

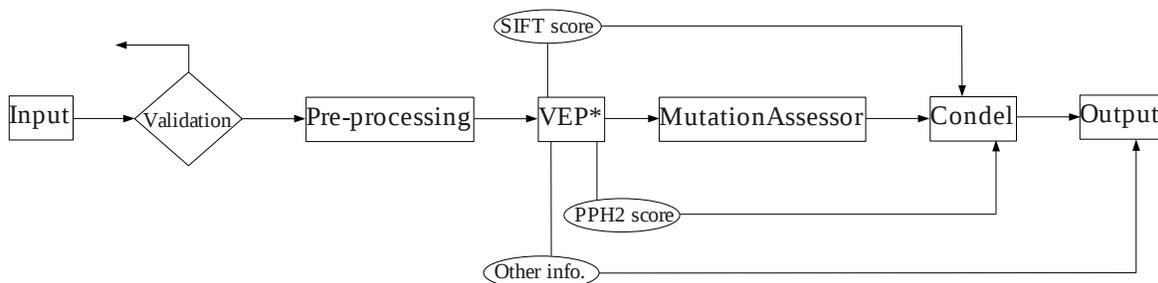
Supplementary data

Section A: Implementation of condel server

Condel-server is a web-application designed modularly using well-known OO design patterns. Four different-decoupled modules compose condel server: task-management, condel-task, condel-web and condel-ws.

Task-management is a generic but simple task manager tool. It is mainly in charge of executing tasks and registering the course of the task executions into a global description tasks registry. Two main agents lead this module: the factory and the task-manager. The **factory** is created during the initialization of the application. It loads in memory the registry file and saves it in disk. Additionally this agent creates task-managers when the application need it . Each **task-manager** (usually one per user) is the agent that response the user events. It is in charge of executing tasks, looking into the registry and canceling or deleting tasks. Every time a new task is created in the system, a new entry is also created in the task registry. The **task registry** is a very simple xml file which contains descriptions of all list of task entries. A **task entry** is the meta-description of the execution of a task. Each task entry contains the following information: an id and a group id of the task, date of creation, date end, input file, output path file, ip of the requester, task status (i.e. pending, executing, error and done) and a short log with the description of the execution of the task. An snapshot of the task registry file is attached in the supplementary material.

Condel-task is the module that implements the condel task. This task contains an associated **context** xml file. The idea of having a context file is to detach the implementation of the processes that intervene in the task from the parameterization with what to execute the processes. This fact drove us to a fast and easy development of the condel task. The context xml file is composed of a name and a description of the task and a list of process descriptions. Each process description contains a name of the process, the url of the executable, and the list of parameters to execute. (The following diagram illustrates the organization of the condel-task module.)



*The Variant Effect Predictor (VEP) output is filtered to retain only SNVs that cause an aminoacid change (non-synonymous SNVs) in at least one of the gene transcripts.

First, the module possesses a data **pre-processing** program, where the input data is validated, then it is converted in a common data format (accepted by the Ensembl-variation Variant Effect Predictor, which includes converting the SNVs from protein coordinates to genomic coordinates if that is the case of the input) and finally this data is partitioned in batches of rows (for a better performance with our local Ensembl-variation MySQL database). After that, and for each input partition we run the **ensembl Variant Effect Predictor (VEP)** with a local installation of the Ensembl-variation and Ensembl

databases. Subsequently, **MutationAssessor** is run for each SNV through its webAPI and finally, the scores of SIFT, PolyPhen2 (PPH2) and MutationAssessor are integrated by the **condel** method. Along the whole process a unique folder is associated to the task where to store and create the initial, final and intermediate files generated by the **condel** task.

Condels-web module is a simple web user interface. The idea behind it is to offer the possibility of running **condel** method to a diversity of users in a simple and easy way. Thus, our purpose was to keep simple and anonymous the execution of **condel** tasks so that any user that with their own SNVs could run **condel**. However we thought that web users could need to manage (e.g. view, download, delete) tasks submitted previously. For this reason, we incorporated into **Condels-web** the option to keep trace of the old user tasks without any heavy registration step. The only pre-requisite for this is to enable the acceptance of cookies in the web browser.

Condels-ws is the module which runs the **condel** web-services. The idea is to offer a very simple API to submit **condel** task in batch mode but also give the possibility to easily integrate **condel** within any other external pipeline or process. The web-services are implemented using the common well-known REST framework. Thus, two main web-services have been created: one for submitting tasks (through a PUT method) and other for retrieving the results of a task (using a GET method).

The orchestration of all the **condel server** modules starts when the application is deployed in the server. Initially the **task-management** module intervenes creating one factory agent for the **condels-web** and one for the web-service module. These agents as mentioned before hold a shared instance in memory of the task registry file. Every time a new user opens their web browser or a web-service call is performed, the factory agent creates a new task-manager (if needed) to carry out the user requests coming from **condels-web** or from **condels-ws** API. Once a new **condel** task is submitted, the task-manager interacts with the **condel-task** module to create a new task for the user. The manager registers a new entry in the registry, creates a new folder in the server and executes in parallel the task. The **condel-task** by it-self decides to change the status when it has already started, finished or if any problem has occurred during its execution.

Additionally, and for maintenance reasons we have created a simple administrative section (with restricted access) in the **condels-web** to allow following up all tasks performed in the server (**condels-web** and **condels-ws**).

The **condel-server** is allocated in our institutional servers. Thus, in order to avoid an overcoming of petitions to our servers we have initially limited the total number of simultaneous tasks to 12 and the number of tasks by session to 2. Additionally all tasks last in our server up to 72h in order to keep space free for new user requests.

Section B: Simple usage tutorial

CONsensus DELeteriousness score of missense SNVs

Home Analysis View Help About

Please access the [home](#) section to know more about the Condel method or check the [help](#) section to know more about how to launch a new task. [Admin](#)

Task

Descriptive task name [*]

Enter your mutation data [*]
(Read about [input format](#) or use this [example](#))

File name:

[*] Mandatory fields

The web server computes the corresponding Condel scores from the outputs of the three tools (SIFT, Polyphen2 and Mutation-Assessor).

Remember:

- Up to 2 tasks running simultaneously
- Up to 20 tasks per session. If you need to execute more tasks, please delete previous old tasks.
- Tasks longer than 72h are cancelled (if they were executing or pending) and removed from the summary table

List of tasks

Once the task is done click on the id link of the task to view the results
This list is being updated automatically every 10 seconds, although you may prefer update it [manually](#)

id	+Name	-DateCreation	DateEnd	+Status	Operations
No Records Found					

Control table: Using its links the user may manage their tasks and access their results

Step 1: Submission of data to create new tasks is done in the Analysis section of condel server. SNVs may be introduced either as genomic coordinates or protein coordinates. They may be cut and pasted in the analysis box, or uploaded within a file. The *input format* link describes the formats accepted by the server. The *example* link contains several SNVs in genomic coordinates. Note that, at this stage, the control table at the bottom of the page appears empty.

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Task

Descriptive task name [*]
some_SNVs

Enter your mutation data [*]
(Read about [input format](#) or use this [example](#))

9	32473858	32473858	A	1
7	43918688	43918688	C	2
7	38471790	38471790	A	3
6	88372821	88372821	A	4
5	41934236	41934236	G	5

File name:

[*] Mandatory fields

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id	+Name	-DateCreation	DateEnd	+Status	Operations
No Records Found					

Step 2: A name has been given to the task (mandatory), and the example link has been hit to fill some SNVs into the analysis box.

Condel
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Task

Descriptive task name [*]

Enter your mutation data [*]
(Read about [input format](#) or use this [example](#))

File name:

[*] Mandatory fields

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List of tasks

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id	Name	DateCreation	DateEnd	Status	Operations
condel-task-534914e1-7477-408b-aa4f-c948a943273f	some_SNVs	2011-07-19 15:12:29		executing	view download details cancel delete

Step 3: The submit button has been hit. A new task has been created and a randomly generated id has been assigned to it. It therefore appears now in the control table at the bottom of the page. Its current status is *executing*. Its status will be updated every 10 seconds until it has finished.

Condel
CONsensus DELeteriousness score of missense SNVs

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Task

Descriptive task name [*]

Enter your mutation data [*]
(Read about [input format](#) or use this [example](#))

File name:

[*] Mandatory fields

The web server computes the corresponding Condel scores from the outputs of the three tools (SIFT, Polyphen2 and Mutation-Assessor).

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- Up to 20 tasks per session. If you need to execute more tasks, please delete previous old tasks.
- Tasks longer than 72h are cancelled (if they were executing or pending) and removed from the summary table

List of tasks

Once the task is done click on the id link of the task to view the results
This list is being updated automatically every 10 seconds, although you may prefer update it [manually](#)

id	Name	DateCreation	DateEnd	Status	Operations
condel-task-534914e1-7477-408b-aa4f-c948a943273f	some_SNVs	2011-07-19 15:12:29	2011-07-19 15:12:43	done	view download details cancel delete

Step 4: The task is now finished (after 14 seconds), so its current status is *done*. Its results may be accessed by clicking on its id or on the view link at its right. Additionally, the user may directly download the results, see the logs generated by condel server while running their task, or delete it using the links at the right of the control table, under *Operations*.

Select task:

Task id: condel-task-534914e1-747f-408b-aa4f-c948a943273f Date in: 2011-07-19 15:12:29
 Name: some_SNVs Date end: 2011-07-19 15:12:43
 Group: condelweb-ee81817f-1ae4-407c-9d9e-9b0ea2696b79 Status: done

[Log details](#)

Columns:

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+Location	+Allele	+Gene	+Symbol	+Protein	+Protein pos.	+AA change	+Sift	+PPH2	+Mass	-Condel	+Condel IBI
7:43918688	C	ENSG00000106608	URGCP	ENSP00000392963	82	L/R	0	0.995	NA	0.997	deleterious
7:38471790	A	ENSG00000078953	AMPH	ENSP00000390734	386	T/M	0.01	0.998	NA	0.994	deleterious
7:38471790	A	ENSG00000078953	AMPH	ENSP00000342268	156	T/M	0	0.983	NA	0.991	deleterious
7:38471790	A	ENSG00000078953	AMPH	ENSP00000415085	137	T/M	0	0.983	NA	0.991	deleterious
7:38471790	A	ENSG00000078953	AMPH	ENSP00000317441	386	T/M	0.02	0.998	NA	0.990	deleterious
6:88372821	A	ENSG00000135336	ORC3	ENSP00000257789	599	A/T	0.01	0.983	NA	0.986	deleterious
7:43918688	C	ENSG00000106608	URGCP	ENSP00000389990	82	L/R	0.09	0.995	NA	0.979	deleterious
7:43918688	C	ENSG00000106608	URGCP	ENSP00000402803	82	L/R	0.05	0.995	NA	0.975	deleterious
9:32473058	A	ENSG00000107201	DDX58	ENSP00000369212	598	L/F	0.01	0.96	NA	0.975	deleterious
7:43918688	C	ENSG00000106608	URGCP	ENSP00000223341	82	L/R	0.05	0.995	NA	0.975	deleterious
7:43918688	C	ENSG00000106608	URGCP	ENSP00000384955	116	L/R	0.05	0.995	NA	0.975	deleterious
9:32473058	A	ENSG00000107201	DDX58	ENSP00000442160	572	L/F	0.01	0.96	NA	0.975	deleterious
7:43918688	C	ENSG00000106608	URGCP	ENSP00000396818	125	L/R	0.05	0.995	NA	0.975	deleterious
7:43918688	C	ENSG00000106608	URGCP	ENSP00000392136	82	L/R	0.05	0.995	NA	0.975	deleterious
9:32473058	A	ENSG00000107201	DDX58	ENSP00000369197	440	L/F	0.01	0.96	NA	0.975	deleterious
7:43918688	C	ENSG00000106608	URGCP	ENSP00000336872	82	L/R	0.05	0.995	NA	0.975	deleterious
9:32473058	A	ENSG00000107201	DDX58	ENSP00000443055	440	L/F	0	0.918	NA	0.961	deleterious
6:88372821	A	ENSG00000135336	ORC3	ENSP00000444995	455	A/T	0.01	0.93	NA	0.960	deleterious
6:88372821	A	ENSG00000135336	ORC3	ENSP00000376586	598	A/T	0.01	0.93	0.965	0.985	deleterious
9:32473058	A	ENSG00000107201	DDX58	ENSP00000369213	643	L/F	0.01	0.96	2.475	0.850	deleterious

[Download data](#)

Step 5: The results of the task may be accessed in HTML format by clicking on the task id link. Note that the user may navigate from one of their tasks to another using the pull-down menu at the top of this page. The results may be downloaded as a tab-separated file hitting the *Download data* link below the control table.

Condel
 CONsensus DEleteriousness score of missense SNVs

Home Analysis View Help About

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Task ?

Descriptive task name

Enter your mutation data
(Read about [input format](#) or use this [example](#))

File name:

[*] Mandatory fields

The web server computes the corresponding Condel scores from the outputs of the three tools (SIFT, Polyphen2 and Mutation-Assessor).

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List of tasks

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 This list is being updated automatically every 10 seconds, although you may prefer update it [manually](#)

id	+Name	-DateCreation	DateEnd	+Status	Operations
condel-task-730c0723-ca65-491f-afbc-efeb9e22147	some_somatic_mutations	2011-07-19 16:04:18	2011-07-19 16:04:28	done	view download details cancel delete
condel-task-534914e1-747f-408b-aa4f-c948a943273f	some_SNVs	2011-07-19 15:12:29	2011-07-19 15:12:43	done	view download details cancel delete

Step 6: Now, note that if a second task is launched by the user, it will appear in the control table upon launching. The tasks will be ordered chronologically, with newer ones at the top.

Select task: **some_somatic_mutations | condet-task-730cd723-cdc5-4917-afbc-efe0b0e22147** ⌵
 some SNVs | condet-task-534914e1-747f-408b-aa4f-c948a943273f
 some_somatic_mutations | condet-task-730cd723-cdc5-4917-afbc-efe0b0e22147
 Task id: some_somatic_mutations | condet-task-730cd723-cdc5-4917-afbc-efe0b0e22147 07-19 16:04:18
 Name: some_somatic_mutations Date end: 2011-07-19 16:04:28
 Group: condetweb-ee81817f-1ae4-407c-9d9e-9b0ea2696b79 Status: done
[Log details](#)

Columns: **summary** ⌵

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+Location	+Allele	+Gene	+Symbol	+Protein	+Protein pos.	+AA change	+Sift	+PPH2	+Mass	+Condel	+Condel lib
17:7578491	T	ENSG00000141510	TP53	ENSP00000269305	147	VII	0.02	0.126	1.38	0.586	deleterious
17:7578491	A	ENSG00000141510	TP53	ENSP00000269305	147	VIF	0	0.993	1.73	0.799	deleterious
17:7578490	T	ENSG00000141510	TP53	ENSP00000269305	147	VID	0	0.989	1.85	0.807	deleterious
17:7578490	C	ENSG00000141510	TP53	ENSP00000269305	147	VIG	0	0.996	1.85	0.812	deleterious
17:7578490	G	ENSG00000141510	TP53	ENSP00000269305	147	VIA	0.04	0.958	1.73	0.758	deleterious
17:7578491	T	ENSG00000141510	TP53	ENSP00000352610	147	VI	0.03	0.019	1.38	0.591	deleterious
17:7578490	T	ENSG00000141510	TP53	ENSP00000352610	147	VID	0	0.973	1.85	0.800	deleterious
17:7578491	A	ENSG00000141510	TP53	ENSP00000352610	147	VIF	0	0.982	1.73	0.793	deleterious
17:7578490	C	ENSG00000141510	TP53	ENSP00000352610	147	VIG	0	0.989	1.85	0.807	deleterious
17:7578490	G	ENSG00000141510	TP53	ENSP00000352610	147	VIA	0.05	0.899	1.73	0.733	deleterious
17:7578491	A	ENSG00000141510	TP53	ENSP00000379735	136	VIF	0	0.997	NA	0.998	deleterious
17:7578490	C	ENSG00000141510	TP53	ENSP00000379735	136	VIG	0	0.998	NA	0.999	deleterious
17:7578490	T	ENSG00000141510	TP53	ENSP00000379735	136	VID	0	0.995	NA	0.997	deleterious
17:7578491	T	ENSG00000141510	TP53	ENSP00000379735	136	VI	0.01	0.214	NA	0.840	deleterious
17:7578490	G	ENSG00000141510	TP53	ENSP00000379735	136	VIA	0.01	0.991	NA	0.991	deleterious
17:7578491	T	ENSG00000141510	TP53	ENSP00000391127	147	VI	0.03	0.007	1.38	0.599	deleterious
17:7578490	G	ENSG00000141510	TP53	ENSP00000391127	147	VIA	0.05	0.777	1.73	0.693	deleterious
17:7578491	A	ENSG00000141510	TP53	ENSP00000391127	147	VIF	0	0.145	1.73	0.658	deleterious
17:7578490	T	ENSG00000141510	TP53	ENSP00000391127	147	VID	0	0.244	1.85	0.675	deleterious
17:7578490	C	ENSG00000141510	TP53	ENSP00000391127	147	VIG	0	0.952	1.85	0.792	deleterious

Step 7: As explained above, the user may navigate between tasks with the pull-down menu at the top of the page. The *Columns* menu allows to add more columns to the result table.

Section C: Description of the HTML output table

Showing 1 to 20 of 60 << < 1 2 3 >>

+Location	+Allele	+Gene	+Symbol	+Protein	+Protein pos.	+AA change	+Sift	+PPH2	+Mass	+Condel	+Condel lbi
17:7578491	T	ENSG00000141510	TP53	ENSP00000269305	147	V/I	0.02	0.126	1.38	0.586	deleterious
17:7578491	A	ENSG00000141510	TP53	ENSP00000269305	147	V/F	0	0.993	1.73	0.799	deleterious
17:7578490	T	ENSG00000141510	TP53	ENSP00000269305	147	V/D	0	0.989	1.85	0.807	deleterious
17:7578490	C	ENSG00000141510	TP53	ENSP00000269305	147	V/G	0	0.996	1.85	0.812	deleterious
17:7578490	G	ENSG00000141510	TP53	ENSP00000269305	147	V/A	0.04	0.958	1.73	0.758	deleterious
17:7578491	T	ENSG00000141510	TP53	ENSP00000352610	147	V/I	0.03	0.019	1.38	0.591	deleterious
17:7578490	T	ENSG00000141510	TP53	ENSP00000352610	147	V/D	0	0.973	1.85	0.800	deleterious
17:7578491	A	ENSG00000141510	TP53	ENSP00000352610	147	V/F	0	0.982	1.73	0.793	deleterious
17:7578490	C	ENSG00000141510	TP53	ENSP00000352610	147	V/G	0	0.989	1.85	0.807	deleterious
17:7578490	G	ENSG00000141510	TP53	ENSP00000352610	147	V/A	0.05	0.899	1.73	0.733	deleterious
17:7578491	A	ENSG00000141510	TP53	ENSP00000379735	136	V/F	0	0.997	NA	0.998	deleterious
17:7578490	C	ENSG00000141510	TP53	ENSP00000379735	136	V/G	0	0.998	NA	0.999	deleterious
17:7578490	T	ENSG00000141510	TP53	ENSP00000379735	136	V/D	0	0.995	NA	0.997	deleterious
17:7578491	T	ENSG00000141510	TP53	ENSP00000379735	136	V/I	0.01	0.214	NA	0.840	deleterious
17:7578490	G	ENSG00000141510	TP53	ENSP00000379735	136	V/A	0.01	0.991	NA	0.991	deleterious
17:7578491	T	ENSG00000141510	TP53	ENSP00000391127	147	V/I	0.03	0.007	1.38	0.599	deleterious
17:7578490	G	ENSG00000141510	TP53	ENSP00000391127	147	V/A	0.05	0.777	1.73	0.693	deleterious
17:7578491	A	ENSG00000141510	TP53	ENSP00000391127	147	V/F	0	0.145	1.73	0.658	deleterious
17:7578490	T	ENSG00000141510	TP53	ENSP00000391127	147	V/D	0	0.244	1.85	0.675	deleterious
17:7578490	C	ENSG00000141510	TP53	ENSP00000391127	147	V/G	0	0.952	1.85	0.792	deleterious

+Location	+Allele
17:7578491	T
17:7578491	A
17:7578490	T
17:7578490	C
17:7578490	G
17:7578491	T
17:7578490	T
17:7578491	A
17:7578490	C
17:7578490	C
17:7578490	G
17:7578491	A
17:7578490	C
17:7578490	T
17:7578491	T
17:7578490	G
17:7578491	T
17:7578490	G
17:7578491	A
17:7578490	T
17:7578490	C

Column 1: Location of the SNV in the format Chromosome:position

Column 2: Alternative allele of the SNV

+Gene	+Symbol
ENSG00000141510	TP53

Column 3: Ensembl ID of the gene affected by the SNV

Column 4: Symbol of the gene affected by the SNV

+Protein	+Protein pos.	+AA change
ENSP00000269305	147	V/I
ENSP00000269305	147	V/F
ENSP00000269305	147	V/D
ENSP00000269305	147	V/G
ENSP00000269305	147	V/A
ENSP00000352610	147	V/I
ENSP00000352610	147	V/D
ENSP00000352610	147	V/F
ENSP00000352610	147	V/G
ENSP00000352610	147	V/A
ENSP00000379735	136	V/F
ENSP00000379735	136	V/G
ENSP00000379735	136	V/D
ENSP00000379735	136	V/I
ENSP00000379735	136	V/A
ENSP00000391127	147	V/I
ENSP00000391127	147	V/A
ENSP00000391127	147	V/F
ENSP00000391127	147	V/D
ENSP00000391127	147	V/G

Column 5: Ensembl ID of the protein affected by the SNV

Column 6: Position of the aminoacid change (protein coordinates)

Column 7: Aminoacid change caused by the SNV

+Sift	+PPH2	+Mass
0.02	0.126	1.38
0	0.993	1.73
0	0.989	1.85
0	0.996	1.85
0.04	0.958	1.73
0.03	0.019	1.38
0	0.973	1.85
0	0.982	1.73
0	0.989	1.85
0.05	0.899	1.73
0	0.997	NA
0	0.998	NA
0	0.995	NA
0.01	0.214	NA
0.01	0.991	NA
0.03	0.007	1.38
0.05	0.777	1.73
0	0.145	1.73
0	0.244	1.85
0	0.952	1.85

Column 8: SIFT score of the aminoacid change

Column 9: PolyPhen2 score of the aminoacid change

Column 10: MutationAssessor score of the aminoacid change

Condel	Condel lbl
0.586	deleterious
0.799	deleterious
0.807	deleterious
0.812	deleterious
0.758	deleterious
0.591	deleterious
0.800	deleterious
0.793	deleterious
0.807	deleterious
0.733	deleterious
0.998	deleterious
0.999	deleterious
0.997	deleterious
0.840	deleterious
0.991	deleterious
0.599	deleterious
0.693	deleterious
0.658	deleterious
0.675	deleterious
0.792	deleterious

Column 11: Condel score

Column 12: Condel classification of the SNV