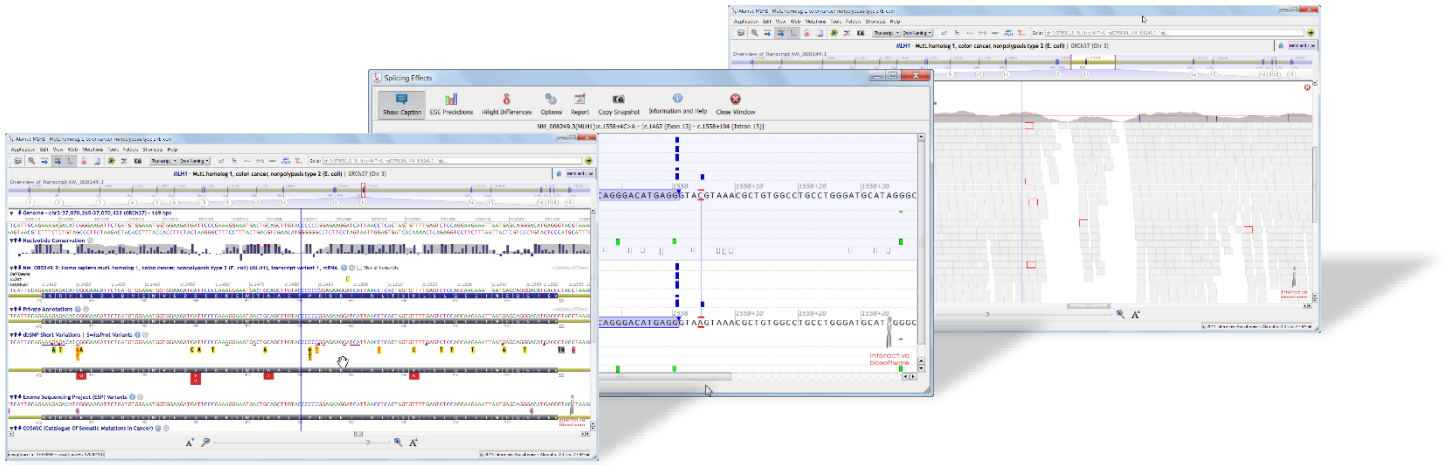
alamut visual

interactive biosoftware



alamut batch

interactive
biosoftware

Société

- Créée en 2007
- Basée à Rouen
- Editeur de logiciels pour la biologie moléculaire
- Principaux produits:

alamut batch alamut focus alamut visual

interactive
biosoftware

Produits

- Alamut Visual
  - Système d'aide à l'interprétation de variations en génétique humaine
  - Analyse visuelle – Bas débit

alamut visual

- Alamut Batch
  - Annotation de variants pour le NGS
  - Analyse automatisée – Haut débit

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- Alamut Focus

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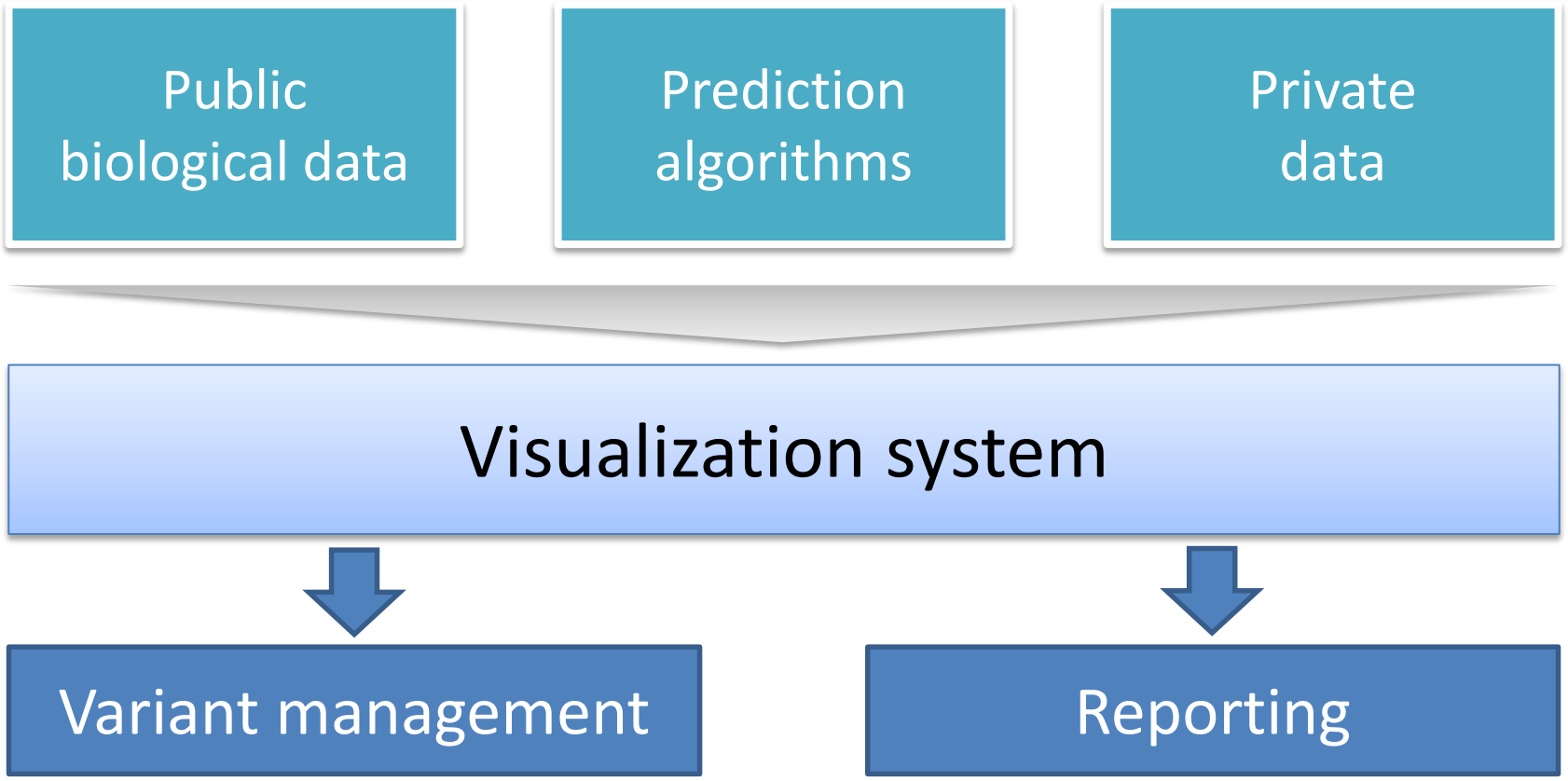
Alamut Visual

- Améliorer la productivité de l'interprétation de variants
  - Convivialité
  - Données pertinentes et à jour
  - Algorithmes de prédiction reconnus
- Support des bonnes pratiques
- Evoluer avec les avancées techniques et scientifiques

alamut visual

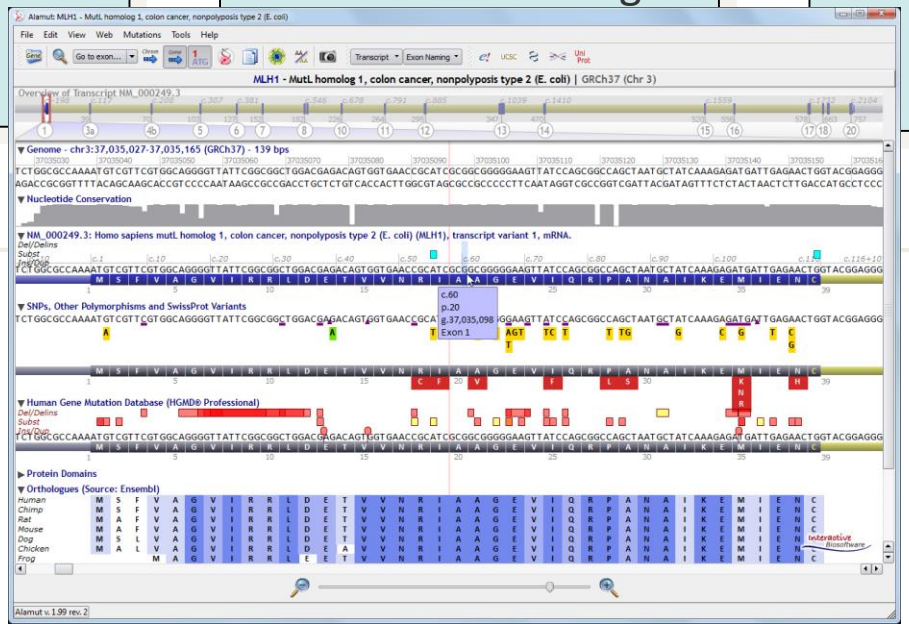
Concepts



alamut visual

Visualization system

Data	Algorithms	GUI
Genome	Coding Effects	Gene Browser
Genes	Nomenclature	Consistent Display
Transcripts	Missense Scoring	Intuitive Navigation and Interactions
Polymorphisms	Splicing Effects	Dynamic Zooming
Mutations	Literature Mining	BAM Viewer
Proteins		



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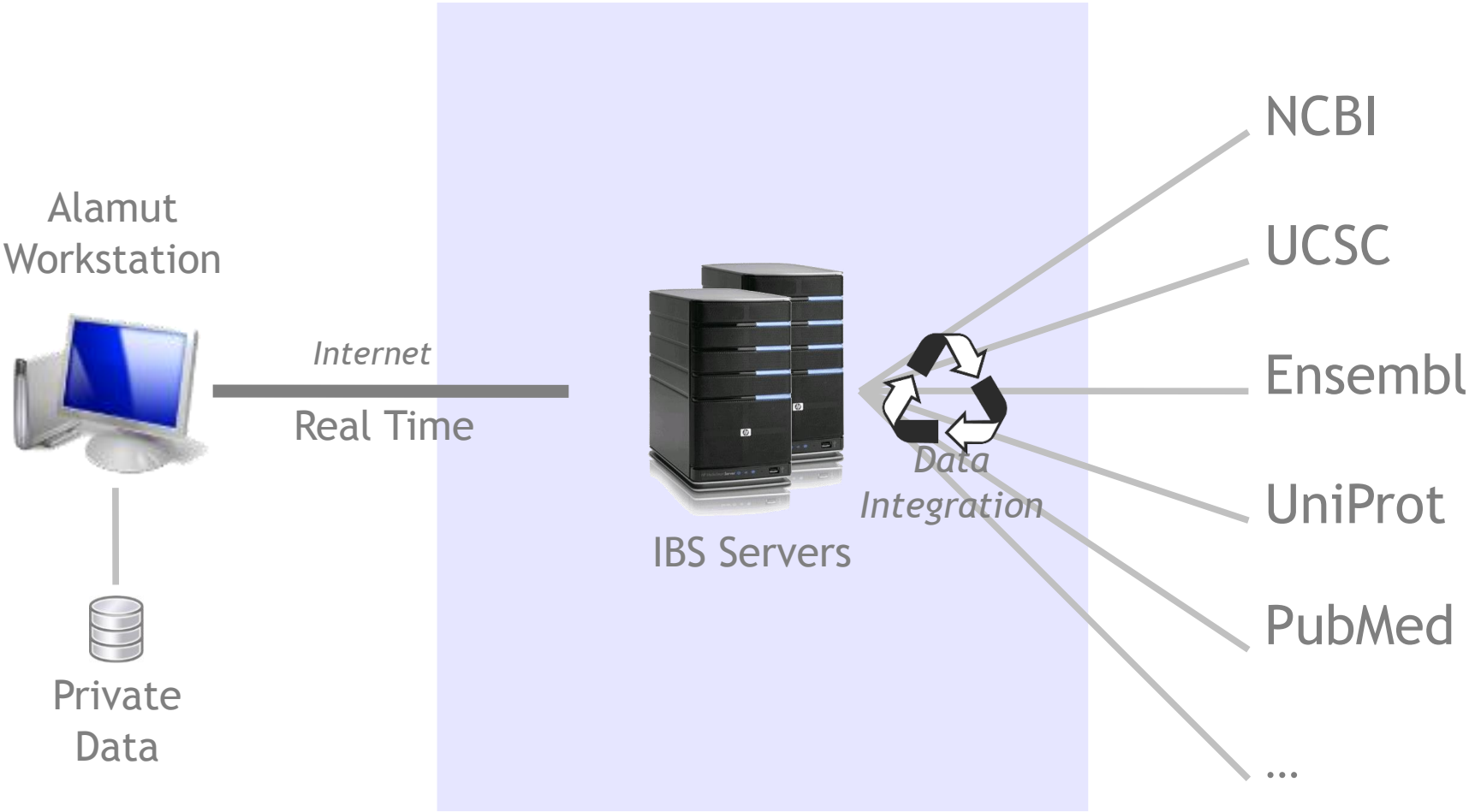
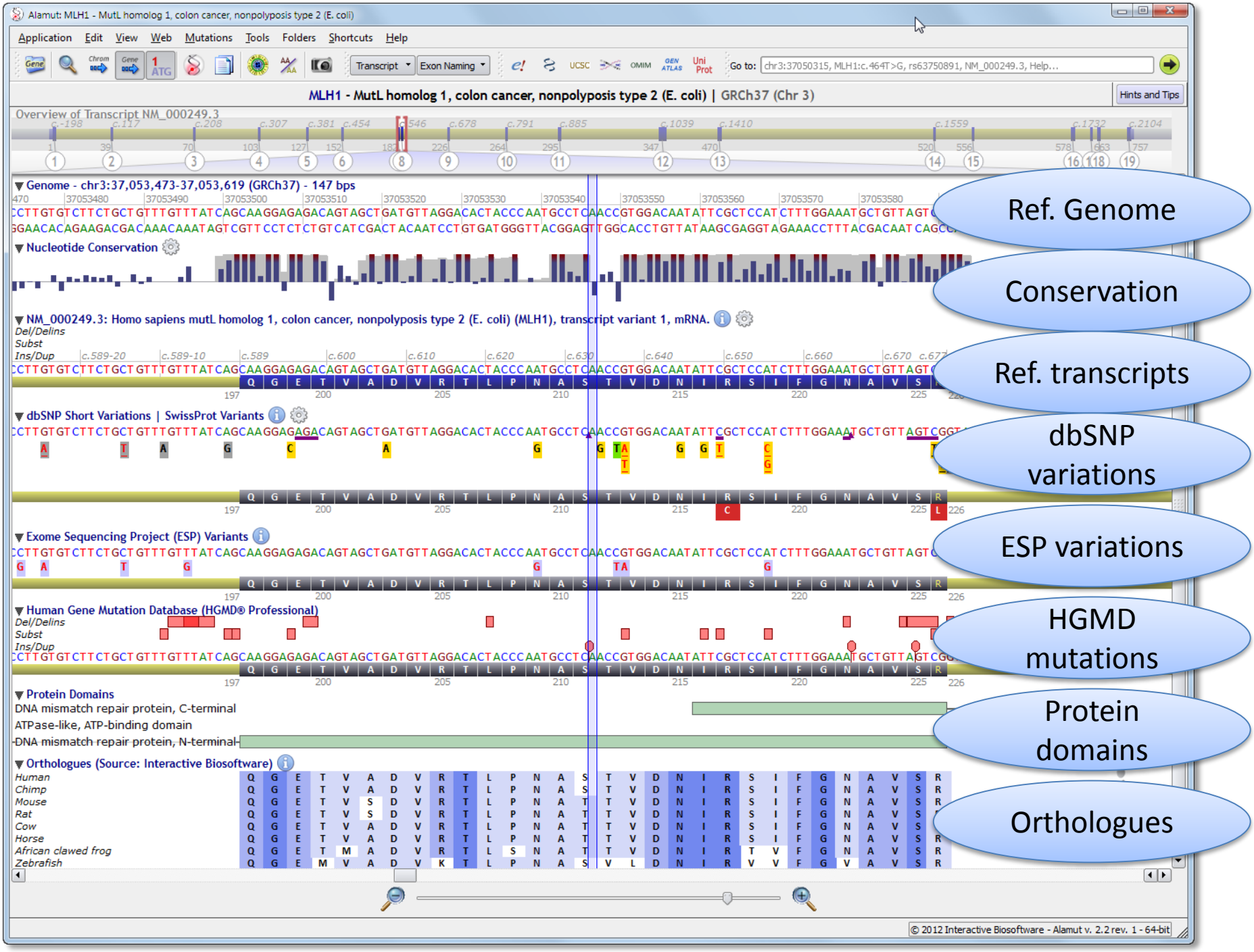
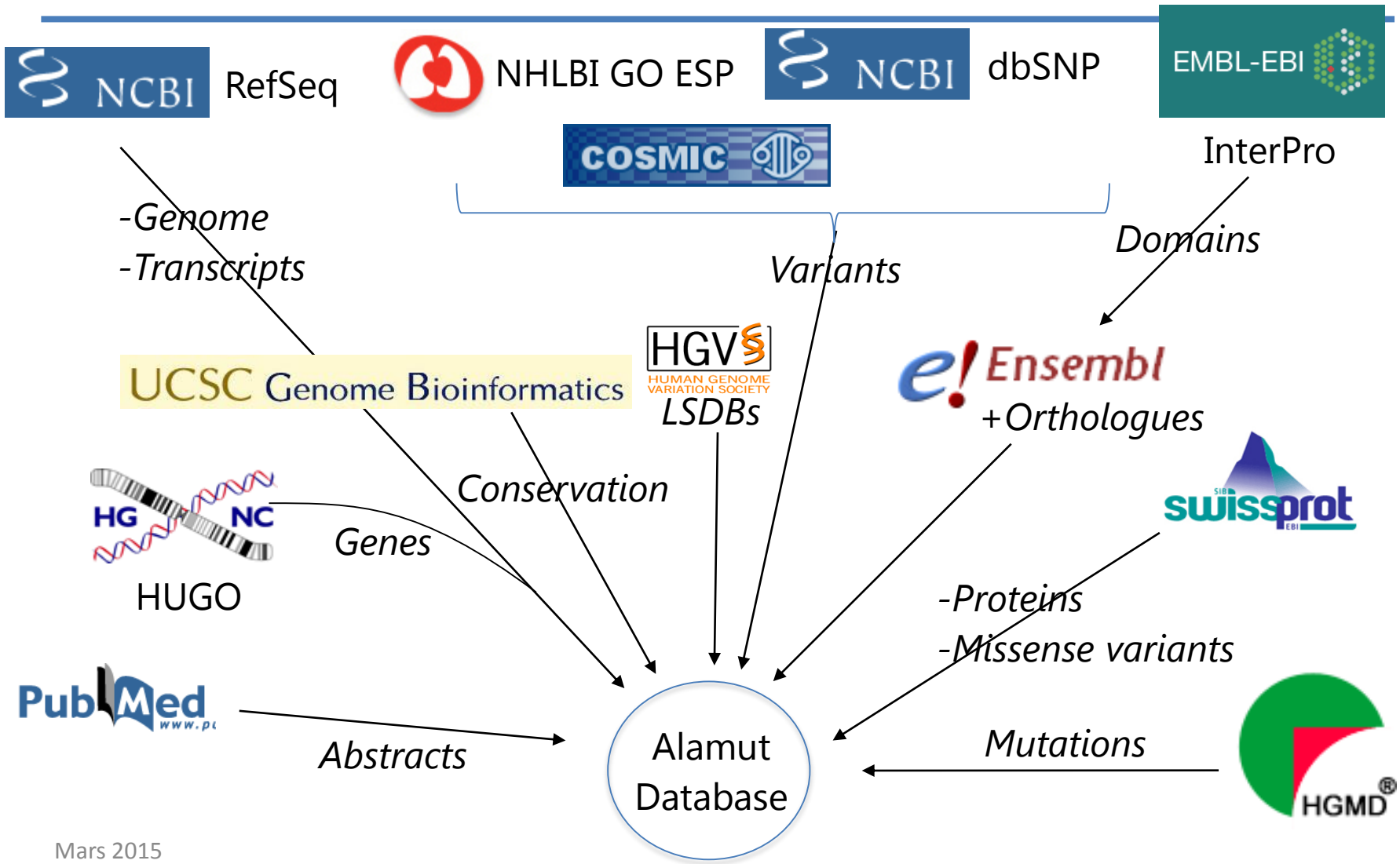
Architecture



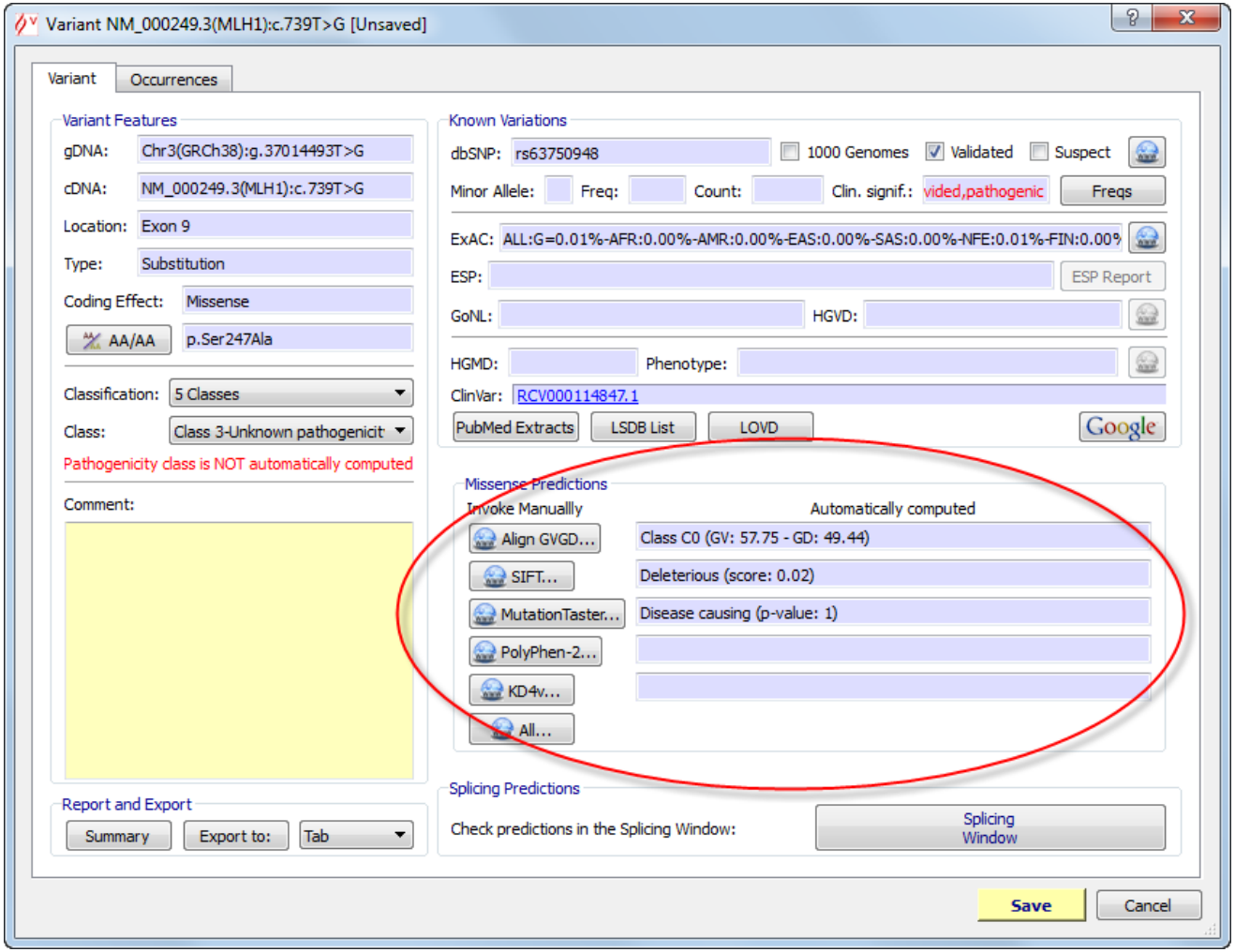

Alamut: MLH1 - MutL homolog 1, colon cancer, nonpolyposis type 2 (E. coli)
Application Edit View Web Mutations Tools Folders Shortcuts Help
Transcript
Exon Naming
Go to:
MLH1 - MutL homolog 1, colon cancer, nonpolyposis type 2 (E. coli) | GRCh37 (Chr 3)
Hints and Tips
Overview of Transcript NM_000249.3
Genome - chr3:37,053,473-37,053,619 (GRCh37) - 147 bps
Nucleotide Conservation
NM_000249.3: Homo sapiens mutL homolog 1, colon cancer, nonpolyposis type 2 (E. coli) (MLH1), transcript variant 1, mRNA.
dbSNP Short Variations | SwissProt Variants
Exome Sequencing Project (ESP) Variants
Human Gene Mutation Database (HGMD® Professional)
Protein Domains
DNA mismatch repair protein, C-terminal
ATPase-like, ATP-binding domain
DNA mismatch repair protein, N-terminal
Orthologues (Source: Interactive Biosoftware)
Human
Chimp
Mouse
Rat
Cow
Horse
African clawed frog
Zebrafish
© 2012 Interactive Biosoftware - Alamut v. 2.2 rev. 1 - 64-bit
Ref. Genome
Conservation
Ref. transcripts
dbSNP variations
ESP variations
HGMD mutations
Protein domains
Orthologues

Data Sources

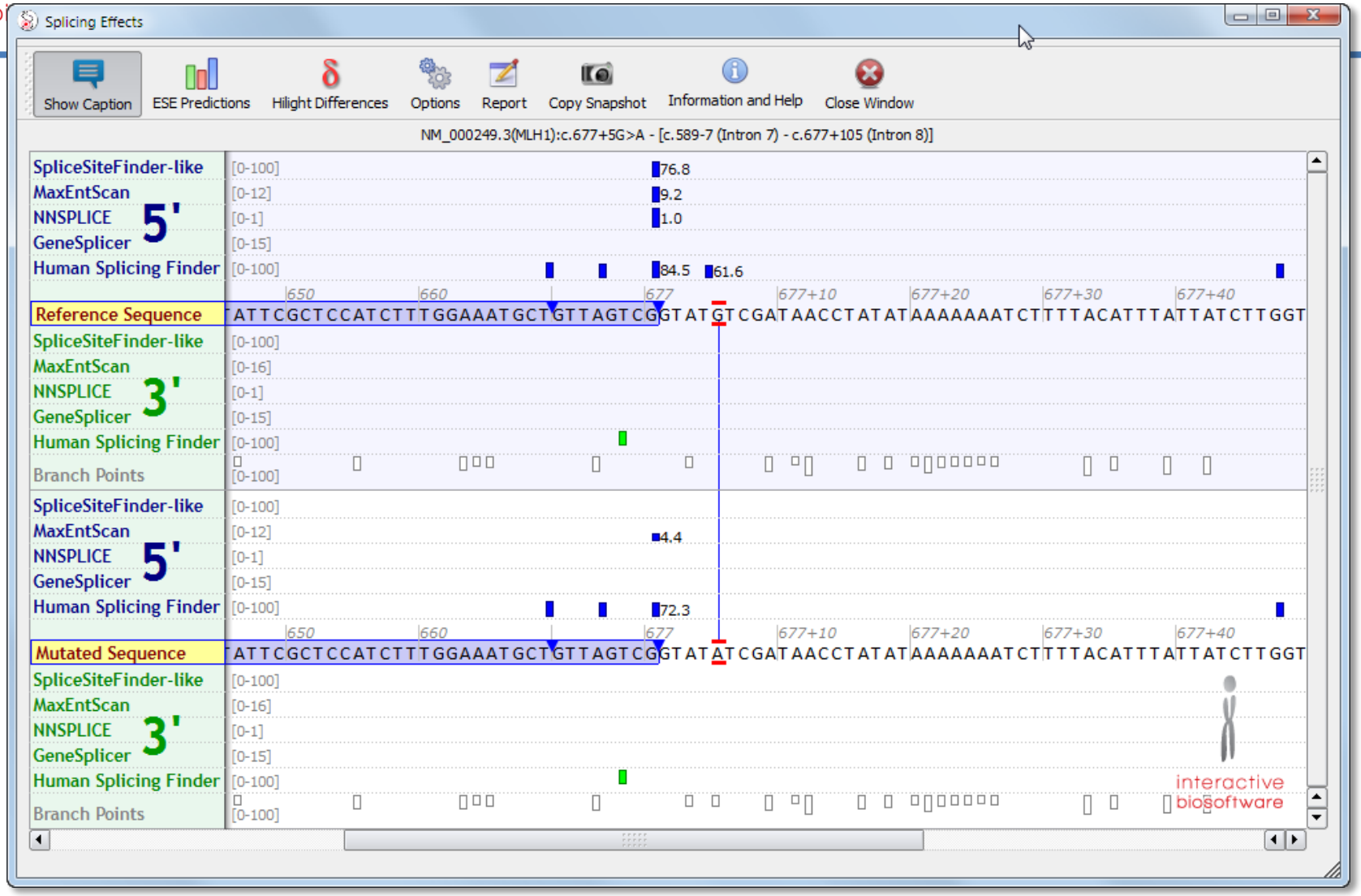


interactive
biosoftware

Missense Predictions



Splicing Predictions



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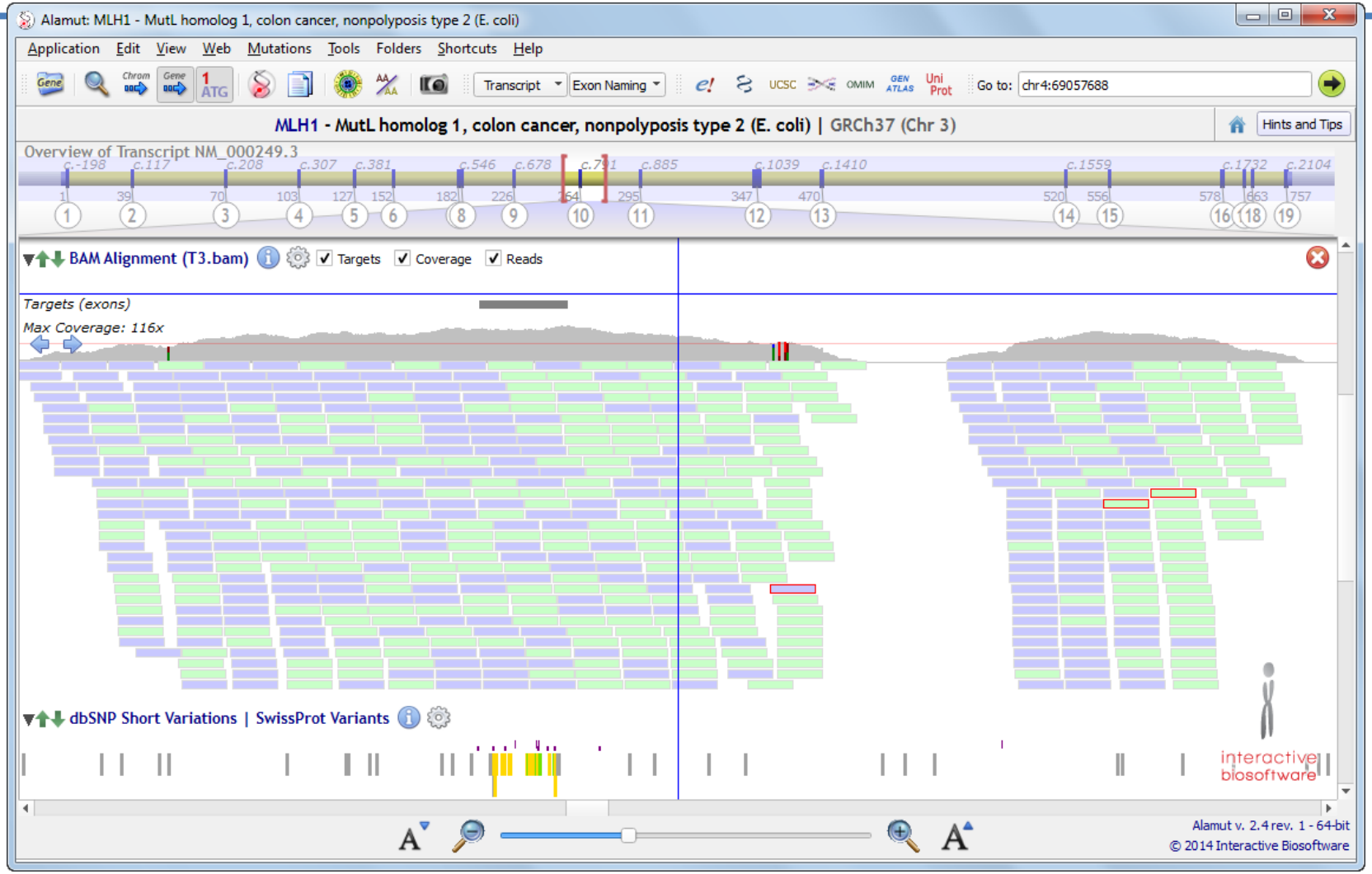
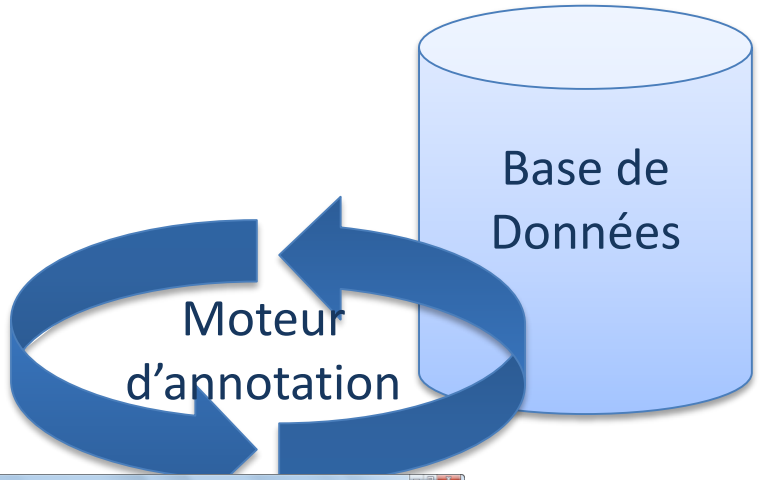
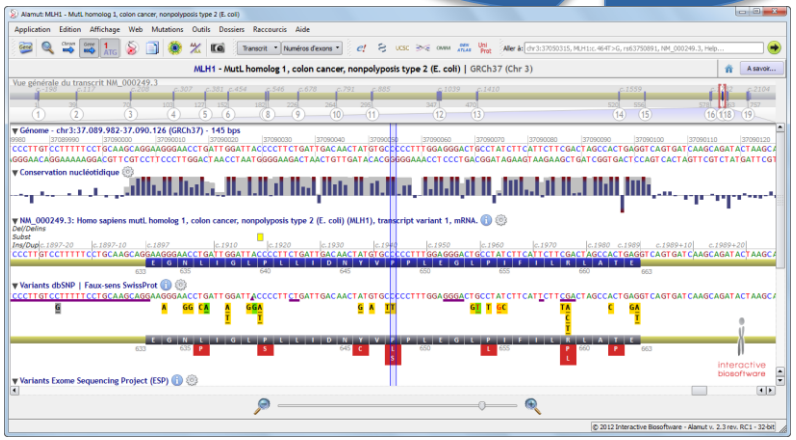
NGS BAM Viewer



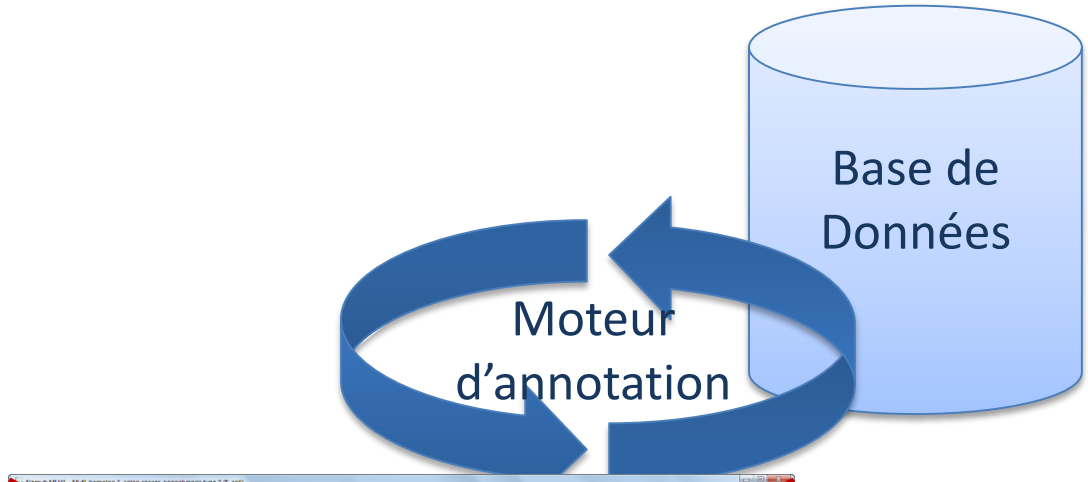
Mars 2015

Visual → Batch



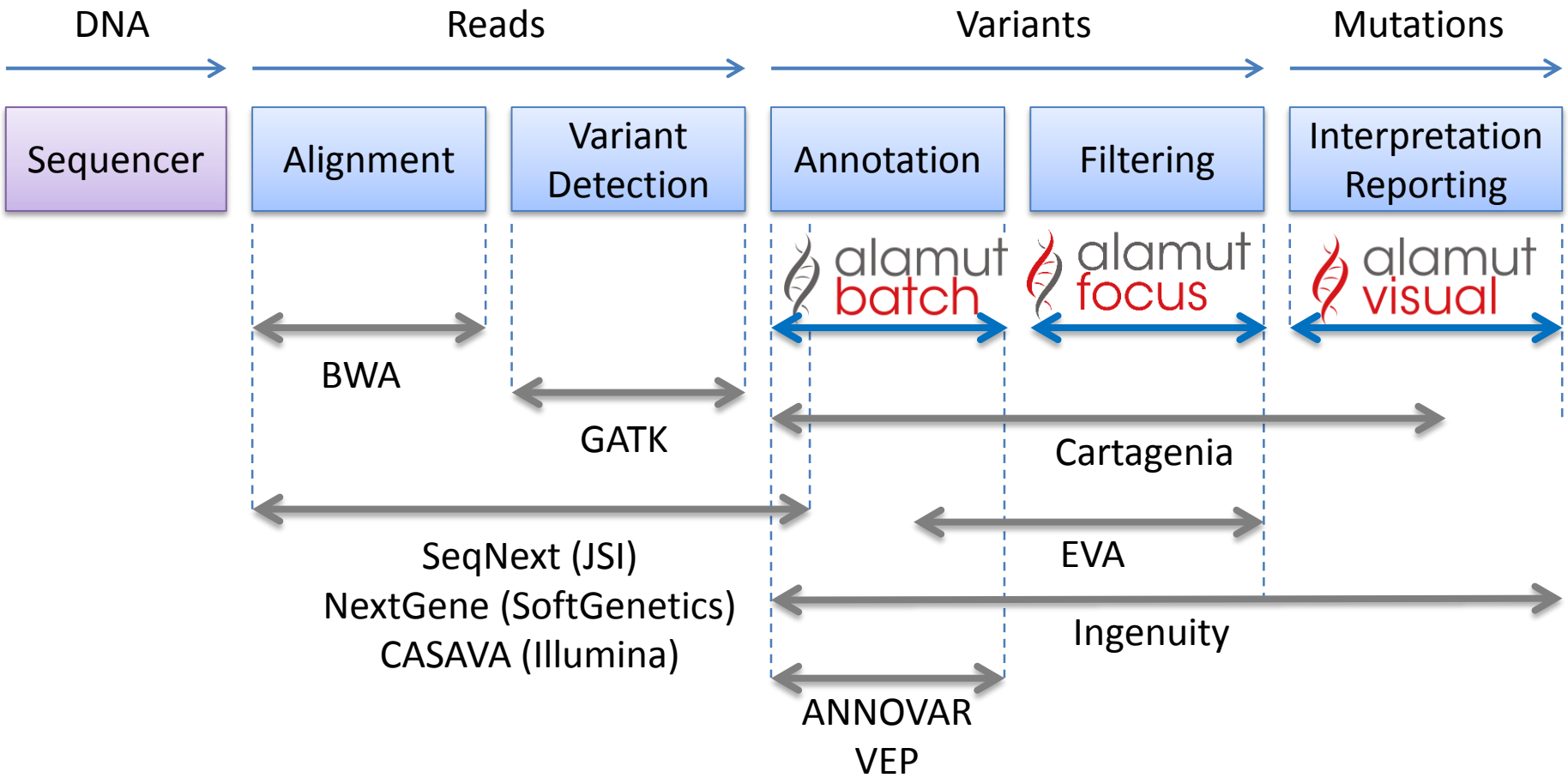


Visual → Batch



interactive biosoftware

Positionnement

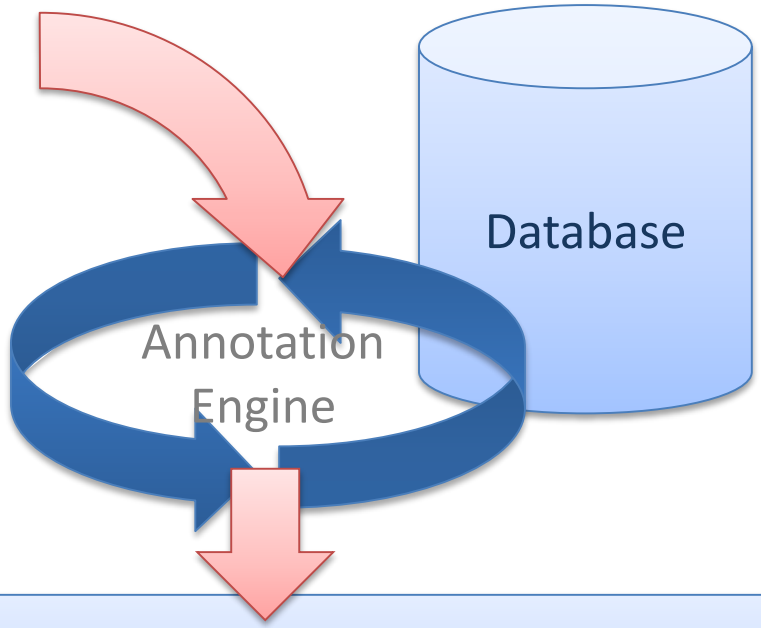


alamut batch

Concepts

Raw variants (VCF)

Chr3:g.37090029C>A
Chr5:g.68876554del
Chr7:g.3962135A>T
Chr13:g.723693insGT
……



Annotated variants

MLH1	NM_000249.3	c.1918C>A	p.Pro640Thr	rs63749792 0.003	…
MLH1	NM_001167617.1	c.1624C>A	p.Pro542Thr	rs63749792 0.003	…
MLH1	NM_001167618.1	c.1195C>A	p.Pro399Thr	rs63749792 0.003	…

…….

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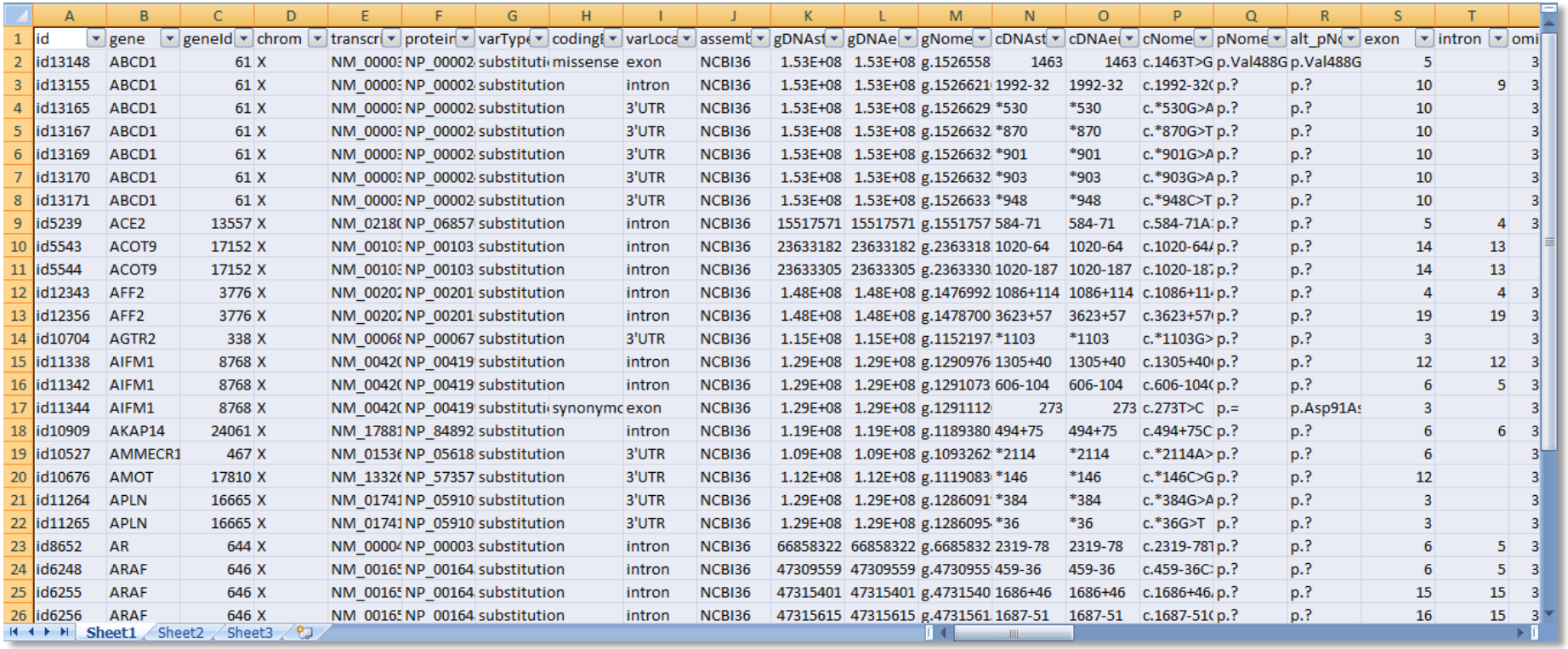
Annotations fournies

- Gène(s), transcrit(s), protéine(s)
- Conservation
- Variant: type, localisation, effet
- Fréq alléliques: dbSNP, 1000g, ESP, ExAC, ClinVar, HGMD, COSMIC
- Protéine/AA: domaines, conservation, scores physico-chimiques
- Faux-sens: Align GVGD, SIFT, MAPP
- Epissage: site naturel le + proche, voisinage du variant

~160 champs

Exemple de sortie



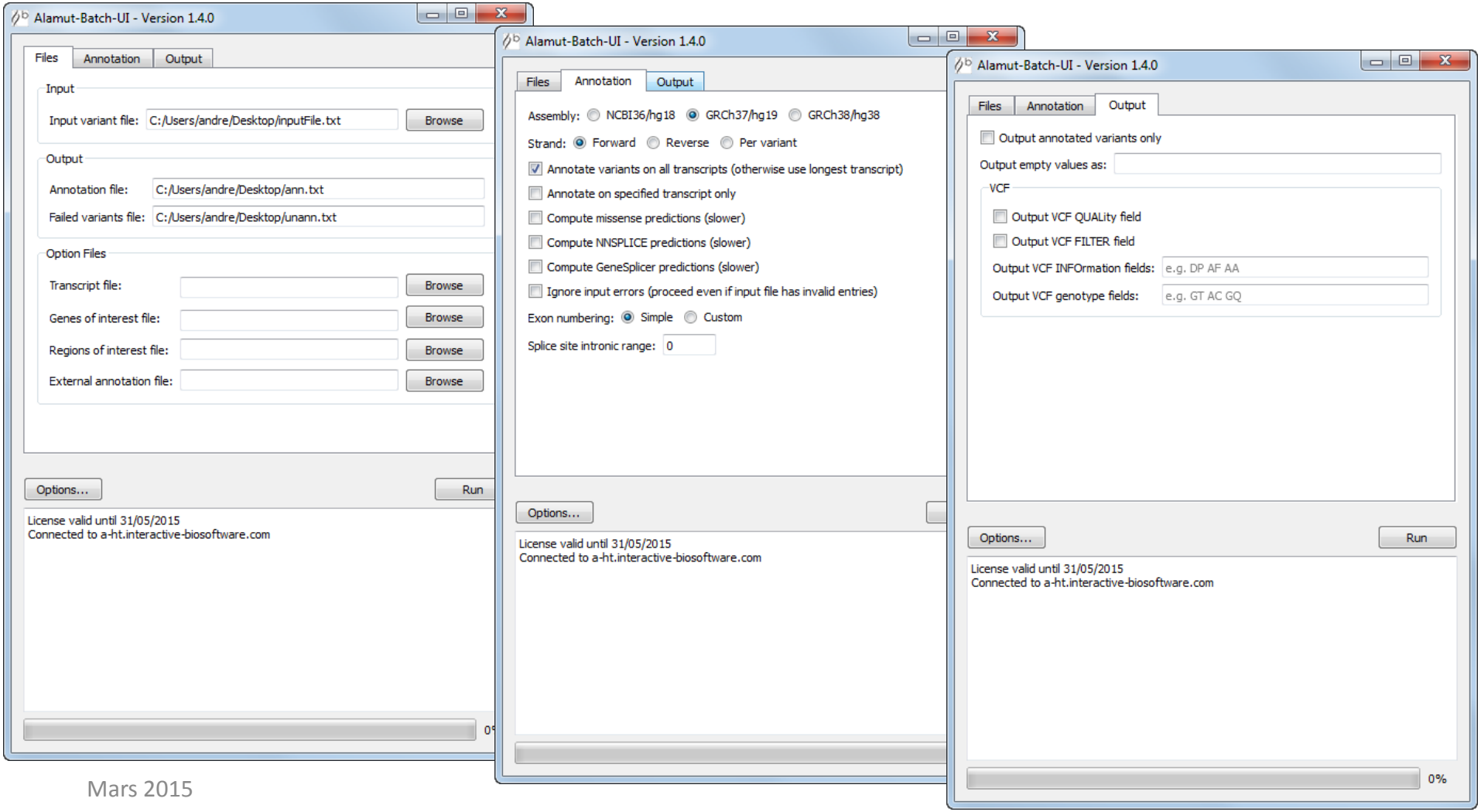
id	gene	geneId	chrom	transcr	protein	varType	codingE	varLoca	assemb	gDNAst	gDNAe	gNome	cDNAst	cDNAe	cNome	pNome	alt_pN	exon	intron	omi
id13148	ABCD1	61	X	NM_0000	NP_00002	substituti	missense	exon	NCBI36	1.53E+08	1.53E+08	g.1526558	1463	1463	c.1463T>G	p.Val488G	p.Val488G	5		3
id13155	ABCD1	61	X	NM_0000	NP_00002	substitution		intron	NCBI36	1.53E+08	1.53E+08	g.1526621	1992-32	1992-32	c.1992-32(	p.?	p.?	10	9	3
id13165	ABCD1	61	X	NM_0000	NP_00002	substitution		3'UTR	NCBI36	1.53E+08	1.53E+08	g.1526629	*530	*530	c.*530G>A	p.?	p.?	10		3
id13167	ABCD1	61	X	NM_0000	NP_00002	substitution		3'UTR	NCBI36	1.53E+08	1.53E+08	g.1526632	*870	*870	c.*870G>T	p.?	p.?	10		3
id13169	ABCD1	61	X	NM_0000	NP_00002	substitution		3'UTR	NCBI36	1.53E+08	1.53E+08	g.1526632	*901	*901	c.*901G>A	p.?	p.?	10		3
id13170	ABCD1	61	X	NM_0000	NP_00002	substitution		3'UTR	NCBI36	1.53E+08	1.53E+08	g.1526632	*903	*903	c.*903G>A	p.?	p.?	10		3
id13171	ABCD1	61	X	NM_0000	NP_00002	substitution		3'UTR	NCBI36	1.53E+08	1.53E+08	g.1526633	*948	*948	c.*948C>T	p.?	p.?	10		3
id5239	ACE2	13557	X	NM_0218(	NP_06857	substitution		intron	NCBI36	15517571	15517571	g.1551757	584-71	584-71	c.584-71A:	p.?	p.?	5	4	3
id5543	ACOT9	17152	X	NM_0010	NP_00103	substitution		intron	NCBI36	23633182	23633182	g.2363318	1020-64	1020-64	c.1020-64/	p.?	p.?	14	13	
id5544	ACOT9	17152	X	NM_0010	NP_00103	substitution		intron	NCBI36	23633305	23633305	g.2363330	1020-187	1020-187	c.1020-187	p.?	p.?	14	13	
id12343	AFF2	3776	X	NM_0020	NP_00201	substitution		intron	NCBI36	1.48E+08	1.48E+08	g.1476992	1086+114	1086+114	c.1086+11(	p.?	p.?	4	4	3
id12356	AFF2	3776	X	NM_0020	NP_00201	substitution		intron	NCBI36	1.48E+08	1.48E+08	g.1478700	3623+57	3623+57	c.3623+57(	p.?	p.?	19	19	3
id10704	AGTR2	338	X	NM_0006	NP_00067	substitution		3'UTR	NCBI36	1.15E+08	1.15E+08	g.1152197	*1103	*1103	c.*1103G>	p.?	p.?	3		3
id11338	AIFM1	8768	X	NM_0042(	NP_00419	substitution		intron	NCBI36	1.29E+08	1.29E+08	g.1290976	1305+40	1305+40	c.1305+40(	p.?	p.?	12	12	3
id11342	AIFM1	8768	X	NM_0042(	NP_00419	substitution		intron	NCBI36	1.29E+08	1.29E+08	g.1291073	606-104	606-104	c.606-104(	p.?	p.?	6	5	3
id11344	AIFM1	8768	X	NM_0042(	NP_00419	substituti	synonymc	exon	NCBI36	1.29E+08	1.29E+08	g.1291112	273	273	c.273T>C	p.=	p.Asp91As	3		3
id10909	AKAP14	24061	X	NM_17881	NP_84892	substitution		intron	NCBI36	1.19E+08	1.19E+08	g.1189380	494+75	494+75	c.494+75C	p.?	p.?	6	6	3
id10527	AMMECR1	467	X	NM_0153(	NP_05618	substitution		3'UTR	NCBI36	1.09E+08	1.09E+08	g.1093262	*2114	*2114	c.*2114A>	p.?	p.?	6		3
id10676	AMOT	17810	X	NM_1332(	NP_57357	substitution		3'UTR	NCBI36	1.12E+08	1.12E+08	g.1119083	*146	*146	c.*146C>G	p.?	p.?	12		3
id11264	APLN	16665	X	NM_01741	NP_05910	substitution		3'UTR	NCBI36	1.29E+08	1.29E+08	g.1286091	*384	*384	c.*384G>A	p.?	p.?	3		3
id11265	APLN	16665	X	NM_01741	NP_05910	substitution		3'UTR	NCBI36	1.29E+08	1.29E+08	g.1286095	*36	*36	c.*36G>T	p.?	p.?	3		3
id8652	AR	644	X	NM_0000	NP_00003	substitution		intron	NCBI36	66858322	66858322	g.6685832	2319-78	2319-78	c.2319-78	p.?	p.?	6	5	3
id6248	ARAF	646	X	NM_0016	NP_00164	substitution		intron	NCBI36	47309559	47309559	g.4730955	459-36	459-36	c.459-36C	p.?	p.?	6	5	3
id6255	ARAF	646	X	NM_0016	NP_00164	substitution		intron	NCBI36	47315401	47315401	g.4731540	1686+46	1686+46	c.1686+46	p.?	p.?	15	15	3
id6256	ARAF	646	X	NM_0016	NP_00164	substitution		intron	NCBI36	47315615	47315615	g.4731561	1687-51	1687-51	c.1687-51(	p.?	p.?	16	15	3

Sheet1 Sheet2 Sheet3

Paramètres

- 1 ou n transcrits
- ± prédictions de faux-sens
- ± prédictions d'épissage
- Gènes d'intérêt
- Régions d'intérêt
- Intégration d'annotations externes
- Extraction d'annotations VCF (ex: génotypes)

Interface


Alamut-Batch-UI - Version 1.4.0
Files
Annotation
Output
Input
Input variant file:
C:/Users/andre/Desktop/inputFile.txt
Browse
Output
Annotation file:
C:/Users/andre/Desktop/ann.txt
Failed variants file:
C:/Users/andre/Desktop/unann.txt
Option Files
Transcript file:
Genes of interest file:
Regions of interest file:
External annotation file:
Options...
Run
License valid until 31/05/2015
Connected to a-ht.interactive-biosoftware.com
Alamut-Batch-UI - Version 1.4.0
Files
Annotation
Output
Assembly:
NCBI36/hg18
GRCh37/hg19
GRCh38/hg38
Strand:
Forward
Reverse
Per variant
Annotate variants on all transcripts (otherwise use longest transcript)
Annotate on specified transcript only
Compute missense predictions (slower)
Compute NNSPLICE predictions (slower)
Compute GeneSplicer predictions (slower)
Ignore input errors (proceed even if input file has invalid entries)
Exon numbering:
Simple
Custom
Splice site intronic range:
0
Options...
License valid until 31/05/2015
Connected to a-ht.interactive-biosoftware.com
Alamut-Batch-UI - Version 1.4.0
Files
Annotation
Output
Output annotated variants only
Output empty values as:
VCF
Output VCF QUALity field
Output VCF FILTER field
Output VCF INFOrmation fields:
e.g. DP AF AA
Output VCF genotype fields:
e.g. GT AC GQ
Options...
Run
License valid until 31/05/2015
Connected to a-ht.interactive-biosoftware.com
0%

Ligne de commande

```
alamut-batch
    [--help]
    [--listgenes <output file name> NCBI36|GRCh37|GRCh38]
     --in <variant file name>
     --ann <annotation file name>
     --unann <unannotated log file name>
     [--from <n>] (start annotating from the nth variant)
     [--to <n>] (annotate up to the nth variant)
     [--assbly NCBI36|GRCh37|GRCh38] (default: GRCh37)
     [--strand 1|-1|0] (default: 1; 0: per variant – not applicable to VCF
                        input)
     [--alltrans] (annotate variants on all transcripts)
     [--spectrans] (annotate variants only on specified per-variant
                    Transcripts – not applicable to VCF input)
     [--translist <transcript file name>] (annotate variants only on listed
                                           preferred transcripts)
     [--glist <gene list file name>] (list of genes of interest)
     [--roilist <ROI list BED file name>] (list of regions of interest)
     [--nomispred] (no missense predictions; faster)
     [--nonnsplice] (no NNSPLICE predictions; faster)
     [--nogenesplicer] (no GeneSplicer predictions; faster)
     [--ignoreInputErrors] (proceed even if input has incorrect entries)
     [--exonnums simple|custom] (default: simple)
     [--ssIntronicRange <n>] (set varLocation as 'splice site' if variant is
                              intronic and within this range)
     [--extAnnFile <external annotation file name>] (include additional
                                        annotations from external file)
     [--outputannonly] (output only annotated variants in annotation output)
     [--outputVCFQuality]
     [--outputVCFFilter]
     [--outputVCFInfo ID ... ID]
     [--outputVCFGenotypeData ID ... ID]
     [--outputEmptyValuesAs <value>] (e.g. NULL)
     [--hgmdUser <HGMD Pro user name>]
     [--hgmdPasswd <HGMD Pro password>]
     [--proxyserver <proxy server name>]
     [--proxyport <proxy server port number>]
     [--proxyuser <proxy user login>]
     [--proxypasswd <proxy password>]
     [--processes <#processes>] (Standalone version only)
```

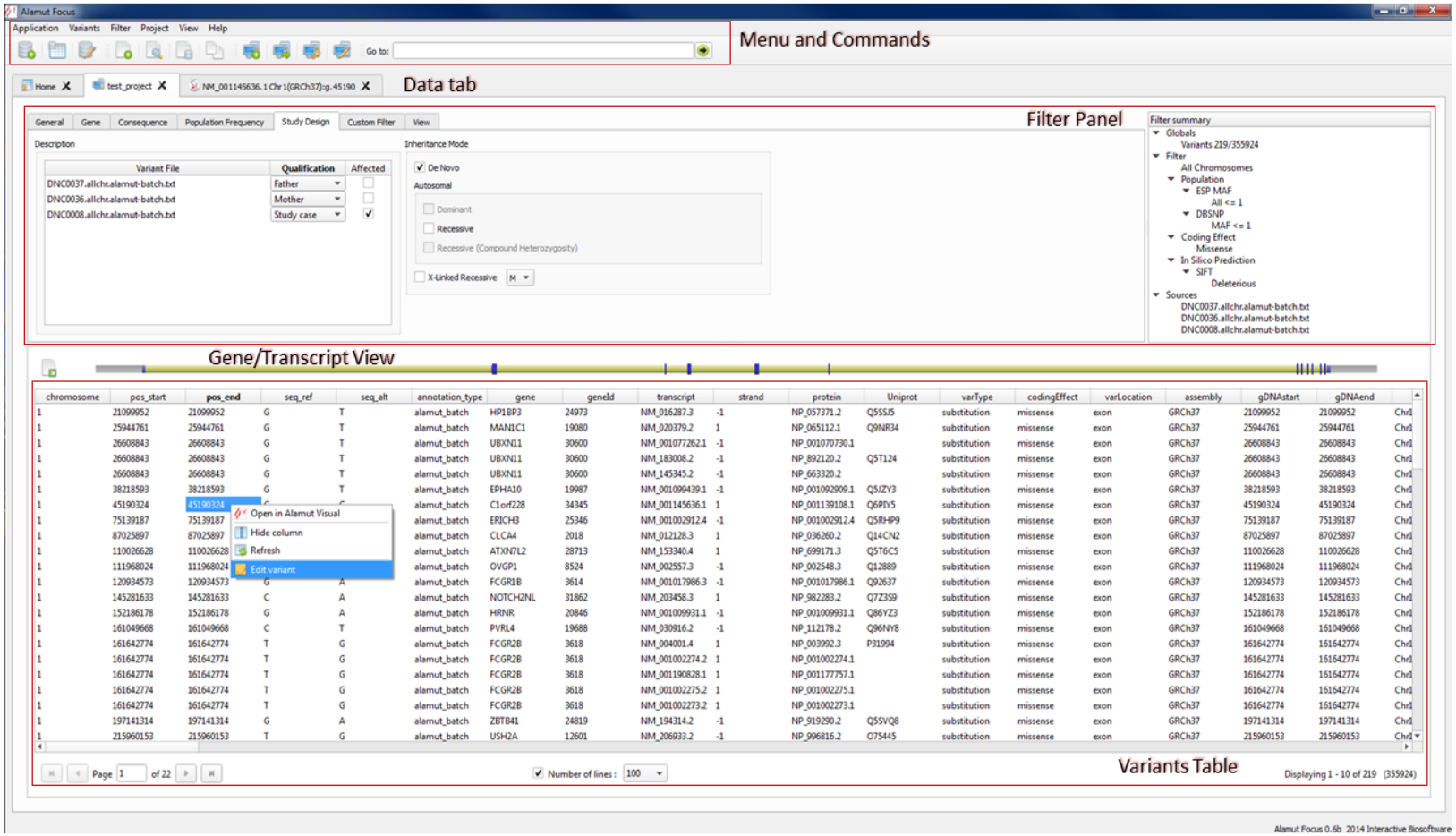
Architecture : 2 versions

- Client/Serveur
  - Base de données distante
  - Annotation locale
  - Performance modeste
- Standalone
  - Base de données locale
  - Annotation locale
  - Performance élevée

Exemples de débits

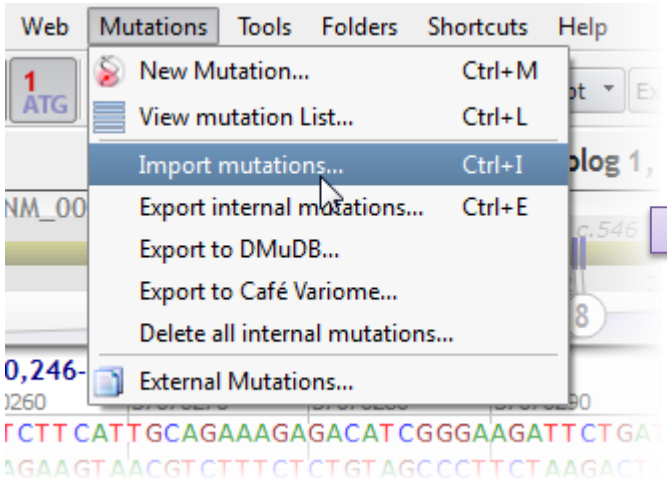
- Ordinateur standard – version client/serveur
  - Avec prédictions: ~4000 variants/h
  - Sans prédictions: ~10.000 variants/h
- Ordinateur puissant – version standalone
  - Avec prédictions: ~15.000 variants/h
  - Sans prédictions: ~100.000 variants/h
- Processus hautement parallélisable

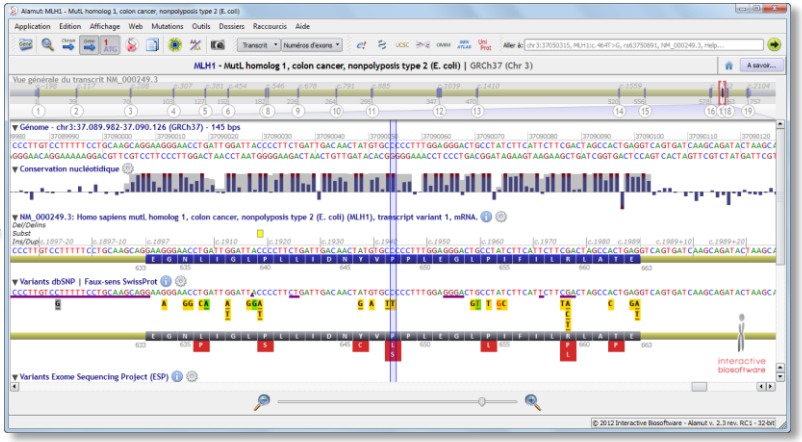
Filtrage de variants annotés



Batch → Visual

1



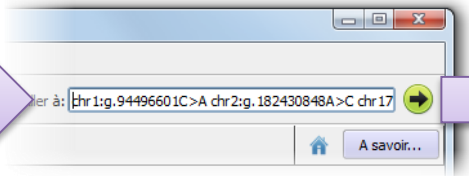


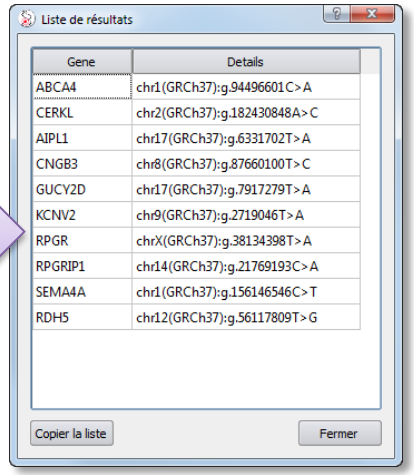
2

copier

	A	B	C	D	E	F	G
1		#id	gene	geneId	chrom	transcript	strand
2	chr1:g.94496601C>A	17	ABCA4	34	1	NM_000350.2	-
3	chr2:g.182430848A>C	49	CERKL	21699	2	NM_201548.4	-
4	chr17:g.6331702T>A	37	AIPL1	359	17	NM_014336.3	-
5	chr8:g.87660100T>C	58	CNGB3	2153	8	NM_019098.4	-
6	chr17:g.7917279T>A	80	GUCY2D	4689	17	NM_000180.3	+
7	chr9:g.2719046T>A	95	KCNV2	19698	9	NM_133497.3	+
8	chrX:g.38134398T>A	178	RPGR	10295	X	NM_000328.2	-
9	chr14:g.21769193C>A	198	RPGRIP1	13436	14	NM_020366.3	+
10	chr1:g.156146546C>T	221	SEMA4A	10729	1	NM_022367.3	+
11	chr12:g.56117809T>G	140	RDH5	9940	12	NM_002905.3	+

coller





Caractères distinctifs

- Orientation clinique (humaine)
  - RefSeq, RefSeqGene, LRG
  - Nomenclature HGVS
- Prédictions d'épissage
  - Jonction proximale
  - Voisinage
- Cohérence avec Alamut Visual
- Produit commercial

Utilisation

- 45 laboratoires

- VaRank: a simple and powerful tool for ranking genetic variants
  Geoffroy V, Pizot C, Redin C, Piton A, Vasli N, Stoetzel C, Blavier A, Laporte J, Muller J. (2015)
  PeerJ 3:e796 https://dx.doi.org/10.7717/peerj.796

- A systematic approach to assessing the clinical significance of genetic variants
  Duzkale H, Shen J, McLaughlin H, Alfares A, Kelly MA, Pugh TJ, Funke BH, Rehm HL, Lebo MS
  Clinical Genetics [2013, 84(5):453-463]