PX structure determination
- allow user to access experimental & computational resources from desktop
- pilot project started 2002

DNA – automating PX data collection experiments

- provides software to collect & process diffraction data
- includes rapid crystal screening
- unfunded collaboration, currently on release 1.0.0

CCP4 Automation Project

- aim to automate structure determination starting from processed data using CCP4 programs
- two programmers at Daresbury

BIOXHIT and PIMS

BIOXHIT - Integrated Technology Platform for High Throughput Protein Crystallography

- Europen project involving 20+ partner institutions
- CCP4 contribution involves development of CCP4i database for project tracking
- one full-time staff member at Daresbury

PIMS – "Protein Information Management System"

- provide LIMS system suitable for high throughput crystallisation experiments in academic environment
- funding from several institutions

The CCP4 Software Suite

Current release is version 5.0.2

Key components:

- Core software libraries
- Programs
- Documentation
- Graphical user interface

Languages:

- Programs: predominantly Fortran 77 (historical), increasingly also C/C++
- Libraries: predominantly C/C++ with Fortran 77
- Also Tcl/Tk (user interface), Java and shell

Platforms:

- Unix/Linux, Windows and Mac OS-X
- source code and binaries available

Philosophy of the CCP4 software suite

- **Modular:**
  - Large number of programs, each covers a small range of functionality
  - Data passed between programs via data files in standard formats
  - Keywords control program function and provide additional data
  - User decides on the sequence of programs to use for a particular task, e.g.

E.g. data reduction starting in CCP4:

`Mosflm` ➡ `Scala` ➡ `Truncate`

Or alternatively starting outside CCP4:

HKL2000/Scalepack ➡ **`Combat`** ➡ **`Scala`** ➡ **`Truncate`**

  - Can easily be used in other software packages (**`ARP/wARP`**, **`autoSHARP`**)

- **Inclusive & redundant:**
  - Includes a number of different programs to do the same job
  - Allows user to choose from different approaches

Core CCP4 Libraries

Provide infrastructure for standardisation of programs

- Data file formats: MTZ, PDB/mmCIF, maps ...
- Keyword parsing
- Handling symmetry and unit cell data
- Features such as **data harvesting**

Freely available for use/modification/redistribution:

- Mixture of LGPL & LGPL-compatible licensing
- Enables **SOLVE**, **SHARP**, **ARP/wARP** to use MTZ files

Advantages of libraries

- Less code to maintain
- Easier/quicker to write new programs/upgrade existing ones

Last release (5.0) focused on upgrading to new C/C++ based libraries

- Move towards more modern code base e.g. scripting interfaces

The CCP4 Suite

- ~180 programs covering all aspects of PX structure determination
- Relatively small subset are significant for most users, e.g.:
  - Data processing and reduction (**mosflm, scala, truncate …**)
  - Experimental phasing (**mlphare**, **acorn**, **rantan**, **oasis**, **bp3 …**)
  - Molecular replacement (**amore**, **molrep**, **beast**, **phaser**)
  - Density modification (**dm**, **solomon**, **pirate**)
  - Refinement (**refmac5**, **sketcher**)
  - Graphics and building (**ccp4mg**, **coot**)
  - Validation and analysis (**sfcheck**, **procheck …**)
  - Utility and conversion programs (e.g. **fft**, **cad**, **revise**, **pdbset, …)**

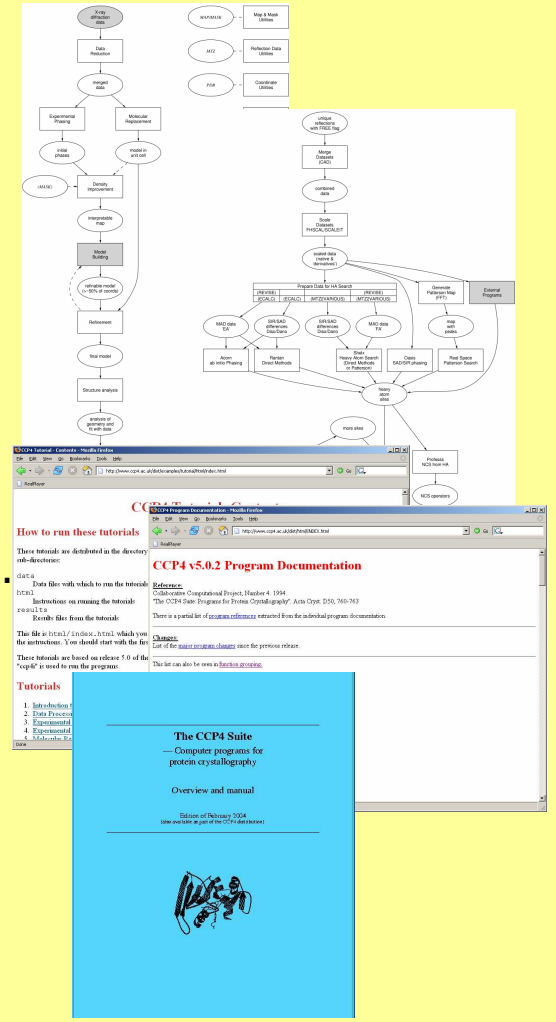
Navigating the suite

Key questions:

- Which program(s) do I need?
- How do I run it/them?

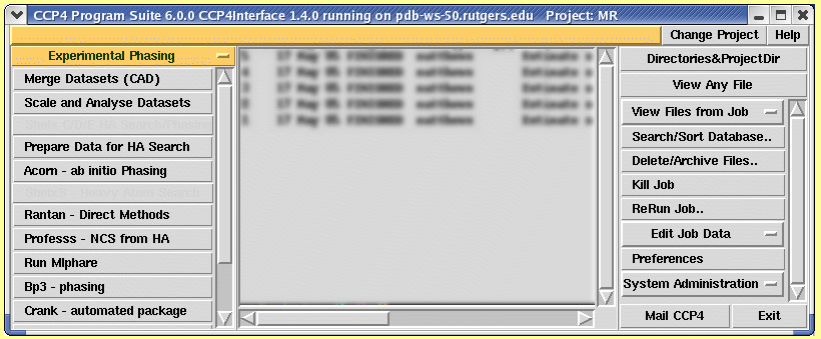
Documentation (http://www.ccp4.ac.uk/docs.html):

- Roadmaps
- Tutorials (html)
- Individual program documentation (html)
  - Function index
  - General background on twinning, reindexing, ..
- Postscript manual
  - Slightly dated but still useful
  - Content distinct from program documentation



Runnable example scripts
Graphical user interface

Graphical User Interface CCP4i



- Sits on top of programs
  - Hides details of individual programs
  - User not locked in
  - Allows mix-and-match approach
- Philosophy:
  - "Task-driven" rather than "program-driven"
  - Interfaces to tasks use "natural language" approach
    - e.g. 

- Key features:
  - Easy-to-use interfaces to major programs and utilities
  - Integrated tools for file viewing and basic project management
  - Customisable
  - Integrated help system
  - Some non-CCP4 programs also interfaced (e.g. ARP/wARP, SHELX)

Helpdesk – Technical Support

- Software is provided with “no warranty” clause
  - in practice we aim to provide support
- Queries sent to **ccp4@ccp4.ac.uk**
  - Problems with installation/usage
  - Bugs in software and documentation
  - Suggestions for improvements
- Central address acts as a clearing house for emails
  - may be forwarded to authors of actively developed software
- DL programmers operate a rota (6 people/1-2 weeks each)
- Known bugs posted on Problems Pages
  - **http://www.ccp4.ac.uk/problems.php**

Making Releases of CCP4

- Increasingly daunting task

Growth of the CCP4 suite since 1998

	March 1998	August 2004
CCP4 version	v3.5	v5.0.2
No. of programs	~150	~180
Size	43.5 Mb	~190 Mb
No. of files	1392	9112
Lines of code	~1.3 million	~4.15 million
Languages	Fortran, C, shell	also C++, Java, Tcl/Tk
Platforms	Unix & VMS	also Linux, Windows, Mac
Binaries provided	No	For all supported platforms
Subscribers to ccp4bb	~1000	~3000

Making Releases of CCP4

- Increasingly daunting task
- Software tools can help
  - CVS for source version control
  - Bugzilla track known issues prior to/after release
  - Automated building on various platforms to test
- Code freeze several weeks before test releases
  - can be difficult to enforce
- Beta releases for testing
  - Next version: test version via **http://www.ccp4.ac.uk/dev/releases.html**
- Patch releases to fix known bugs after release
- Long process (typically now 3-4 months)

Improvements to installation/update

- **Originally source code only**
  - Provision of binaries (2001)
  - Windows version (2002)
- **Automated installation and updates**
  - Binary downloader scripts (2004)
  - Prototype updater (2005) – fetch & apply source patches
  - InstallShield for Windows (2005)

Next release of CCP4: version 6.0

New packages:

- **PHASER:** maximum-likelihood molecular replacement
- **Pirate:** statistical phase improvement
- **CCP4MG:** CCP4 Molecular Graphics package
- **Coot:** graphical model building tools
- **Superpose:** secondary structure alignment
- **BP3**: heavy atom phasing refinement
- **CHOOCH:** anomalous scattering factors from raw fluorescence spectra

Updates to **REFMAC5**, **MOLREP**, **SFCHECK**, **SCALA**, **PDBEXTRACT** and others

CCP4i:

- **CRANK:** automated structure solution via SAD, SIR, SIRAS
- **SHELXC/D/E** interface
- Database search and sort utility

Plus many bug fixes and minor improvements

Some major new programs in CCP4 v6.0

Phaser

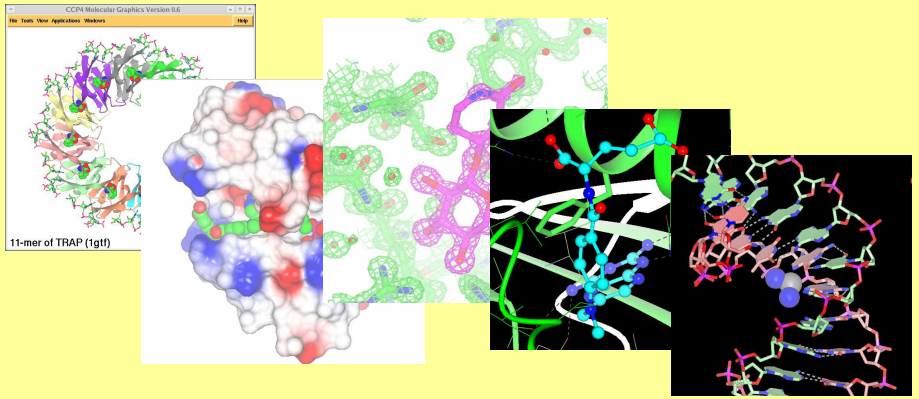
- maximum likelihood phasing
- currently has methods for molecular replacement
- uses ensembles of many models (with estimate of similarity to target)
- experimental phasing methods under development

Pirate

- statistical phase improvement (replacement for dm)
- uses phases from known reference structure with features similar to unknown structure
- doesn't require knowledge of solvent content

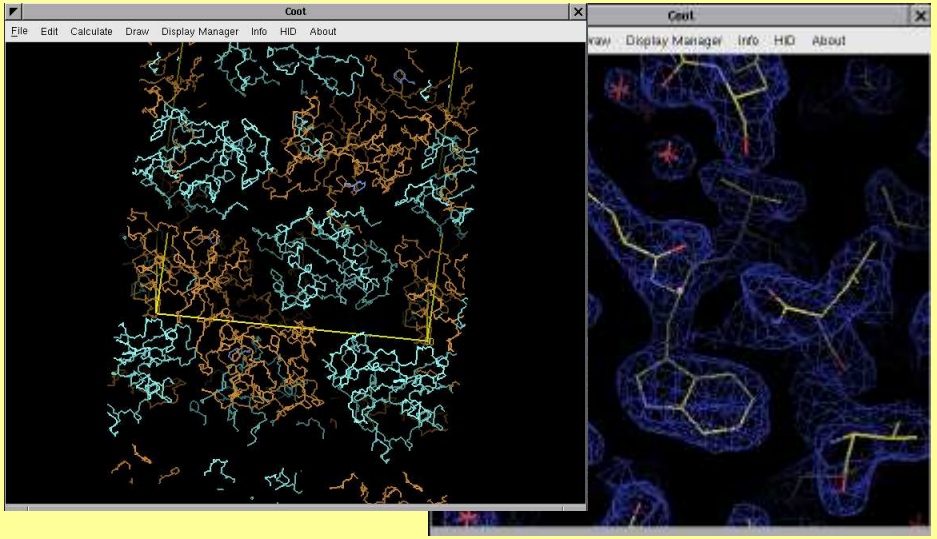
CCP4 Molecular Graphics

CCP4MG



- Focused on presentation graphics
- Rendering surfaces, superposition, structure analysis, movies …

Coot



- Platform for semi-automated model building tools
- Real space refinement, rigid-body fitting, ligand search, solvation, rotamers, Ramachandran plots …

Status of CCP4 version 6.0

Test version 5.99.2 available:

- see **`http://www.ccp4.ac.uk/dev/releases.html`**

Downloads divided into a number of packages:

- Basic CCP4 (about the same as v5.0)
- **`Phaser`**
- ***`cctbx`*** *(libraries)*
- **`CCP4mg`**
- **`Coot`**
- **`CHOOCH`**
- *plus dependencies* (**`Tcl/Tk/BLT`**, **`Python`** …)

New download pages:

- allow user to select required packages and dependencies
- download a single file for installation
- source code and/or binaries

Future Developments

Software

- Increasing automation
  - programs
  - automated pipelines
- More integration of “external” software packages
- Increasing use of scripting to develop applications
  - already seen in other projects e.g. PHENIX
- Significant update/revision of user interface
- Associated projects start to deliver software for distribution

Delivery of suite

- More modular package
- Installation/update procedure will change
  - easier for users (to compensate for increasing complexity)

Challenges and Issues

- Legitious environments (software patents and licensing issues)
- Changing user expectations (user base)
- Changing code base (size/diversity)
- Changing ways that software is used (webservices/GRID)
- Use of complementary experimental techniques (NMR, EM, XAFS, CD …)

Acknowledgements

CCP4 working group members

- Jim Naismith

CCP4 staff and contributors past and present

- Everyone who has ever contributed to the project
- *Far too many to mention here*

Martin Noble and Johan Turkenburg

Helen Berman & people at the RCSB-PDB

Cathy Lawson

You all for listening

- Thank you!