Databases and ontologies

**MPIDB: the microbial protein interaction database**

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**ABSTRACT**

Summary: The microbial protein interaction database (MPIDB) aims to collect and provide all known physical microbial interactions. Currently, 22,530 experimentally determined interactions among proteins of 191 bacterial species/strains can be browsed and downloaded. These microbial interactions have been manually curated from the literature or imported from other databases (IntAct, DIP, BIND, MINT) and are linked to 24,060 experimental evidences (PubMed ID, PSI-MI methods). In contrast to these databases, interactions in MPIDB are further supported by 8,150 additional evidences based on interaction conservation, co-purification and 3D domain contacts (IPFam, 3did).

**Availability:** http://www.jcvi.org/mpidb/

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1 **INTRODUCTION**

As of today, about 600 bacteria have been completely sequenced and fragments of thousands of others have been determined as part of metagenomics projects (http://www.genomesonline.org/). Relationships among these genes and proteins are now being determined in a systematic manner. One such relationship that can be measured experimentally is a physical interaction between two proteins. High-throughput methods have generated large interaction networks. Such datasets have not only been shown to reveal functional clues about hypothetical proteins (Titze et al., 2008), but also that highly connected proteins are important for survival—afact that makes them ideal targets for antibiotics (Jeong et al., 2001). Several databases have been established for interaction data (Table 1). In addition to experimental data, databases such as STRING (Von Mering et al., 2007) provide predicted interactions. However, except for the latter, there is surprisingly little overlap between different databases. Hence users need to download and combine several microbial datasets.

The aforementioned databases have other shortcomings: none of them provides information on whether an interaction is conserved in another species and how similar the homologous proteins are. They do not include domain pairs that are known to form close contacts in 3D structures. Some even do not allow to search for species-specific information or only to a very limited extent, e.g. IntAct currently provides only searches for cryptic species abbreviations or NCBI taxon ids.

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| Table 1. Overview of imported interaction data |
|---|---|---|---|
| Dataset | No. of interactions | No. of unique interactions | Reference |
| INTACT | 16,322 | 16,059 | (Kerrien et al., 2007b) |
| MPI-EXP | 3,171 | 3,544 | (Titze et al., 2008) |
| MINT | 1,720 | 284 | (Zanoni et al., 2002) |
| BIND | 1,564 | 180 | (Alfarano et al., 2005) |
| DIP | 1,413 | 117 | (Salwinski et al., 2004) |
| MPI-LIT | 748 | 656 | unpublished data |

**MPIDB’s top species**

| Protein–protein interactions | No. of interactions | No. of evidences |
|---|---|---|
| Campylobacter jejuni | 11,873 | 12,401 |
| Treponema pallidum | 3,664 | 3,818 |
| Synechocystis sp | 3128 | 3148 |
| Helicobacter pylori | 1,629 | 1,647 |
| Escherichia coli | 1,292 | 1,811 |

Date April 6, 2008. *Numbers may include different strains.

We describe the microbial protein interaction database (MPIDB), a new web resource that addresses such questions and provides unified access to available microbial interaction data.

2 **MICROBIAL INTERACTION EVIDENCES**

Protein–protein interactions are defined as unique pairs of microbial UniProt accessions (UniProt Consortium, 2008). For each interaction, MPIDB features experimental and additional evidences (Fig. 1). An interaction is reported if there is at least one experimental evidence.

2.1 Experimental evidences

Experimental evidences are based on interaction experiments that identify two physically associated proteins. An evidence is defined by its interaction detection method (PSI-MI vocabulary (Kerrien et al., 2007a) in combination with its publication. Interactions from pull-down studies were only included if a bait protein purified only one prey protein. Overall, we integrated 24,060 experimental evidences from the scientific literature (MPI-LIT), from in-house two-hybrid experiments (MPI-EXP) and from other databases (Table 1). These experiments describe a unique set of 22,530 protein–protein interactions.
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2.2 Additional evidences
Interactions were used to identify homologous interactions (interologs) in the same or different species. A protein sequence comparison of interacting proteins revealed 5465 interolog evidences among 110 species/strains (BLAST E-value \( \leq 10^{-5} \), Fig. 1A). Interacting proteins were co-purified by 1029 pull-down experiments (bait–prey or prey–prey, Fig. 1B) and 1441 Pfam domain combinations among interacting proteins have been found to form close contacts in 3D structures [Pfam (Finn et al., 2005), 3jid (Stein et al., 2005), Fig. 1C]. Whenever an interaction from another study is mentioned in an article without experimental evidence in the same paper, we add the referenced study as a ‘secondary reference’ (Fig. 1D). Finally, multimeric 3D structures were integrated whenever both interacting proteins were part of a protein complex (homodimers have been excluded, Fig. 1E).

3 WEB INTERFACE
MPIDB can be searched by species/strain and/or by protein names (common gene name, ordered locus name and UniProt accession). More specific requests may be made using the advanced search option. Found interactions are displayed as protein pairs ordered by supporting interaction evidences. Lists of interactions may be downloaded as PSI-MI tab delimited files and can be imported by visualization tools, such as Cytoscape (http://www.cytoscape.org/). Clicking on the number of evidences shows experimental and additional evidences along with links to the source databases.

4 DISCUSSION
Experimental and/or predicted protein interactions are provided by several publicly available databases. Although some of them feature microbial interactions, the majority emphasise eukaryotic interactions while none of them provide access to all microbial data: each database stores interactions that are not reported by another (see No. of Unique interactions in Table 1). While features of these databases have influenced MPIDB, its manual literature curation efforts (meanwhile as an IMEx observer member http://imex.sourceforge.net/) and supporting evidences such as interologs and domain-domain interactions are unique to our database. In contrast to other repositories, we do not include binary interactions inferred from pull-down experiments. While STRING predicts interactions de novo, we treat predictions with caution and only add them as additional evidences to experimentally verified ones. Finally, users are requested to suggest additional features of interest.

Conflict of Interest: none declared.

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