To Authors:
To begin with the paper is well written in terms of technical and implementation aspects.

Thank you!

What I see is that author's do not clearly present difference between the earlier versions with the current version of BioMoby. It would be really helpful if the authors could explain this using a concrete example to understand the functioning of the BioMoby framework.

This is, in fact, the first publication of the BioMoby framework, though other publications have discussed, in very general terms, the various ontologies and their interpretations. The earliest publication that describes BioMoby (Wilkinson & Links, 2002) – which is often cited as the "canonical" publication – merely outlines an idea for a proposal; at that time no formal technical proposal nor robust implementation of that proposal had been developed. As such, there really is no "earlier version" to compare this to. BioMoby has developed, incrementally, over a period of several years, often with several small changes every day or every week. Though we have had a number of code releases, these releases did not correspond to any specific stepwise advances in functionality, but rather to points of functional-stability in the codebase along the more continuous development path. In this sense, there is no useful statement that could be made about prior versions, nor any particularly useful (to the reader) comparisons between them.

The paper looks more like a user manual with technical specification rather than any scientific implication to the readers. The authors could improve the paper by providing a strong biological input as motivation for developing such a framework.

It is always useful to contextualize the creation of a novel technology, and as such I have added an additional paragraph at the beginning of the introduction describing the bottleneck for Systems Biology research being the complexity of Web-based data access, as well as the lack of standards for Systems Biology data representation, which has thwarted our ability to create software systems that can integrate this data. We then use this as the framing motivation for the technology-development that was undertaken within the BioMoby project. However, while we agree with the reviewer's observation that the "results" portion of the manuscript reads, at times, like a technical manual, this is perhaps unsurprising given that the manuscript is specifically intended to describe a novel technology! We further feel that the extensive discussion section, which takes-up nearly half of the manuscript and lays-out numerous “philosophical” comparisons with peer technologies, constitutes a valid scientific discussion of the technology’s implications. It is our understanding that the PLoS ONE journal accepts manuscripts from a wide range of domains, including both biologically-oriented and technologically-oriented manuscripts, and it is important to note that this manuscript was not “aimed at” a biologically-oriented audience. As such, it may be that the reviewer’s expectations of how the manuscript should be written do not parallel our intentions.

As I read through the paper I see the author’s speak about semantic web services. It would be interesting for the readers to know what the other semantic web services and how BioMoby is better. Is it possible for u to demonstrate it with an example?

Last paragraph of Introduction has been extensively edited to define what we mean by Semantic Web Service, and to point out the primary difference between BioMoby’s approach and those of its peers. Detailed comparisons between the three major peer technologies – BioMoby, myGrid, and caBIO – have already been published elsewhere, and we agree that we should have referenced these discussions in this manuscript. References to the two key comparative papers have been added to the bibliography (reference 18, 19). Beyond this, the discussion section of this manuscript already includes an extensive (3 ½ page) sub-section entitled “BioMoby vs. peer semantic and schema technologies” where we go into more specific detail on finer points of the comparison, and include comparison of peer technologies other than myGrid, and caBIO. In this discussion we point out not only the aspects of BioMoby that are better, but also the aspects where it fails to achieve what other standards have. To provide explicit comparative examples would require the addition of significant amounts of code and/or XML, which would make this manuscript considerably more technical (which the reviewer has already objected to).

In the results section the author’s speak about Namespaces Ontology wherein there are 300 different Namespaces that includes prominent public data resources. It would be interesting to know weather BioMoby also supports PSI MI, MAGE standards that are also coming in from prominent databases.

There seems to be some confusion in this question between Namespaces and Objects, and this may be the root of what is apparently a mis-understanding. For Moby, PSI-MI and MAGE are not Namespaces, they are Objects. In the manuscript section “The Object Ontology – How is that data represented?” we explicitly state that we support legacy and third-party data-types; nevertheless, in response to this comment I have added “MAGE-ML” to the list of examples we gave in the text. It is important to point out, in response to this comment, that this brief list of examples was not meant to be exhaustive (nor could it be!). The point made in the last sentence of that paragraph is that we intend to support ALL existing data-types; quote "Importantly, the Object Ontology does not re-define legacy or third-party data-types, it simply makes their type explicit, thus the myriad of existing parsers and analytical tools that consume these file formats can still be utilized."

In the Object Ontology the author's specify BioMoby framework can receive any data-type and it does not re-define the legacy of the data type. Please provide a more concrete example for this point.

It seems the reviewer may have missed the example given in that very same paragraph. We provide a concrete example in the text, and it is in fact diagrammed in Figure 2B, where an EMBL record – one of a wide range of legacy data-types we support – is being passed in a Moby Object.

In BioMoby web services Second Paragraph the author's say:
"The providers do not need to be concerned about the exact structure of incoming data and do not need to query the ever- changing BioMoby ontology".
1. Justify this statement.

It is unfortunate that, through the course of migrating and cleaning-up the BioMoby documentation, this directive has somehow been lost from the most recent version of the API document. It was, however, published in the Proceedings of the Virtual Conference on Genomics and Bioinformatics, 2003 (http://biomoby.org/VCGB_130.pdf). It's "justification" is that it represents a ***directive*** within the BioMoby API, and therefore does not constitute a hypothesis or a speculation on our part. It is part of the ***definition*** of BioMoby's behaviour – that providers need not (in fact, ***should not***) validate the nature of an incoming object; it is either structured how you expect it to be structured, or you fail.

Though we discuss this issue extensively in the section entitled "BioMoby vs. OWL/RDF", I will reiterate the supporting argument briefly here: Given that all defined objects derive from, or contain other defined objects; and given that one cannot over-ride the definition of a contained or inherited object, it is therefore impossible to modify those aspects of the DOM coming from contained or inherited object. As such, if I am provider being accessed by a well-behaved client application (where "well behaved" means that it provides me with the data-type I have registered, or one of its derivative child types, as per the Moby API), I am guaranteed that the data I expected to receive will be at a predictable location within the incoming DOM ***regardless of what the exact data object is that I have***

been given. I do not need to look-up that object's type in the ontology (though I could if I wanted to!) because the system is designed to never give me a piece of data that I cannot interpret simply by querying the DOM model. If any of this is not true, then I pass an error back to the client application, since they are not being API-compliant.

2. Summaries what are the BioMoby's ontology's that was present in the earlier and in the current version.

I apologize, but I am unable to understand the intent of this question. There has never been any "version" of any of the ontologies, nor (with one arcane exception that would only serve to confuse the reader) have any changes in the ontology been linked to any fundamental version-change in the core BioMoby code. The object ontology is changing almost daily. It is not versioned, nor do we track what is contained in the ontologies at any given point in time, though we agree that this might be of historical interest to some people. Unfortunately, I suspect that we would be unable to answer this question due to lack of available data, even if it were clear what the underlying intent of the reviewers question was.

3. How can you compare it with the other semantic web services ontology's?

As mentioned above, the final paragraph of the introduction now points out the fundamental difference between BioMoby's ontologies and those used by other Semantic Web Services projects, and provides citations to two published manuscripts where this comparison is made in significant detail.

Justify how SOAP concept implemented in BioMoby is better than the others service providers that could improve the interoperability of the framework.

We do not claim that we have implemented SOAP in any novel way. What we have implemented is a way of defining message structure and semantics within the body of a normal SOAP message. Most existing Web Service providers utilize SOAP with message-bodies that are opaque except to software applications that were designed to utilize them. We embed the meaning into the message-body by giving the message a structured syntax that is grounded in an external ontology. Other Semantic Web Service providers utilize external ontologies to explicitly describe the meaning of the various fields in a SOAP interface, but they do not strictly/reliably define the syntax by which those fields will be represented. The predictability of syntax in BioMoby is what causes BioMoby to have improved interoperability over other Web Service systems. The manuscript, in toto, contains the justification for why we believe our implementation of messaging is better than other service providers; this issue is the purpose and point of the entire BioMoby project! We discuss the issue explicitly throughout the manuscript, but I will copy/paste one of the arguments, verbatim, here. From the beginning of the Discussion section: “The first distinguishing feature of BioMoby is that it operates in an extensible, but closed-world of data semantics. The XML Schema within a traditional WSDL document defines valid XML tags for any given service, but these are not (predictably) bound to any standard external machine-readable interpretation. Thus the XML tags, and the content of these tags, from one Web Service are not reliably compatible with the XML tags or content from another arbitrarily chosen Web Service. As a result, automated pipelining of non-coordinated services in other interoperability initiatives is extremely difficult. In contrast, the Object, Namespace, and Service Ontologies provide a common binding for all services and client software in the BioMoby framework such that a given XML tag appearing in any BioMoby message has one and only one interpretation, and this interpretation is available in a shared ontology. In this way, BioMoby finesses the extremely complex problem of open-world Web Service composition by defining the allowable world of data syntax and semantics via publicly extensible ontologies.”

Through out the paper the author’s have introduced various terms as ontology. It is quite misleading for me to associate these different ontology under one roof of BioMoby.

I apologize, but I cannot understand what the reviewer is asking here. We claim to have built three ontologies: Object, Namespace, Service. We use one term – ontology – to define what kind of data structures they are, and they are all part of the BioMoby project specification, and therefore rightly belong “under one roof”.

Finally, I feel that BioMoby is one of the most prominent approaches in the bioinformatics community.

Thank you!!

The paper contains less scientific inputs and more technical inputs. The paper does not contain strong examples to validate various arguments.

I feel I must disagree with the reviewer. Though this manuscript is specifically intended to be an announcement of a novel technology, and thus by design contains many details about the technical specifications for the framework, nearly one half of the manuscript is dedicated to a discussion of the science and theory behind the decisions we made when designing the BioMoby system. We provide explicit examples, relevant to our target audience, in the text and in figures.

My understanding is that the reviewer wishes to see more explicit *biological* examples in the manuscript text. In this regard, I have included an extensive "story" detailing how a biologist might interact with the BioMoby system in the course of their normal daily activities. This is presented in the final section of the Results, headed "An example of the utility of BioMoby for the biologist". Hopefully this is the kind of example that the reviewer is looking for?