Sequence analysis and bioinformatics using Debian GNU/Linux

Andreas Tille

Libre Software Meeting

LSM, Nantes 2009

Overview

1. Debian Med
   - Debian Pure Blend for medical care and health science
   - Why Debian
2. Implementation
   - Available packages
   - Biological databases
3. Looking beyond
   - Alternatives and prospectus

Scope of Debian Med

- Free management systems for patients in medical practice and hospitals are rare

GNUmed	Patient record documentation for general practicians
MedinTux	Practice management system written for French health care system
Vista	Comprehensive software suite for hospitals (U.S. Department of Veterans Affairs)
Care2x	Web based hospital management system
Others	...

- However, people who hear the sound “Debian Med” just *assume* we provide a practice management system ...
- ... even if you tell them explicitly it is not
- So what are the real strengths of Debian Med?

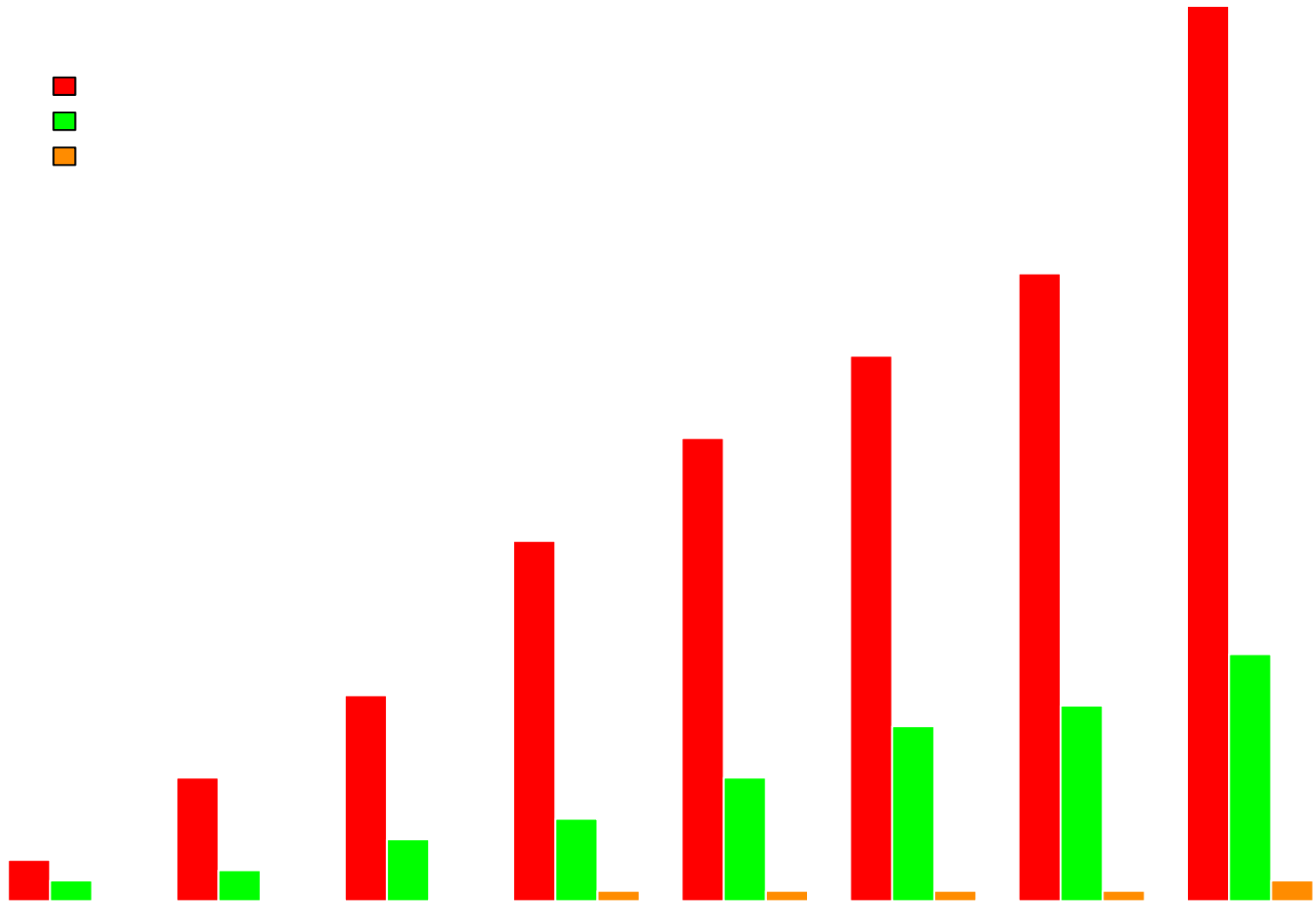
Medical imaging

- Debian Med can only include *existing* software
- Fair amount of high quality Free Software for medical imaging
  - Aeskulap, Amide: Medical image viewers
  - Dcmtk: OFFIS DICOM toolkit
  - Sofa: Simulation Open Framework Architecture
  - Fsl: analysis tools for brain imaging
  - ...
- Complete overview on *Debian Med imaging tasks page*

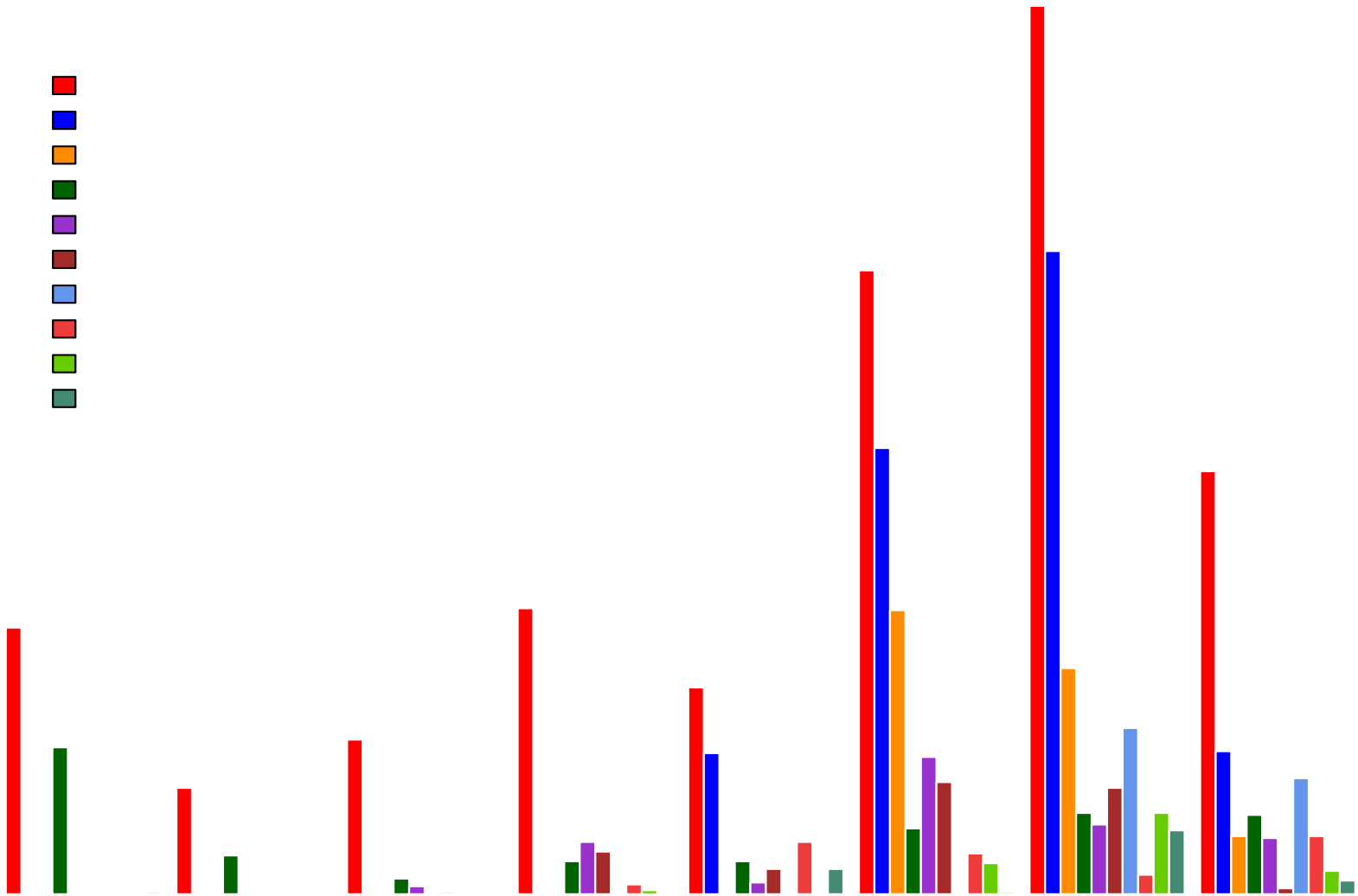
Molecular and structural biology, bioinformatics

- Most established branch of Debian Med because of good coverage by upstream software
- Fostering
  - Development at universities
  - Organised funding
- Hindering
  - Advertising for proprietary software
  - Different preferences of initiators

Selected metapackages of Debian Med



Top 10 posters on *debian-med@lists.debian.org*



Differences to commercial distributions

Commercial distributor		Debian
Company	Structure	Organisation
Employees	Persons	Volunteers
CDs, Service	Sells	Nothing
Business plan	Release	If 0 RC-bugs
Certified	Oracle, SAP, etc.	Runs in principle
Beginners	Preferred by	Administrators
Rpm	Packages	Deb
Market	Customisation	Do-O-Cracy

Customising Debian

- Debian $>$ 20000 packages
- Focus on *medical subset* of those packages
- Easy installation and configuration
- Automatic installation $\longrightarrow$ cloud computing
- Maintaining a general infrastructure for medical users
- Propagate the idea of Free Software in medicine
- Completely integrated into Debian - **no fork**

Basic idea: Do not make a separate distribution but make Debian fit for medical care instead

Debian - adaptable for any purpose?

- Developed by about 1000 volunteers
- Flexible, not bound on commercial interest
- Strict rules (policy) glue all things together
- Common interest of each individual developer:
  Get the best operating system for himself.
- Developers have children in real life or work in the field of medicine etc.
- In contrast to employees of companies every single Debian developer has the freedom and ability to realize his vision
- Every developer is able to influence the development of Debian - he just has to *do* it.

Do-O-Cracy = "The doer decides"

Programming language support

BioPerl	Collection of Perl tools for computational molecular biology
BioPython	Python library for computational molecular biology
BioRuby	Ruby tools for computational molecular biology
BioJava	Java API to biological data and applications
BioSQUID	library of C code functions for sequence analysis

Widely used software

BLAST2 Basic Local Alignment Search Tool
official NCBI version of this famous sequence alignment program (Note that databases are not included in Debian; they must be retrieved manually.)

EMBOSS European Molecular Biology Open Software Suite
EMBOSS is a free Open Source software analysis package specially developed for the needs of the molecular biology (e.g. EMBnet) user community

Statistics using GNU R

R-cran-genetics GNU R package for population genetics
: The package provides a library for the statistics environment R that contains classes to represent genotypes and haplotypes at single markers up to multiple markers on multiple chromosomes.

R-cran-haplo.stats GNU R package for haplotype analysis
: The package provides routines for the GNU R statistics environment for statistical Analysis of indirectly measured Haplotypes with Traits and Covariates when Linkage Phase is Ambiguous

Bioconductor GNU R tools for the analysis and comprehension of genomic data.
: Not yet packaged for Debian but work in progress to automate packaging of CRAN and Bioconductor packages.

There are some more general R packages recommended by `med-statistics`

Phylogenetic analysis

Altree	Perform phylogeny based analyses
fastdnaml	Construction of phylogenetic trees of DNA sequences
Njplot	phylogenetic tree drawing program
Tree-puzzle	Reconstruction of phylogenetic trees by maximum likelihood
Treeviewx	Displays and prints phylogenetic trees
Phylip	Package of programs for inferring phylogenies
Treetool	Interactive tool for displaying phylogenetic trees

Genetics and analysis of RNA sequences

Genetics:

Fastlink	Faster version of pedigree programs of Linkage
Loki	MCMC linkage analysis on general pedigrees
Plink	Whole-genome association analysis toolset
R-cran-qtl	GNU R package for genetic marker linkage analysis

Analysis of RNA sequences:

Infernal	Inference of RNA secondary structural alignments
Rnahybrid	Fast and effective prediction of microRNA/target duplexes

Sequence alignments and related programs

amap-alig	Protein multiple alignment by sequence annealing
Boxshade	Pretty-printing of multiple sequence alignments
Dialign(-tx)	Segment-based multiple sequence alignment
Exonerate	Generic tool for pairwise sequence comparison
Gff2aplot	Pair-wise alignment-plots for genomic sequences in PostScript
Hmmer	Profile hidden Markov models for protein sequence analysis
Kalign	Global and progressive multiple sequence alignment
Mafft	Multiple alignment program for amino acid or nucleotide sequences
Mummer	Efficient sequence alignment of full genomes
Muscle	Multiple alignment program of protein sequences

Sequence alignments and related programs (cont.)

Poa	Partial Order Alignment for multiple sequence alignment
Probcons	PROBabilistic CONSistency-based multiple sequence alignment
Proda	Multiple alignment of protein sequences
Seaview	Multiplatform interface for sequence alignment and phylogeny
Sibsim4	Align expressed RNA sequences on a DNA template
Sigma-align	Simple greedy multiple alignment of non-coding DNA sequences
Sim4	Tool for aligning cDNA and genomic DNA
T-coffee	Multiple Sequence Alignment
Wise	Comparison of biopolymers, commonly DNA and protein sequences

Molecular modelling and molecular dynamics

Adun.app	Molecular Simulator for GNUstep
Autogrid	Pre-calculate binding of ligands to their receptor
Gamgi	Construct, view and analyse atomic structures
Garlic	Visualisation program for biomolecules
Gdpc	Visualiser of molecular dynamic simulations
Ghemical	GNOME molecular modelling environment
Gromacs	Molecular dynamics simulator, with building and analysis tools
Pymol	Molecular Graphics System
R-other-bio3d	GNU R package for biological structure analysis
Rasmol	Visualise biological macromolecules

Autodocktools	GUI to help set up, launch and analyse AutoDock dockings

High-throughput sequencing

- “Next-generation sequencing”
- Chip-systems to sequence a genome
- Reads are very short (40 nucleotides rather than traditionally about 600)
- Enormous amount of chromosomal regions covered

Last-align Genome-scale comparison of biological sequences

Maq Maps short fixed-length polymorphic DNA sequence reads to reference sequences

Ssake Genomics application for assembling millions of very short DNA sequences

Velvet Nucleic acid sequence assembler for very short reads

Mikrobiological packages

- More than 80 Packages
- Overview at
  according tasks page of Debian Med project
- Software developed by
  - *National Center for Biotechnology Information (NCBI)*
  - *Sanger Institute*
  - *The Institute for Genomic Research (TIGR)*
  - ...

DebTags

```
udd=# SELECT tag, COUNT(*) FROM debtags
      WHERE tag LIKE '%bio%'
      GROUP BY tag ORDER BY tag;
                tag                 | count
------------------------------------+-------
 biology::emboss                    |     2
 biology::format:aln                |     9
 biology::format:fasta              |     9
 biology::nuceleic-acids            |    11
 biology::peptidic                  |    12
 field::biology                     |   174
 field::biology:bioinformatics      |    86
 field::biology:molecular           |     8
 field::biology:structural          |    16
(9 rows)
```

How to install large databases

- Bundling into Debian package makes no sense
  - Size costs bandwidths and mirror space
  - Moving target: Stable distribution will be out of date soon
  - Remote service seems appropriate
- Solution also works for astronomy and meteorology

getData

- Obtain data from external source
- Move data to local mirror
- Preparation of configuration file for particular system that deals with the database
- getData is still in a proof of concept stage
- People are much welcome to join this development (Google Summer of Code project)

Open Database License (ODbL) v1.0

- *Open Data Commons*
- License agreement intended to allow users to freely share, modify, and use this Database while maintaining this same freedom for others
- Databases can contain a wide variety of types of content (images, audiovisual material, and sounds all in the same database, for example)
- ODbL only governs the rights over the Database, and not the contents of the Database individually

Alternatives

BioLinux

- Based on Debian
- Create a policy incompatible structure in `/usr/local/biolinux`
- Some software not yet available in Debian but really sloppy with licenses
- We try to include the missing stuff in Debian to create a policy compliant, really free system
- Hope BioLinux people will adopt this

FreeBSD ports collection Biology

- Also contains a fair amount of biological software
- Only a few unimportant missing in Debian

Prospectus

- There are good requisites in Debian
- Most important tools of molecular biology, structural biology and bioinformatics for use in life sciences are included
- Further increase of interest of developers and users and getting them involved in the project
- Turning Debian into the distribution of choice for people working in the field of medicine because there is best support for free medical software

This talk is available at
http://people.debian.org/~tille/talks/
Andreas Tille <tille@debian.org>