Annotation Guidelines BIONLP-ST 2016 SeeDev task

Estelle Chaix, Bertrand B. Dubreucq, Dialekti Valsamou, Abdelhak Fatihi, Louise Deleger, Robert R. Bossy, Pierre Zweigenbaum, Philippe Bessières, Loic L. Lepiniec, Claire Nédellec

Annotation Guidelines BIONLP-ST 2016 SeeDev task

Campaign: Scientific literature on *Arabidopsis Thaliana.*

Estelle Chaix[1], Bertrand Dubreucq[2], Dialekti Valsamou[1,3], Abdelhak Fatihi[2], Louise Deléger[1], Robert Bossy[1], Pierre Zweigenbaum[3], Philippe Bessières[1], Loïc Lepiniec[2], Claire Nédellec[1]

[1] MaIAGE, INRA – Jouy en Josas, France; [2] Institut Jean-Pierre Bourgin, INRA–Versailles, France; [3] LIMSI, CNRS, Orsay, France.

A. Annotation Scheme

Parts of the document are declared as completely annotated by the [*Completely_Annotated*] label.

A.1. Entities

Entities are all terms belonging to relevant predefined semantic types.

A.1.1 Color scheme

Here you can see the annotation scheme with the colors used in the Annotation Editor (AlvisAE). In the following, we use this color coding to highlight entity mentions, and refer to Annotated entities.

[*Completely_Annotated*] : In the [*Completely_Annotated*] text, all entities should be annotated, even if they do not participate in a relation.

Entity types:

Molecule : DNA : *Gene*, *Gene_Family*, *Box* , *Promoter*

DNA product : *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*

Hormone: *Hormone*

Dynamic Process : *Regulatory_Network*, *Pathway*

Context : *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*

In the following, we use the conventions defined below to distinguish between relation names, roles in relation and entities:

- Entities are noted in italic font with the color scheme previously described (e.g. *Tissue*), and in sentences are between brackets (*e.g.* [*Tissue*])
- Relation names are noted in straight font with the color scheme described below (e.g. Protein_Domain_Composition),
- Roles of relation are noted in black and bold (*e.g.* **Tissue**)

A.1.2 Entity annotation

When an entity includes another, all possible entities are annotated with the relevant types (which may be different). For example, in “embryo development” we annotate the [*Development_Phase*] (embryo development) as well as the [*Tissue*] (embryo). “*WRI1*-like group” is another example where “*WRI1*” is a [*Gene*] and “*WRI1*-like”a [*Gene_Family*] . Embedded entities may be linked by relationships. The entity span may include in rare cases prepositional phrases or even relative clauses, if they are modifiers of the entity and if they contribute to specify its nature.

Examples:

- cotyledons that are initiated outside of the seed environment
- later stages of morphogenesis
- organs with embryonic features
- organs and tissues derived from double fertilization in flowering plants
- proteins which start to be expressed coordinately in the endosperm of maize 8 to 10 days after pollination .

Annotation of words denoting an entity type:

When entities are "named" (*e.g.* [*Gene*], [*Protein*]), the general words that denote the type of the entity (*e.g.* "gene") should not be included in the annotation (the name itself is sufficient).
Examples : *BCCP2* gene, AP2 protein

When entities do not have proper names (*e.g.* [*RNA*], [*Protein_Family*], [*Promoter*]), words denoting the entity type (e.g. "mRNA") should be included in the annotation when they are needed to identify the entity.
Examples : AGL16 mRNA (where "AGL16" is a [*Protein*]), AP2 family (where "AP2" is annotated as a [*Protein_Domain*] and "AP2 family" the [*Protein_Family*] that contain AP2 domain)

Entities should be noun or adjectival phrases, such as "FA biosynthesis" or "FA biosynthetic" (in "FA biosynthetic genes").

Entities (in particular developmental phases) should include the preposition occurring before when it expresses temporal or spatial information, such as "before" or "after" (but not "during") (e.g. AGL15 was present before embryogenesis).

Discontinuity:

Discontinuous entities are allowed when they are syntactically coherent. In particular, they are used for the annotation of coordinated structures.
Example : *BCCP2* and *PKp-ß1* promoters

- "*BCCP2* [...] promoters" is a discontinuous entity and should be annotated as [*Promoter*]

Discontinuity is not allowed between elements that are not in the same sentence or that are *too far* from each other in the sentence.
Counter example : "An analysis of genetic factors affecting *Arabidopsis* seed mass used a segregating population from a cross between small-seeded and large-seeded ecotypes to show that both maternal and nonmaternal QTL affect seed mass"

- "Arabidopsis [...] small-seeded" and "Arabidopsis [...] large-seeded" should NOT be annotated as a discontinuous entity

Inclusion of entities

All entities must be annotated with the correct type, even if they are included in a larger one.

Example: "central cell of female gametophyte"

- ➢ The whole term "central cell of female gametophyte" should be annotated as [*Tissue*]
- ➢ but also "female gametophyte" as [*Tissue*]
- ➢ and "gametophyte" as [*Tissue*]

Entities should be linked by a relation such as "*Localization*" : "central cell of female gametophyte" *Localization* "female gametophyte"

Errors in the text:

When the typography (italic and case) is not consistent with the intended type of entities, entities should be annotated with their intended type (e.g. italic instead of plain text used for protein names as in "interaction between *WRI1* and the *BCCP2* promoter.", "*WRI1*" is annotated as [*Protein*] and not as [*Gene*])

Some sentences may contain errors from the authors (*e.g.* gene names used to refer to proteins, protein names used to refer to RNA). **These sentences should be excluded from the annotated paragraphs when possible**.

An exception is made for enumerations where the intended type of the entities is clearly stated in the context (e.g. "RNAs include ..."). In this case, annotation is permitted and entities should be annotated with their intended type (since it can easily be inferred from the context).

Example : These RNAs include 12S storage proteins, oleosin and steroleosin

- ➢ "12S storage proteins", "oleosin" and "steroleosin" are annotated as [*RNA*] even though they are protein names.

A.1.3 DNA Entities

Gene

Description:

Definition: DNA sequence coding for a mRNA.

Gene names are in italic and uppercase. The [*Gene*] type includes artificial design, for instance with a reporter gene denoted : gene1::gene2 or promoter::gene.

It excludes overgeneral terms such as *these genes*. In this case, the antecedent should be annotated and linked to the relevant arguments (*e.g.* PHAP2A and AP2 extends throughout the whole protein, suggesting that these genes (...)).

Genes belonging to a set of genes that is not a family are annotated with the [*Gene*] type. However, plasmids should **not** be annotated (*e.g.* GAL4-DBD).

Full names of genes (e.g. *APETALA2*) and locus of gene (e.g. At4g38130) should also be annotated (and should be linked to their abbreviation (e.g *AP2*) with a Sequence_Identity relation).

Examples: *FUS3* ; *FUS3::GUS* ; *ABI3* ; *APETALA2* ; At4g38130

Gene_Family

Description:
A family of genes mentioned by their common function, including coding for a same [*Protein_Family*] (*e.g.* albumin genes), or their common ancestor. It should not be confused with proteins (*e.g.* B3 transcription factors).
Words that do not designate the [*Gene_Family*] should be excluded from the name. For instance, in "three new MADS-box", the words *three new* should be excluded.

Examples: LEC genes ; AP2-like ; albumin genes ; B3 transcription factors genes
Counter examples:
GA-biosynthesis genes ; glycolytic biosynthetic genes ; genes involved in acquisition of desiccation tolerance ; B3 transcription factors
Databases:
http://www.arabidopsis.org/browse/genefamily/index.jsp

Box

Description:
Definition: A (short) DNA sequence that corresponds to a **binding site** for a "product" (the transcription machinery or a transcription factor). It also includes DNA elements such as "response elements".
Examples: AFL targets ; TT targets ; WRI1 targets ; dehydration response elements ; AACA
Databases:
More on http://arabidopsis.med.ohio-state.edu , http://www.athamap.de/, or http://bioinformatics.psb.ugent.be/ATCOECIS/

Promoter

Description:
Definition: Upstream region of a gene that binds the polymerase for gene transcription.
It can be designated as a regulatory region of a gene. It may happen that it is not named, such as in the expression "promoters of *At2S3*" where "*At2S3*" is a gene name or in "5' flanking regions followed by promoter". The expression "5' flanking region" **without any gene information** should not be annotated because it is too general and not informative. It may be a set of promoters, such as "albumin promoters". The promoter name should not be confused with the gene name.

The expression "upstream of" should be annotated as a promoter **only** if it refers to the DNA region located before the gene: *e.g.* in "The WRI1 binding sites in the upstream regions of Pl-PK β 1" the expression should be annotated as promoter, but **not** in "*GL2* acts upstream of *MUM4*" which refers to a genetic relationship.

Examples: *BCCP2* promoter ; AGL15 regulatory regions ; 35s; 5' flanking regions of LEC2-induced genes ; promoters of seed storage protein genes
Databases:
http://urgv.evry.inra.fr/projects/FLAGdb++/HTML/index.shtml

A.1.4 Gene product entities

RNA

Description:
Definition: Gene product.
an RNA entity is generally named with the gene name followed by the word "mRNA" (*e.g.* *AGL16* mRNA) or transcript (*e.g.* *TTG1* transcript). In some cases, it may be named with the gene name or protein name (metonymy). For instance, "These RNAs include 2S and 12S storage proteins, oleosin, and steroleosin"
In this case, the gene or the protein is annotated with the [*RNA*] type (see above). This generates ambiguities and should be avoided when possible.
Examples: *CLV3* mRNA ; LEC2-induced RNAs ; *CBF2* transcript

Protein

Description:
Definition: RNA product
Protein names are in plain letters and uppercase (*e.g.* CLV3). If a protein name is followed by the word "protein", the word "protein" should not be annotated. (*e.g.* CLV3 protein). If a protein is denoted by the gene name followed by the word "expression" or "protein", the whole phrase is annotated as a protein (*e.g.* *ABI3* expression)
Examples: CLV3 ; LEC1 ; GLABRA3

Protein_Family

Description:
Definition: A family of proteins mentioned by their common biologic function (*e.g.* kinase) or by their common ancestor.
[*Protein*] should not be confused with [*Gene*]. Proteins should not be confused with protein domains or families.
A protein family can also be defined by a common domain shared by the members of the family (*e.g.* B3 domain), which can be ambiguous with the protein domain type and should be avoided as much as possible.
Proteins mentioned by their common pathway, such as "enzymes of the glycolysis" should not be annotated as a [*Protein_Family*].

Examples: MADS-domain proteins ; MYB ; bHLH protein ; bZIP transcription factor families ; seed storage proteins
Counter examples: enzymes of the glycolysis ; transcription factors ; sequence-specific DNA binding proteins

Databases:
http://planttfdb.cbi.edu.cn/index.php?sp=At
http://arabidopsis.med.ohio-state.edu/AtTFDB/

Protein_Complex

Description:
Definition: A group of proteins that physically interact together.
Examples: PolycombGroupProtein (PCG) ; MYB-bHLH-WD40 (MBW) ; AFL (ABI3-FUS3-LEC) ; SERK1 complex

Protein_Domain

Description:
Definition: A protein domain is a protein sequence and structure that can evolve, function and exist independently, a motif is a sequence that is widespread and has biological significance.
[*Protein_Domain*] should not be confused with [*Protein*] or [*Protein_Family*] .
Examples: B3 domain ; C-terminal region ; non-LEC1-type B domain ; basic helix-loop-helix (bHLH)

A.1.5 Other molecule entities

Hormone

Description:
Definition: A hormone is a plant molecule that influences plant physiology and development.
It does not include sensitivity to the hormone, such as in "ABA sensitivity" where the whole expression should be annotated as [*Regulatory_Network*] , but only "ABA" should be annotated as [*Hormone*]. If a hormone was artificially added, such as in "ethylene treatment", the expression should be annotated as [*Environmental_Factor*].
Examples: auxin ; ethylene ; abscisic acid (ABA) ; GA Gibberellic ac (GA) ; Cytokinin (CK) ; strigolactone ; Brassinosteroid ; Salicylic Acid (SA), Nitric oxide (NO)

A.1.6 Dynamic process

Regulatory_Network

Description:
Definition: A set of DNA products and/or DNA that control the expression of a gene, a pathway.

Generally, regulatory functions should be annotated by [*Regulatory_Network*].

- ➢ Sensitivity to a factor (*e.g.* sensitivity to abscisic acid),
- ➢ Response to a factor (*e.g.* sugar responses),

- ➢ Acquisition of properties (*e.g.* acquisition of desiccation tolerance)
- ➢ Fate (*e.g.* embryonic cell fate) in the sense of determination of the cell destiny.
- ➢ Processes and functionality involving several genes (*e.g.* meristem function, control of seed size, maturation-specific genes)
- ➢ are regulatory networks.

- ❑ In the case of the specific expression "control of" such as "control of seed size", the whole expression should not be annotated : only the words that follow "control of" should must be annotated as a [*Regulatory Network*].

- ❑ In some cases, regulatory networks are designated by the genes that achieved a function. The annotation depends on the action verb (regulate, associated to, involved in) and the action ([*Pathway*] / [*Regulatory_Network*] / [*Development_Phase*]):

  - ➢ *The genes that regulate*[*Pathway*] / [*Regulatory_Network*] / [*Development_Phase*]: the whole expression should be annotated as a [*Regulatory_Network*]

Ex: The genes that regulate female reproductive tract development.

  - ➢ *The genes regulate* [*Pathway*] / [*Regulatory_Network*] / [*Development_Phase*]: the genes are related to the [*Development_Phase*] by the relation they regulate the activity of (option involvement).

Ex: The genes regulate female reproductive tract development.

  - ➢ *The genes involved in/related to* [*Development_Phase*], [*Regulatory_Network*]: the whole expression should be annotated as a [*Regulatory_Network*]

Ex: Genes involved in the female reproductive tract development.

  - ➢ *The genes involved in/related to* [*Pathway*]: the expression should not be annotated as a [*Regulatory_Network*]

Ex: Genes involved in the accumulation of storage protein [*Pathway*].

- ❑ Abnormal development such as "incomplete cytoplasmic rearrangement" and formation of tissues that occurs in abnormal conditions such as "vegetative organs" or "patterning defects" should be annotated as [*Regulatory_Network*] because it means that the development and tissue formation has been triggered by regulation (*e.g.* embryo formation in vegetative organs, somatic embryo or embryonic mode)

- ❑ In "acquisition of desiccation tolerance" the whole term is annotated by [*Regulatory_Network*], and the term "desiccation tolerance" is also annotated as a [*Pathway*].

Examples: germination sensitivity to abscisic acid ; sensitivity to ABA inhibition of

germination ; sensitivity to sugar ; salt responses ; auxin responses ; seedling responses to sugars ; acquisition of desiccation tolerance ; fate of embryonic cells ; vegetative leaf fate ; formation of ectopic trichome on embryos

Counter examples:

- "the expression of genes involved in fatty-acid biosynthesis"
  - This is not a [*Regulatory_Network*], only "fatty-acid biosynthesis" should be annotated as a [*Pathway*]
- "Genes related to the biosynthesis and storage of triacylglycerols"
  - This is not a [*Regulatory_Network*], only "biosynthesis…of triacylglycerols" and "storage of triacylglycerols" should be annotated as [*Pathway*]

Pathway

Description:

Definition: [*Pathway*] means here metabolic pathway, for instance synthesis or degradation.

A pathway represents a group of genes or corresponding products that are involved in a same metabolic, physiological or developmental pathway. In reality, a set of any entities that are involved in such a pathway can be annotated as a pathway here. The biological function of the pathway is also annotated as a pathway (e.g. regulation of storage protein synthesis). It may happen that "storage protein synthesis" is abbreviated into "storage protein".

In the example "LEC2 regulates the accumulation of storage protein", the word "accumulation" should be annotated in the pathway entity span. The *relation* Regulation_Of_Process should be used.

In "acquisition of desiccation tolerance" the whole term is annotated as regulatory network. The term "desiccation tolerance" is a pathway.

The word "pathway" is included in the annotation only when it is part of the name of the pathway. Typically, when it is followed by an adjective:

- fatty acid biosynthetic pathway → "pathway" is included
- glycolysis pathway → "pathway" is not included

The signaling pathways must be annotated as [*Regulatory_Network*] and not as [*Pathway*].

Examples: metabolic pathways ; lipid/triacylglycerol/oil pathway ; fatty acid pathways; storage protein pathways ; starch pathway ; carbohydrate pathway ; secondary metabolite pathways ; flavonoid pathway ; tannin pathway

Database:

ftp://ftp.plantcyc.org/Pathways/

A.1.7 Context

Genotype and Species

(Genotype type)
Description:
Definition: A genotype is given part or the whole genetic information (genetic composition) expressed by an organism genome. In this case, for *Arabidopsis thaliana*. It includes ectopic, as for example in "ectopic expression", which means the expression of the non-modified organism.

In the corpus, it mainly concerns the mutant organism resulting from a genetic modification (*e.g.* insertion or deletion of a gene). They are denoted by the gene name with all letters in lowercase and italic (e.g. *fus3* mutant). If the gene name has a gene typography (italic and all letters in uppercase) and it is followed by the word "mutant", the whole expression should be annotated as a genotype (e.g. *Fus3* mutant), and the gene name should be annotated as a gene.
The non-mutant is called wild-type and should be annotated with [*Genotype*].

The entity text span **includes** the terms qualifying a change in the expression as a result of a mutation, like overexpression. For example, in "plants that overexpress floral MADS factors, such as AP1, AG, or AP3 with PISTILLATA" the whole expression "plants that overexpress floral MADS factors" should be annotated as [*Genotype*].

However, the entity **excludes** the terms qualifying a change in the expression as a result of an exterior factor.

The entity [*Genotype*] should be annotated with all its modifiers (i.e., the largest text span is annotated), such as in "Ectopic postembryonic expression of the *LEC1* gene in vegetative cells induces the expression [..]."

Species: referring to the biological nomenclature.
The expression *in planta* should be annotated as [*Genotype*]; but *in vivo* should be annotated as [*Environmental_Factor*].

Examples: serk2 null mutant ; variety ; cultivar ; cross ; mutation ; mutant cyanobacteria ; plants ; yeast ; animals ; ciliates ; oilseed rape ; soybean ; maize ; eukariotic organisms ; plants that overexpress AP1 ; *fus3* ; *fusca3* ; *Fus3* mutant ; wild-type

Tissue, Cell and Organ

(Tissue type)
Description:
Definition: A tissue is a group of cells, not necessarily identical, that carry out a specific function together. Organs are then formed by the functional grouping together of multiple tissues.
The Tissue type includes organs, as well as entities on the intra-cellular level, such as the "nuclei of endosperm" for example.

The entity span includes all characteristics of the tissue. The state of the tissue should be included in the annotation span (e.g. maturating seed). The species should be included in the annotation span (e.g. endosperm of maize).

When a tissue is described as a part of another tissue, both tissues should be annotated, and linked by a relationship (e.g. in aleurone layer of mature embryos, the whole expression is annotated as [*Tissue*], as well as "mature embryos", and the two are also linked by the relation Localization)

Examples: vegetative tissues ; reproductive tissues ; seedling ; cotyledon ; root ; stem ; leaf ; bud ; flower ; fruit ; silique ; seed ; testa ; integument ; chalaze ; micropyle ; enveloppe ; embryo ; endosperm ; epiderm ; ovule ; pollen ; green seed ; germinating seed ; embryo-like structures from vegetative tissues ; endosperm of maize ; cytoplasm ; nuclei ; cytosol ; Golgi apparatus
Counter examples:
Cell (too general)
Databases:
http://bar.utoronto.ca/efp/cgi-bin/efpWeb.cgi and more specifically for seed:
http://seedgenenetwork.net/

Development_Phase

Description:
Definition: A growth stage.
It includes identity (cotyledon identity), dormancy (bud dormancy), development (cotyledon development), growth (etiolated growth).
It should not be confused with [*Tissue*], such as developing tissues (e.g. embryonic cotyledons, nuclei of of young embryos) or maturing tissue (e.g. maturing A.th seeds).
It should not be confused with abnormal development such as "earlier flowering" or "precocious germination" : the whole expression should be annotated as [*Regulatory_Network*], and only "flowering" and "germination" should be annotated as [*Development_Phase*]

Examples: number of days after fertilization (daf) ; flowering ; maturation ; juvenile phase ; globular stage
Databases:
As for the [*Tissue*], nomenclature can be found at
http://bar.utoronto.ca/efp/cgi-bin/efpWeb.cgi and more specifically for seed at
http://seedgenenetwork.net/

Environmental_Factor

(Environmental or experimental conditions)
Description:
Definition: Any factor, abiotic or biotic, that influences living organisms (e.g. temperature, light).
They are rare in the corpus. They should not be confused with mutants, such as *tnp*

mutants that should be annotated as genotypes.
Expressions such as "laboratory conditions" should not be annotated as [*Environmental_Factor*] because it is too general and not informative.
However, expression "*in vitro*", "*in vivo*" and "yeast two-hybrid" should be annotated as [*Environmental_Factor*].

Examples:
Temperature ; drought ; salt ; heat ; abiotic stress ; biotic stress ; ethylene treatment

A.2. Events

Events (or relations) are n-ary and directed named (typed) relations between entity arguments of the types defined above. All events have two required arguments and may have between 0 and 6 optional secondary arguments (except for Presence_In_Genotype).

In the following, we use the conventions defined below to distinguish between relation names, roles in relation and entities:

- Entities are noted in italic font with the color scheme previously described (e.g. *Tissue*), and in sentences are between brackets (*e.g.* [*Tissue*])
- Relation names are noted in straight font with the color scheme described below (e.g. Protein_Domain_Composition),
- Roles of relation are noted in black and bold (*e.g.* **Tissue**)

For readability, roles are usually not notified in binary examples, but are detailed in the case of n-ary examples.

n-ary event example with 2 arguments:
"Three VP1/ABI3-LIKE genes [*Gene_Family*] encode B3 proteins [*Protein_Family*]"

- **Relation:**
- Transcription_or_Translation : **Source**= VP1/ABI3-LIKE genes [*Gene_Family*] + **Product**=B3 proteins [*Protein_Family*]

n-ary event example with 4 arguments (2 required arguments and 2 optional arguments)
"In addition to the ectopic localization of protoderm [*Tissue*] markers in the suspensor [*Tissue*], globular [*Developmental_Phase*] dcl1-5[*Genotype*] suspensors [*Tissue*] had reduced levels of WOX8 transcripts [*RNA*]"

- **Relation:**
- Localisation : **Functional_Molecule**= WOX8 transcripts [*RNA*] + **Target_Tissue**= suspensor [*Tissue*] + **Organism_Genotype**= dcl1-5 [*Genotype*] + **Developmental_Stage**= globular [*Developmental_Phase*]

A.2.1 Required arguments of relations

The **roles of relation arguments** are also typed. Groupings of entity types have

been created for better readability and are used for naming the argument roles when applicable:

- ➔ **Molecule :**
  - ◆ **DNA :** *Gene*, *Gene_Family*, *Box* , *Promoter*
  - ◆ **Functional_Molecule**
    - ● **DNA product :**
      - ○ *RNA*
      - ○ **Amino acid sequence :** *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*
    - ● *Hormone*
- ➔ **Dynamic Process :** *Regulatory_Network*, *Pathway*
- ➔ **Context :**
  - ◆ **Biological context** *Tissue*, *Development_Phase*, *Genotype*,
  - ◆ *Environmental_Factor*

For **required arguments**, not all combinations are possible. [X | Y] stands for the union of type X and Y, meaning that the argument can be either of type X or of type Y. In the following, we describe each of the main arguments allowed for each event.

A.2.2 Event type and color scheme

Here you can see the event types of our model, classified in large groups, as well as the annotation color scheme used in the Annotation Editor (AlvisAE).

Where and When

- Presence_In_Genotype
- Occurrence_In_Genotype
- Presence_At_Stage
- Occurrence_During
- Localization

Function

- Involvement_In_Process
- Transcription_Or_Translation
- Functional_Equivalence

Regulation

- Regulation_Of_Accumulation
- Regulation_Of_Expression
- Regulation_Of_Development_Phase
- Regulation_Of_Molecule_Activity
- Regulation_Of_Process
- Regulation_Of_Tissue_Development

Composition and Membership

- Primary_Structure_Composition
- Protein_Complex_Composition
- Protein_Domain_Composition
- Family_Membership

- Sequence_Identity

Interaction

- Interaction
- Binding

A.2.3 Extra-properties of events

To limit the number of relations, qualifications of given relations are represented by parameters. A default is set for each relation. All relations have parameters. In this task, only one kind of parameters exists:

➢ Modalities: Negation (Y/N) : describe the status of the knowledge

A.2.4 Event for specific case

➢ **Specific case of entities with synonyms**

Generally, synonyms are linked by a "Sequence_Identity" relation.

These synonyms may be included in an other relation, also to avoid double annotations, the following rules are used, in **this significance order**:

1. The abbreviated form is preferred to the full form

e.g. Diacylglycerol acyltransferase 1 (DGAT1) belongs to DGAT

➢ "Sequence_Identity" relation between DGAT1 [*Protein*] and Diacylglycerol acyltransferase 1 [*Protein*]

➢ "Family_Membership" relation between DGAT1 [*Protein*] and DGAT [*Protein_Family*]

2. The most precise form is preferred to the generic form :

e.g. MIKC contain a second weakly conserved coiled-coil motif (the K domain)

➢ "Sequence_Identity" relation between K domain [*Protein_Domain*] and coiled-coil motif [*Protein_Domain*]

➢ "Protein_Domain_Composition" relation between K domain [*Protein_Domain*] and MIKC [*Protein_Family*]

3. The entity in text is preferred to that between brackets :

e.g. Arabidopsis (*Arabidopsis thaliana*) has two *HDAC1* orthologs, *HDA19* and *HDA6*.

➢ "Sequence_Identity" relation between Arabidopsis [*Genotype*] and *Arabidopsis thaliana* [*Genotype*]

➢ "Presence_In_Genotype" relation between *HDA19* [*Gene*] and Arabidopsis [*Genotype*]

➢ "Presence_In_Genotype" relation between *HDA6* [*Gene*] and Arabidopsis [*Genotype*]

A.2.5 "Where and When" events

Presence_In_Genotype

Description: A **Molecule** or **Element** is present ***in*** a given **Genotype**.
Arguments:

Molecule: Molecule (*Gene*, *Gene_Family*, *Box* , *Promoter*, *RNA* , *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone*)

Element: Biological context (*Tissue*, *Development_Phase*, *Genotype*)

Genotype: *Genotype*

(**Molecule** et **Element** are mutually exclusive)

The relation Presence_In_Genotype should be used in case of genes that are found specifically in species/genotype (e.g. : "*VP1* of maize"), because it means genes are found in plant, and not necessarily expressed

Vocabulary: identified, conserved, possesses
Examples:

- Proteins containing homologues of the AP2 domain [*Protein_Domain*] have been identified in cyanobacteria [*Genotype*]
- *Yeast* [*Genotype*] *has only one HDAC* [*Protein_Family*]

Occurrence_In_Genotype

Description: A **Process** occurs ***in*** a given **Genotype**.
Arguments:

Process: Dynamic_Process (*Regulatory_Network*, *Pathway*)

Genotype: *Genotype*

Vocabulary: occurs, observed, described, present
Examples:

- It is becoming increasingly apparent that autoregulatory loops are a common phenomenon in the regulation of MADS-box genes [*Regulatory_Network*] in plants [*Genotype*]

Presence_At_Stage

Description: A **Molecule** is present ***during*** a given **Developmental phase**.
However, the relation Presence_At_Stage should not be used in case of a specific expression of genes during a developmental phase (e.g. : "expression of the *LEC1* gene in embryogenesis"), because **all** genes are found in cells at any developmental stage (but not necessarily expressed).
However, the relation Regulation_Of_Expression should be used :

- "embryogenesis" [*Developmental_Phase*] Regulation_Of_Expression "*LEC1*" [*Gene*]

Arguments:

Functional_Molecule: Functional_Molecule (*RNA* , *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone*)

Development : *Development_Phase*

Vocabulary: expressed during, accumulates during, present during
Examples:

- We showed that *LEC2* RNA [*RNA*] accumulates primarily during seed development [*Developmental_Phase*]

Occurrence_During

Description: A **Process** occurs ***during*** a given **Developmental Phase**.
Arguments:

Process: Dynamic_Process (*Regulatory_Network*, *Pathway*)
Development: *Development_Phase*

Vocabulary: implicated during, established during, occurs during, active during
Examples:

- Higher plant embryogenesis [*Developmental_Phase*] is divided conceptually into two distinct phases: early morphogenetic processes [*Regulatory_Network*] […]

Localization

Description : A **Molecule** is found ***in*** a **Tissue**
However, the relation Localization should not be used in case of a specific expression of genes in tissues (e.g. : "expression of the *LEC1* gene in vegetative cells"), because **all** genes are found in cells (but not necessarily expressed).
However, the relation Regulation_Of_Expression should be used :

- "vegetative cells" [*Tissue*] *Regulation_Of_Expression* "*LEC1*" [*Gene*]

Arguments:

Functional_Molecule: Functional_Molecule (*RNA* , *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone*)
Process: Dynamic_Process (*Regulatory_Network*, *Pathway*)
Target_Tissue: *Tissue*
(**Functional_Molecule** et **Process** are mutually exclusive)

Vocabulary: accumulate in, within, possess, present in, active in
Examples:

- FUS3 mRNA [*RNA*] accumulates in seed [*Tissue*]
- AGL15 [*Protein*] was initially present in the cytoplasm of cells [*Tissue*]

Counter examples:

- expression of the *LEC1* [*Gene*] gene in vegetative cells [*Tissue*]

A.2.6 "Function" events

Involvement_In_Process

Description: A **Molecule** is involved ***in*** a **Dynamic Process**.
Arguments:

Participant: Molecule (*Gene*, *Gene_Family*, *Box* , *Promoter*, *RNA* , *Protein*,

Protein_Family, *Protein_Complex*, *Protein_Domain*, *Hormone*)

Process: Dynamic_Process (*Regulatory_Network*, *Pathway*)

Vocabulary: involved in, includes, mediating

Examples:

- A complex process of differentiation [*Regulatory_Network*] that includes the biosynthesis and secretion of pectinaceous mucilage [*Pathway*]
  - biosynthesis of pectinaceous mucilage [*Pathway*] Involvement_In_Process process of differentiation [*Regulatory_Network*]
  - secretion of pectinaceous mucilage [*Pathway*] Involvement_In_Process process of differentiation [*Regulatory_Network*]
- *MUM4* [*Gene*] encodes an enzyme involved in RGI biosynthesis [*Pathway*]

Transcription_Or_Translation

Description: A **DNA** entities encodes for **RNA** (Transcription) or **RNA** entities encodes a **Protein** (Translation). Often, reference is made to the gene encoding the protein, without mention of the RNA.

Arguments:

Source: DNA|RNA (*Gene*, *Gene_Family*, *RNA*)

Product: DNA_Product (*RNA* , *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*)

Vocabulary: encodes

Examples:

- Three VP1/ABI3-LIKE (VAL) [*Gene_Family*] genes encode B3 proteins [*Protein_Family*]

Functional_Equivalence

Description: A **Molecule**, **Dynamic Process** or **Context** compared to another similar **Molecule**, **Dynamic Process** or **Context**.
Functional_Equivalence relation is to be used to link similar products in different species, such as homolog/ortholog proteins.

- [...] BnSCL1, an ortholog of the *Arabidopsis* SCARECROW-like protein 15 (SCL15)

Arguments:

Element1: All entities (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone* , *Regulatory_Network*, *Pathway* , *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*)

Element2: All entities (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone* , *Regulatory_Network*, *Pathway* , *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*)

Vocabulary : ortholog, homolog

Examples :

- *WER* [*Gene*] and *GL1* [*Gene*] encode functionally equivalent proteins
- Rice homologs of ABI3 and ABI5 (OSVP1 and TRAB1, respectively)
  - ABI3 [*Protein*] Functional_Equivalence OSVP1 [*Protein*]
  - ABI5 [*Protein*] Functional_Equivalence TRAB1 [*Protein*]

A.2.7 "Regulation" events

Use of "Regulation" relations when there is a genotype involved

The **agent** of the Regulation relation is always the **genotype**, even when the gene involved in the genotype is specified, **if no information on the direct role of the agent is given**. If direct information on the agent is given, genotype is indicated in the optional argument **Organism_Genotype** [*Genotype*].

Examples :

- RNA interference of *L1L* function [*Genotype*] has been shown to cause embryo arrest [*Regulatory_Network*]
  → "RNA interference of L1L function" [*Genotype*] Regulation_Of_Process "embryo arrest" [*Regulatory_Network*], even though the gene "*L1L*" is mentioned, because the subject is "RNA interference of L1L function", and the role of *L1L* is not clearly defined.

- Ectopic expression of LEC1 [*Genotype*] is sufficient to induce embryo formation [*Regulatory_Network*]
  → "Ectopic expression of LEC1" [*Genotype*] Regulation_Of_Process "embryo formation" [*Regulatory_Network*], even though the gene "LEC1" is mentioned.

- *val1 val2* double-mutant [*Genotype*] seedlings form no leaves [*Tissue*]
  → "*val1 val2* double-mutant" [*Genotype*] Regulation_Of_Tissue_Development "leaves" [*Tissue*] (no gene is mentioned).

Counter examples:

- WRI1 [*Protein*] is able to regulate *in planta* [*Genotype*] the activity of the *BCCP2* promoters [*Promoter*]
  → Here, the direct role of WRI1 [*Protein*] is given : WRI1 *Regulation_Of_Expression* *BCCP2* promoters, with the **Organism_Genotype** instance "*in planta*".

Regulation_Of_Accumulation

Description: A **Molecule**, **Dynamic Process** or **Context** regulates the accumulation of a **Functional Molecule** (in particular, [*Protein*], [*RNA*], [*Hormone*] entities).

Arguments:

Agent: All entities (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone* , *Regulatory_Network*, *Pathway* , *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*)

Functional_Molecule: Functional_Molecule (*RNA* , *Protein*, *Protein_Family*, *Protein_Complex*, *Hormone*)

Vocabulary: activates, induces, enhances, trigger, inhibits, accumulation, steady state-level, concentration, increase

Examples:

- AGL15 [*Protein*] induces accumulation of AGL18 transcript [*RNA*]
- Finally, the results of our studies of somatic embryogenesis [*Development_Phase*] indicate that AGL15 [*Protein*] accumulates even when embryos [*Tissue*] arise de novo from cells in other phases of the life cycle.
  - Regulation_Of_Accumulation : **Agent**= somatic embryogenesis [*Development_Phase*] + **Functional_Molecule**= AGL15 [*Protein*] + **Tissue** =embryos [*Tissue*]

NB: the target of this relation **cannot** be a [*Pathway*] or a [*Regulatory_Network*]. In those cases, the relation "Regulation_Of_Process" should be used instead.

Regulation_Of_Expression

Description: A **Molecule**, **Dynamic Process** or **Context** regulates the expression of a DNA entity. DNA entity includes [*Promoter*] and [*Box*].

Argument:

Agent: All entities (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone* , *Regulatory_Network*, *Pathway* , *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*)

DNA: DNA (*Gene*, *Gene_Family*, *Box* , *Promoter*)

Vocabulary: activates, induces, enhances, trigger, inhibits, gene expression or gene transcription

Examples:

- WRI1 [*Protein*] is a limiting factor of lipogenic gene [*Gene_Family*] expression in seeds [*Tissue*], directly induces the transcriptional activation of these genes at the onset of the maturation phase [*Development_Phase*].
  - Regulation_Of_Expression: **Agent**= WRI1 [*Protein*] + **DNA**= lipogenic gene [*Gene_Family*] + **Tissue**= seeds [*Tissue*] + **Development_Stage**=maturation phase [*Development_Phase*]
- Expression of the *LEC1* [*Gene*] gene in vegetative cells [*Tissue*]
- We suggest that VAL [*Gene_Family*] targets Sph/RY [*Box*] -containing genes

Counter example:

- WRI1 [*Protein*] directly enhances the expression of genes involved in glycolysis [*Pathway*] : even if "genes" is mentioned, the relation was made between [*Protein*] and [*Pathway*] with the "Regulation_Of_Process" relation

Regulation_Of_Development_Phase

Description: A **Molecule**, **Dynamic Process** or **Context** regulates the activity of a **Development** phase.

Arguments:

Agent: All entities (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone* , *Regulatory_Network*, *Pathway* , *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*)

Development: *Development_Phase*

Vocabulary: activates, induces, enhances, trigger, inhibits, influences, blocks

Examples:

- Biologically active GAs [*Hormone*] have been suggested to have a role in embryogenesis [*Development_Phase*]
- Genetic analysis shows that termination of the primary shoot meristem [*Development_Phase*] in l28 mutants [*Genotype*] requires an active CLV signaling pathway [*Pathway*]
  - Regulation_Of_Development_Phase: **Agent**= CLV signaling pathway [*Pathway*] + **Development**= termination of the primary shoot meristem [*Development_Phase*] + **Organism_Genotype**= l28 mutants [*Genotype*]

Regulation_Of_Molecule_Activity

Description: An **Agent** (**Molecule**, **Dynamic Process** or **Context**) regulates the activity of a **Molecule**, such as [*Protein*].

Arguments:

Agent: All entities (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone* , *Regulatory_Network*, *Pathway* , *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*)

Molecule: Amino acid sequence| Hormone (*Protein*, *Protein_Family*, *Protein_Complex*, *Hormone*)

Vocabulary: control, regulate, phosphorylate

Examples:

- p97/VCP [*Protein_Complex*] can be phosphorylated by the JAK-2 [*Protein*] kinase

Regulation_Of_Process

Description: A **Molecule**, **Dynamic Process** or **Context** regulates the activity of a Dynamic Process.

Arguments:

Agent: All entities (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone* , *Regulatory_Network*, *Pathway* , *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*)

Process: Dynamic Process (*Regulatory_Network*, *Pathway*)

Vocabulary: restrict, regulate, induce

Examples:

- ➢ The stem cells in turn signal back via the CLV3 [*Protein*] peptide to restrict the size of the OC [*Regulatory_Network*]
- ➢ WRI1 [*Protein*] directly enhances the expression of genes involved in glycolysis [*Pathway*]

Regulation_Of_Tissue_Development

Description: A **Molecule**, **Dynamic Process** or **Context** regulates the activity of a Dynamic Process.

Arguments:

Agent: All entities (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone* , *Regulatory_Network*, *Pathway* , *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*)

Target_Tissue: *Tissue*

Vocabulary: produce, generate, developped, repress, possess

Examples:

- ➢ The results of our study of organs [*Tissue*] produced during precocious germination [*Regulatory_Network*]

A.2.8 "Composition and Membership" events

Primary_Structure_Composition

Description: A specific sequence of nucleotide is found in a molecule of **DNA**

Arguments:

DNA_Part: *Box* | *Promoter*

DNA: DNA (*Gene*, *Gene_Family*, *Box* , *Promoter*)

Vocabulary: possess, motif, core of, located, sequence, contained

Examples:

- ➢ We show that mutations in the AACCCA [*Box*] element of the *BCCP2* promoter [*Promoter*]
- ➢ The WRI1 binding sites in the upstream region of Pl-PK β 1 [*Promoter*] contained the conserved AW-box [*Box*]

Protein_Complex_Composition

Description: A specific DNA product is found in a **protein complex**.

Arguments:

Amino_Acid_Sequence: Amino acid sequence (*Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*,)

Protein_Complex: *Protein_Complex*

Vocabulary: presence, associated, complex, detected, component of, composition of

Examples:

- ➢ The identification of two members of the BR signaling pathway, the main BR receptor BRI1 [*Protein*] and its coreceptor BAK1 [*Protein*] (SERK3 [*Protein*]) as components of the SERK1 complex [*Protein_Complex*].

Protein_Domain_Composition

Description: A specific **Protein Domain** is found in an Amino acid sequence. It can be used to link products that are part of a factor, such as [*Protein_Domain*] Protein_Domain_Composition [*Protein*].

Arguments:

Domain: *Protein_Domain*

Product: DNA_Product *(RNA , Protein, Protein_Family, Protein_Complex, Protein_Domain)*

Vocabulary: contains, presence, characterized by

Examples:

- ➢ Proteins of the RAV family [*Protein_Family*] contain one AP2 domain [*Protein_Domain*]

Family_Membership

Description: A **DNA, RNA** or **Protein** belongs to another DNA, Product or Factor. This relation is to be used between entities of the same nature, to denote members of a set (e.g. [*Gene*] belonging to [*Gene_Family*], [*Protein*] to a [*Protein_Family*], sub-families to families, etc.).
Family_Membership should **not** be used for entities that are part of another entity (e.g. [*Protein_Domain*] that are part of [*Protein*]). The more generic relation Protein_Domain_Composition should be used instead.

Arguments:

Element: *Gene, Gene_Family, RNA, Protein, Protein_Family, Protein_Domain*

Family: *Gene_Family, RNA, Protein_Family*

Vocabulary: member of, family , belongs

Examples:

- ➢ AP2 [*Protein*] belongs to AP2/EREBP [*Protein_Family*] family
- ➢ *AGL15* [*Gene*] from the large group of floral MADS box genes [*Protein_Family*]
- ➢ bZIP10 [*Protein*] and bZIP25 [*Protein*], which have been classified into group C [*Protein_Family*]

Counter examples:

- ➢ The LEC2 [*Protein*] protein contains a DNA-binding B3 domain [*Protein_Domain*]
  → Protein_Domain_Composition between B3 domain and LEC2

Sequence_Identity

Description: A **Molecule**, **Dynamic Process** or **Context** compared to another similar **Molecule**, **Dynamic Process** or **Context**.
The Sequence_Identity relation is to be used to link identical products as well as synonyms, full form and abbreviation .

Arguments:

Element1: All entities (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone* , *Regulatory_Network*, *Pathway* , *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*)

Element2: All entities (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone* , *Regulatory_Network*, *Pathway* , *Tissue*, *Development_Phase*, *Genotype*, *Environmental_Factor*)

Vocabulary : identical, synonym
Examples :

- The SUN6 gene [*Gene*] is identical to the previously described ABI4 gene [*Gene*]
- LEAFY COTYLEDON2 [*Protein*] (LEC2)[*Protein*]

A.2.9 "Interaction" events

Binding

Description: A **functional molecule** physically binds to a **molecule**. In most cases, a protein binds to a promoter or a gene.

When the interaction between two protein is specifically performed "*in vitro*" or in "yeast two-hybrid", the relation Binding is used (and not Interaction, which is less precise)

- **Example:** FUS3 [*Protein*] interacts with LEC2 [*Protein*] *in vitro*

In the specific case of a homodimeric interaction, the agent and the target of the Binding relation is the same entity:

- **Example:** BRI1 [*Protein*] can also form homodimers in the plasma membrane [*Tissue*]
  - In this case: Binding **Functional_Molecule**= BRI1 [*Protein*] + **Molecule**= BRI1 [*Protein*] + **Tissue**=plasma membrane [*Tissue*]

Arguments:

Functional_Molecule: Functional_Molecule (*RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone*)

Molecule: Molecule (*Gene*, *Gene_Family*, *Box* , *Promoter* , *RNA*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*, *Hormone*)

Vocabulary: binds, physically interacts, co-precipitates, co-migrate
Examples:

- Interaction between WRI1 [*Protein*] and the *BCCP2* promoter [*Promoter*], both *in vitro* and in yeast

- ➢ TT2 [*Protein*] interacts with TT8-TTG1 [*Protein_Complex*] in yeast two-hybrid studies.
- ➢ CLV3 [*Protein*] acts as an extracellular ligand of the CLV1 receptor kinase complex [*Protein_Complex*]

Interaction

Description: A **molecule** interacts with another **molecule**.
The relation Interaction should be used between DNA-DNA, and in the case of indirect interaction. It may be applied to a DNA or Amino acid sequence, but Binding, Regulation_Of_Molecule_Activity or Regulation_Of_Expression must be used when possible.
It excludes the case where the interaction is direct (physical): the more specific relation Binding must be used in this case.

Arguments:

Agent: DNA | Amino acid sequence (*Gene*, *Gene_Family*, *Box*, *Promoter*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*)

Target: DNA | Amino acid sequence (*Gene*, *Gene_Family*, *Box*, *Promoter*, *Protein*, *Protein_Family*, *Protein_Complex*, *Protein_Domain*)

Vocabulary: cooperate, synergistic antagonist, counteract relationships, effects
Examples:

- ➢ *SAP18* [*Gene*] alone repressed *LEA* and *CBF2*, possibly through interaction with *AGL15* [*Gene*]
  - ○ Genetic interaction
- ➢ AGL15 [*Protein*] interacts with members of the SIN3 histone deacetylase (HDAC) complex [*Protein_Complex*]
  - ○ Physically bind unproved

Counter example:

- ➢ CLV3 [*Protein*] presumably acts as an extracellular ligand of the CLV1 [*Protein*] receptor kinase complex
  - ○ Here, the relation Binding should be used
- ➢ Ternary complex formation between the bZIP [*Protein_Family*] heterodimers and ABI3 [*Protein*]
  - ○ Here, the relation Binding should be used

A.2.10 Optional arguments of relations

6 optional arguments are possible to describe n-ary event. 5 of them require an entity identifier as argument. For these, only one entity type per role is authorized. These arguments can exist in ALL types of relations (except for Presence_In_Genotype).

- ➢ **Tissue**:
  - ○ *Tissue*

- **Developmental_Stage**:
  - *Development_Phase*
- **Organism_Genotype**:
  - *Genotype*
- **Environmental_Factor**:
  - *Environmental_Factor*
- **Hormone**:
  - *Hormone*

A specific optional argument is Prerequisite_Event which accepts events as argument.

- **Prerequisite event:**
  - Primary_Structure_Composition
  - Interaction
  - Localization
  - Protein_Domain_Composition

Optional arguments are used to handle cases when we have some conditional information of the type:

- "A [*Protein*] accumulates in B [*Tissue*] when there exists C [*Hormone*] ."
- In this fictional example we have a Localization relation between A [*Protein*] & B [*Tissue*], and the optional argument **Hormone** is C [*Hormone*].

In a second fictional example we can see the second scenario :

- "A [*Protein*] activates B [*Gene*] in the flower [*Tissue*], if C [*Hormone*] exists."
  - Here we have a Regulation_Of_Expression event:
    - **Agent** A [*Protein*] Regulation_Of_Expression **DNA** B [*Gene*] , **Tissue** flower [*Tissue*] , **Hormone** C [*Hormone*]

In a third and fourth fictional example, we can see scenarios illustrating the difference between arguments in conjunction vs. arguments in disjunction. When arguments are in conjunction, only one relation is annotated with all the arguments.

- "A [*Protein*] accumulates in B [*Tissue*] when there exists C [*Hormone*] **and** D [*Environmental_Factor*]."
  - Here : we have a Localization relation between **Functional_Molecule** A [*Protein*] & **Target_Tissue** B [*Tissue*], and the 2 optional arguments: **Hormone** C [*Hormone*] and **Environmental_Factor** D [*Environmental_Factor*]

When arguments are in disjunction, two separate relations are annotated.

- "A [*Protein*] accumulates in B [*Tissue*] when there exists C [*Hormone*] **or** D [*Environmental_Factor*]."
- Here : we have two relations :
  - First relation : Localization relation between **Functional_Molecule** A [*Protein*] & **Target_Tissue** B [*Tissue*], and an optional argument:

Hormone C [*Hormone*]

- Second relation : Localization relation between **Functional_Molecule** A [*Protein*] & **Target_Tissue** B [*Tissue*], and an optional argument: **Environmental_Factor** D [*Environmental_Factor*]

In a fifth fictional example, we can see the scenario where a prerequisite event is needed.

➢ "A [*Protein*] binds to B [*Protein_complex*] if C [*Hormone*] is found in D [*Tissue*]."

- First relation: Event identifiant: Event1: Localization relation between **Functional_Molecule** C [*Hormone*] & **Target_Tissue** C [*Tissue*]
- Second relation: Binding relation between **Agent :** A [*Protein*] **Target:** B [*Protein_complex*] **Pre-requisite event:** Event1

A.2.1 Extra properties

Negation

All types of relations have an extra field to mark the negation of an event.

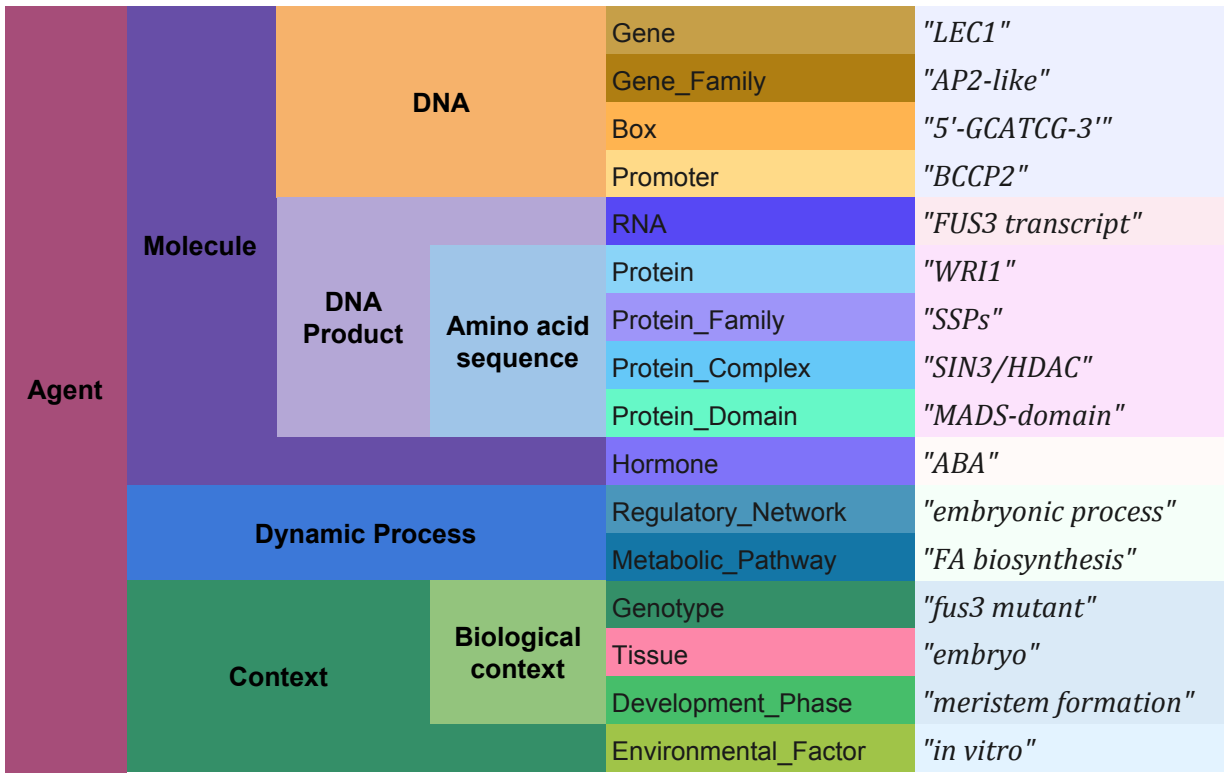
Example :

➢ Trichomes [*Tissue*] are present on Arabidopsis leaves and stems but **not** on wild-type [*Genotype*] cotyledons [*Tissue*]

➢ Notably, **none** of the proposed downstream components of BRI1, such as BES1 [*Protein*], BZR1 [*Protein*], or BIN2 [*Protein*] was detected in the SERK1 complex [*Protein_Complex*].

B. Figures

B.1 Entity types and Categories



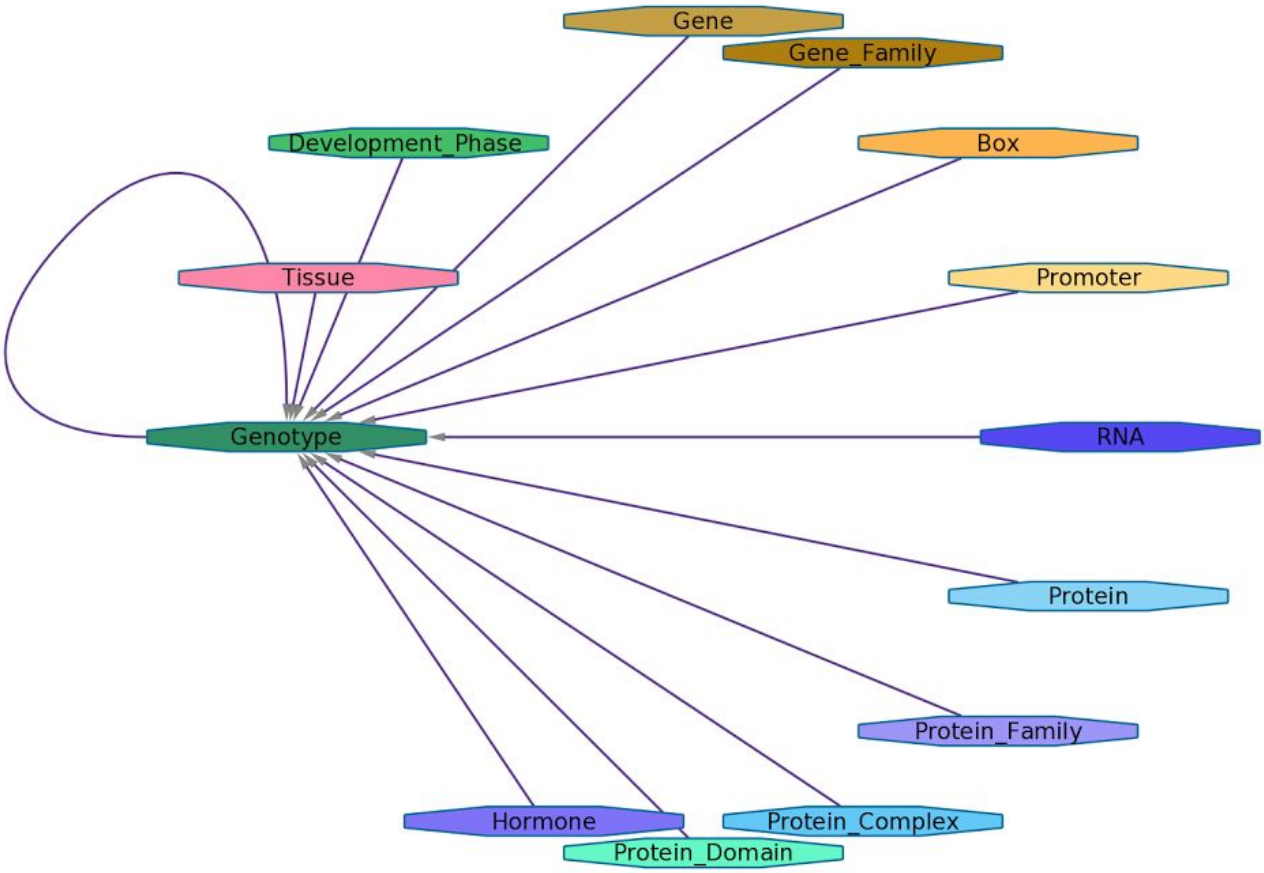
B.2 Relation classification

BIONLP-ST task See-Dev have two subtasks: *binary relation extraction* and full *event extraction* The labels are the same, except Is_Linked_To relation, which is specific to the binary framework :

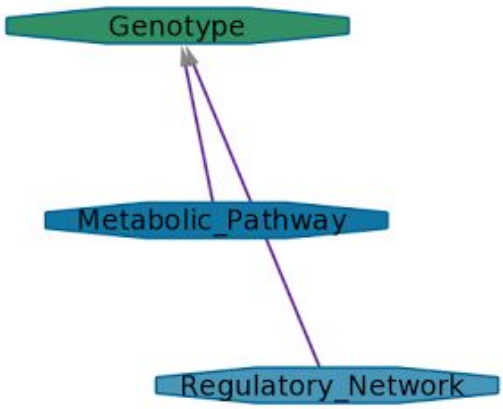
Set of relation type	N-ary relation name	Binary relation name
Where and When	*Presence_At_Stage*	*Exists_At_Stage*
Where and When	*Presence_In_Genotype*	*Exists_In_Genotype*
Where and When	*Localization*	*Is_Localized_In*
Where and When	*Occurrence_During*	*Occurs_During*
Where and When	*Occurrence_In_Genotype*	*Occurs_In_Genotype*
Function	*Functional_Equivalence*	*Is_Functionally_Equivalent_To*
Function	*Involvement_In_Process*	*Is_Involved_In_Process*
Function	*Transcription_Or_Translation*	*Transcribes_Or_Translates_To*
Regulation	*Regulation_Of_Accumulation*	*Regulates_Accumulation*
Regulation	*Regulation_Of_Development_Phase*	*Regulates_Development_Phase*
Regulation	*Regulation_Of_Expression*	*Regulates_Expression*
Regulation	*Regulation_Of_Molecule_Activity*	*Regulates_Molecule_Activity*
Regulation	*Regulation_Of_Process*	*Regulates_Process*
Regulation	*Regulation_Of_Tissue_Development*	*Regulates_Tissue_Development*
Composition and Membership	*Primary_Structure_Composition*	*Composes_Primary_Structure*
Composition and Membership	*Protein_Complex_Composition*	*Composes_Protein_Complex*
Composition and Membership	*Sequence_Identity*	*Has_Sequence_Identical_To*
Composition and Membership	*Family_Membership*	*Is_Member_Of_Family*
Composition and Membership	*Protein_Domain_Composition*	*Is_Protein_Domain_Of*
Interaction	*Binding*	*Binds_To*
Interaction	*Interaction*	*Interacts_With*
Interaction	XXXX	*Is_Linked_To*

B.3 Schematical representation of Arguments and Events

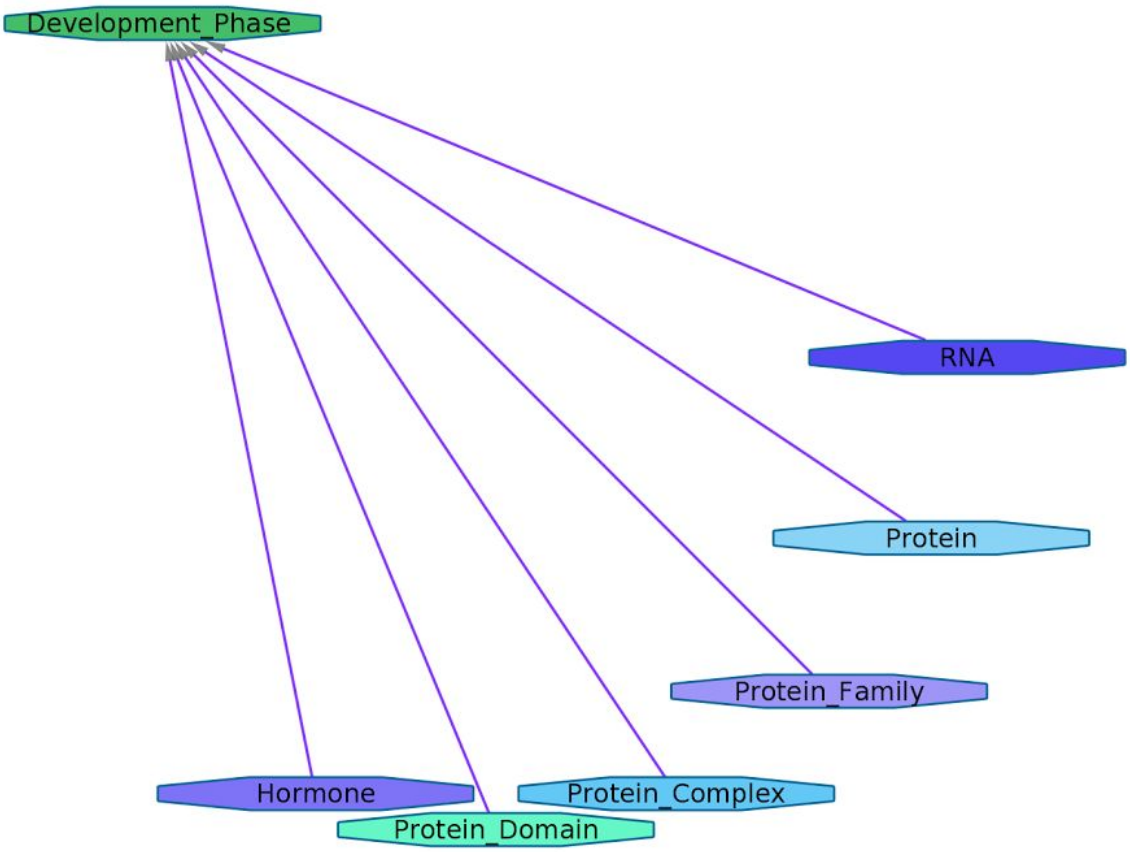
B.3.1 Presence_In_Genotype



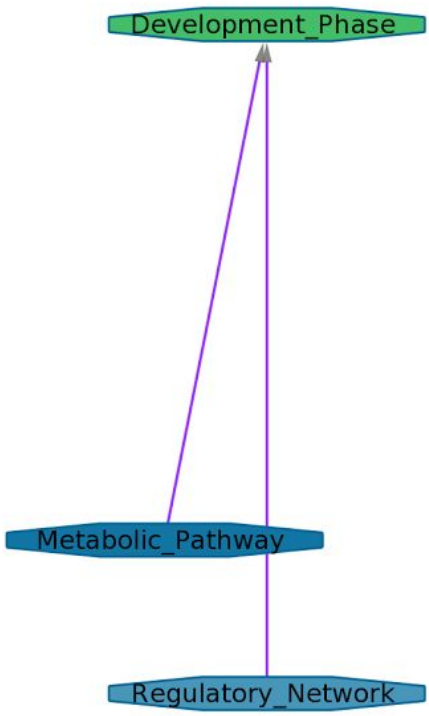
B.3.2 Occurrence_In_Genotype



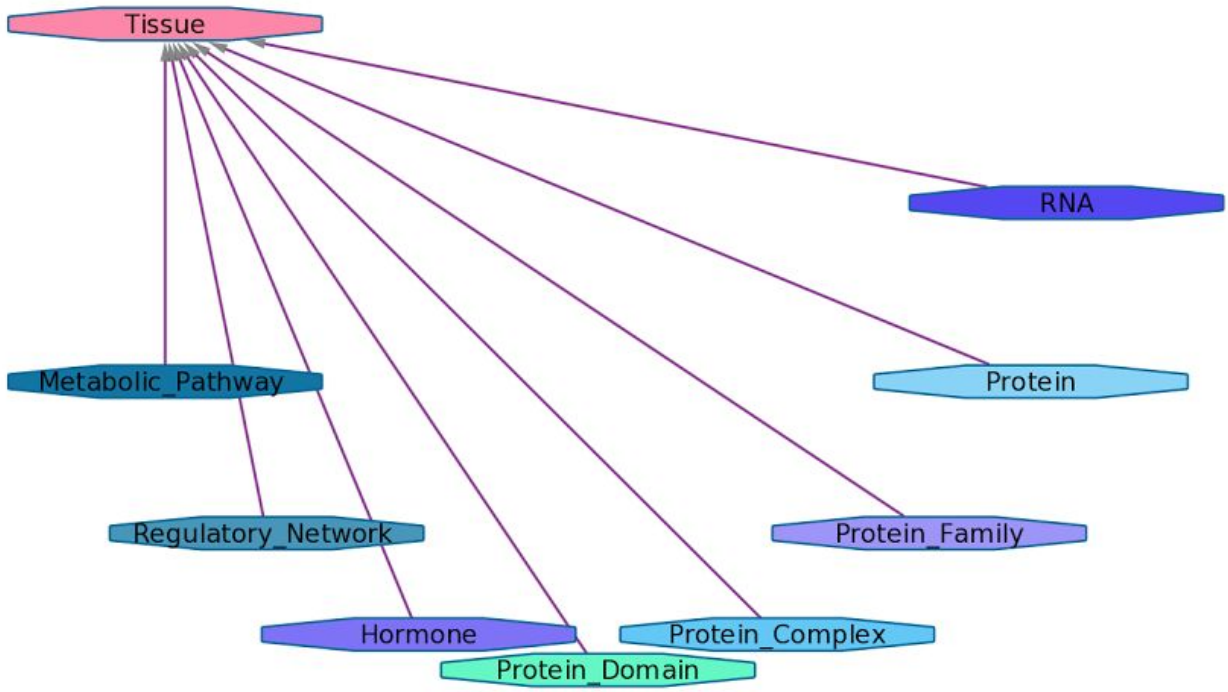
B.3.3 Presence_At_Stage



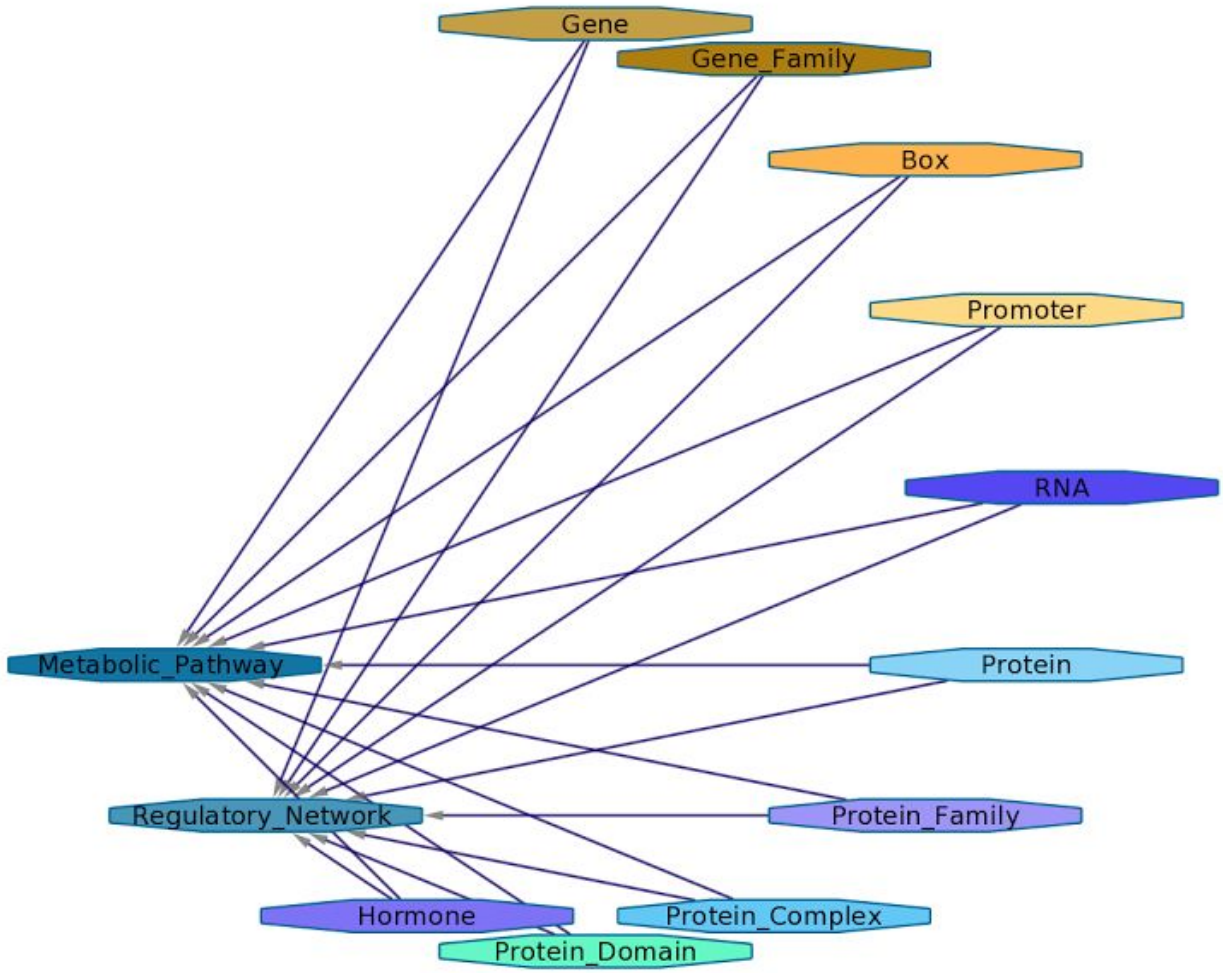
B.3.4 Occurrence_During



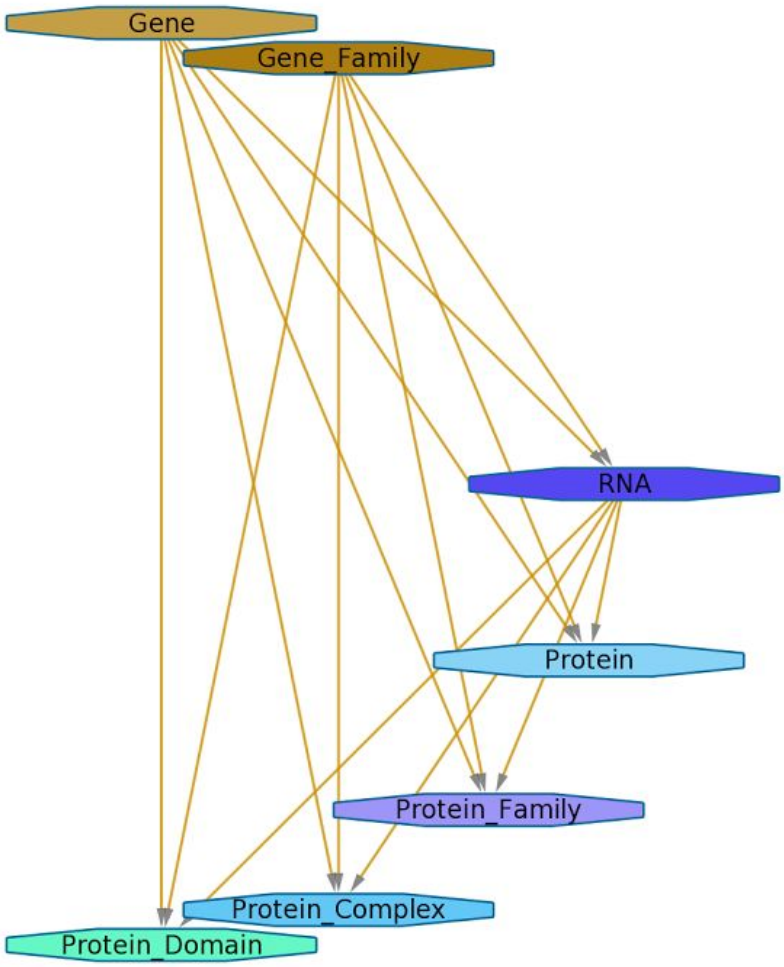
B.3.5 Localization



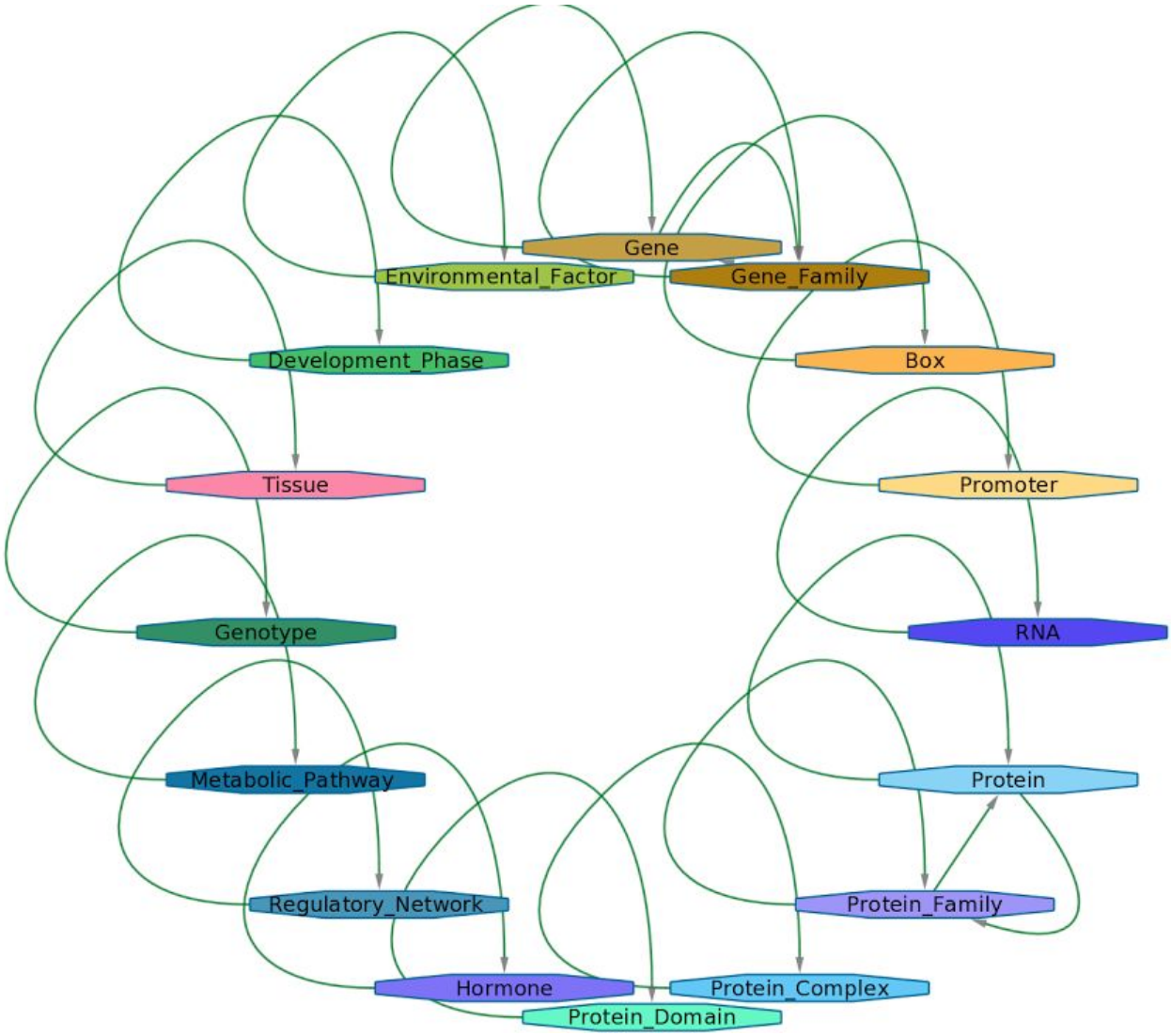
B.3.6 Involvement_In_Process



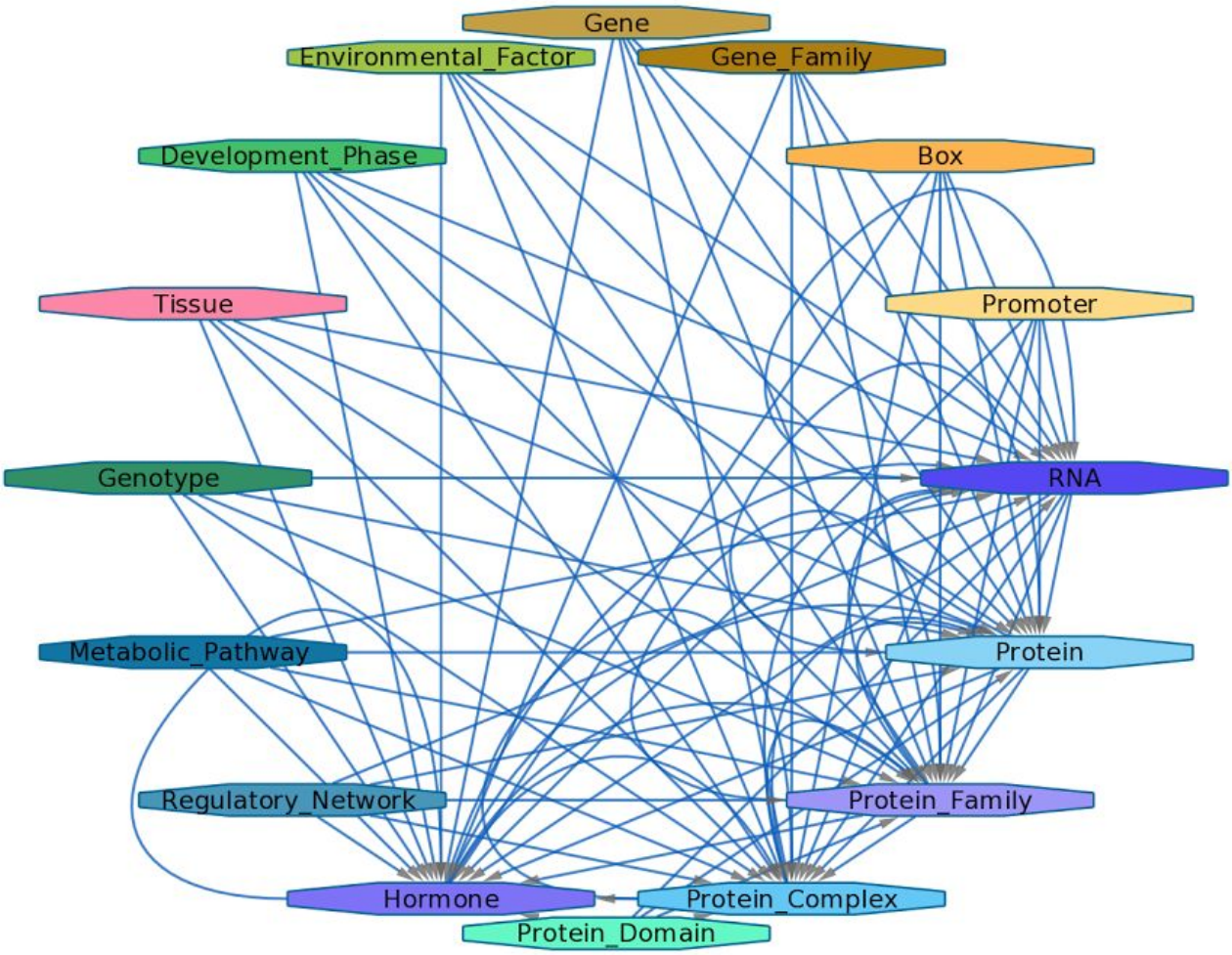
B.3.7 Transcription_Or_Translation



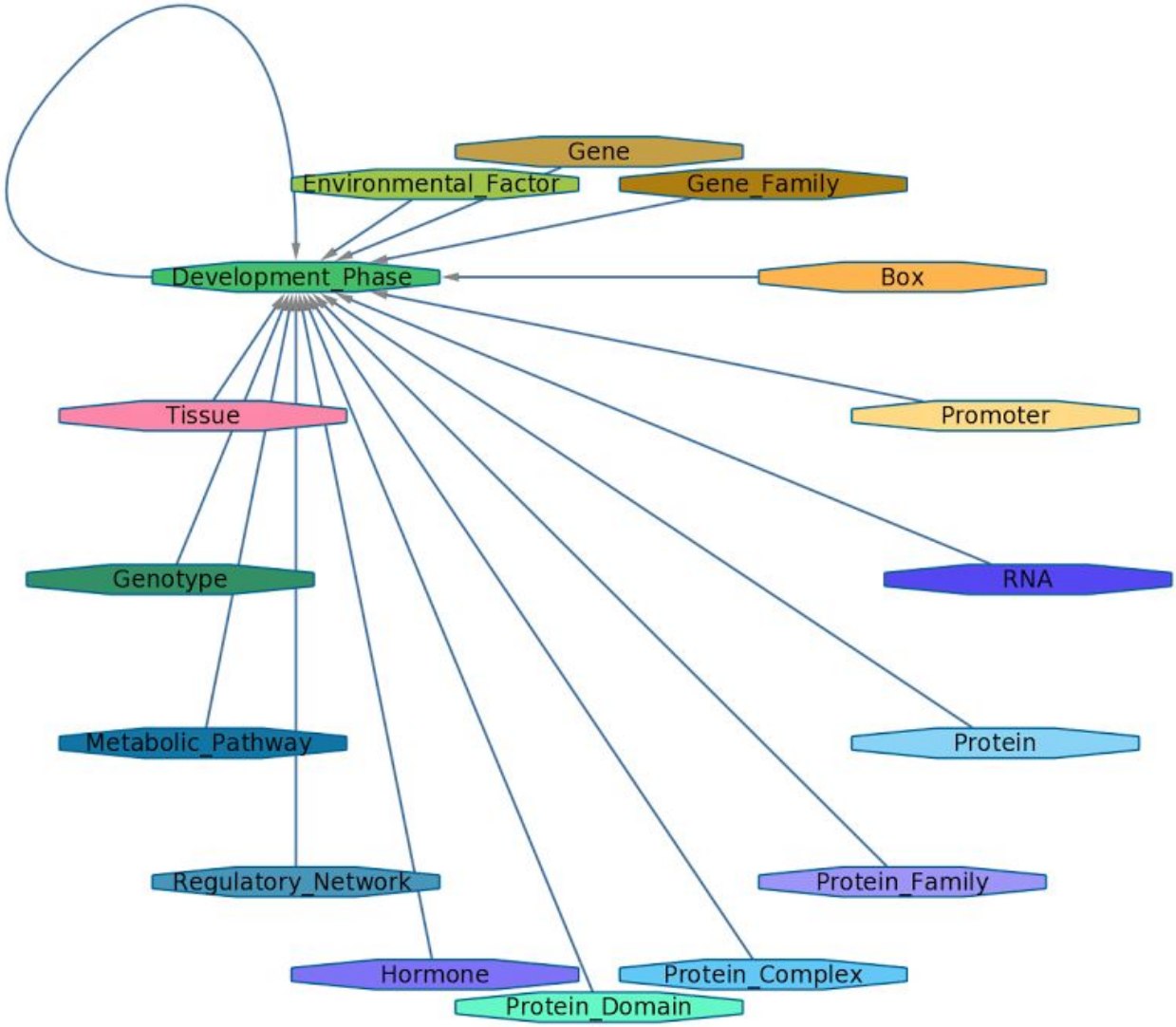
B.3.8 Functional_Equivalence



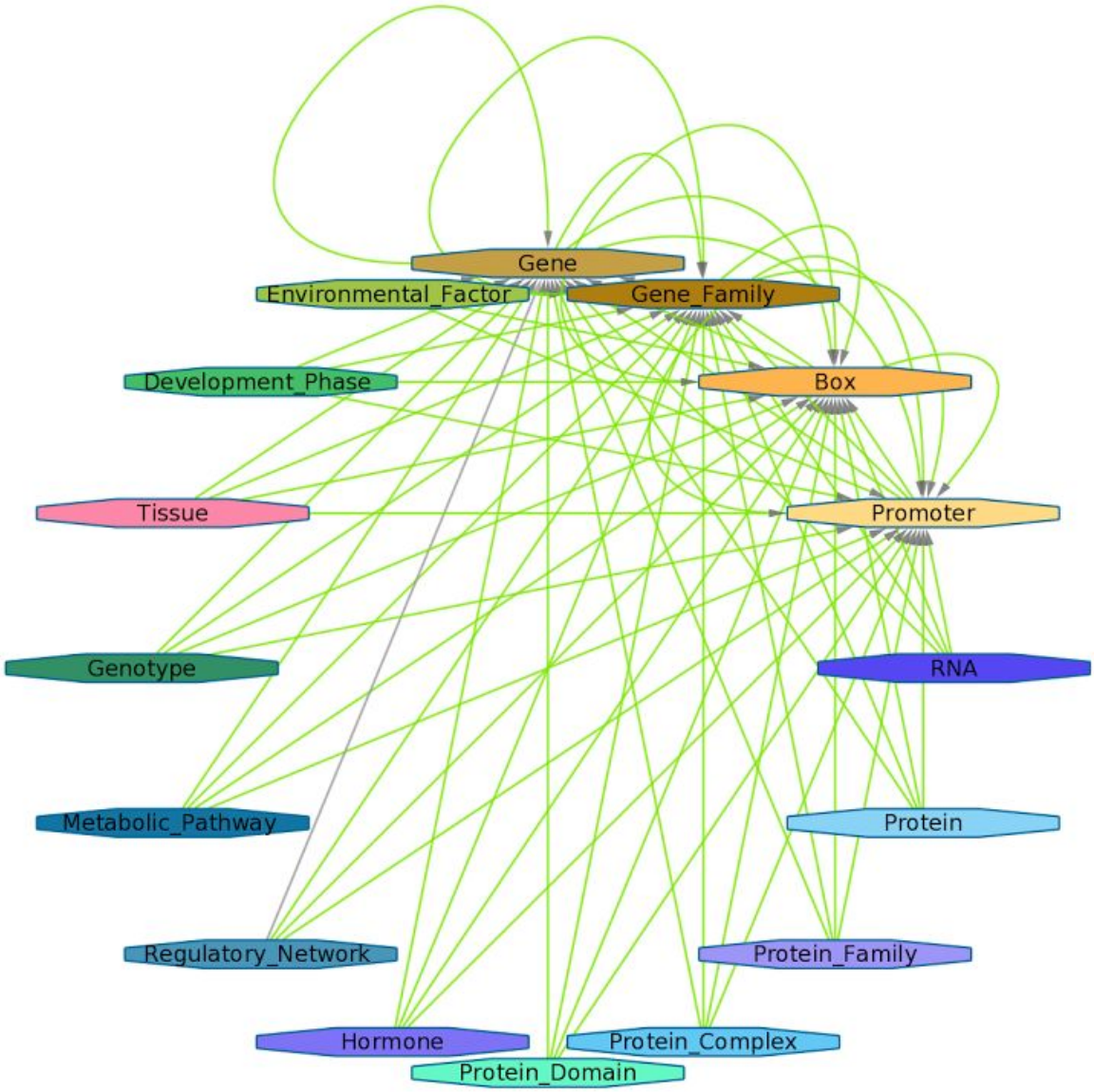
B.3.9 Regulation_Of_Accumulation



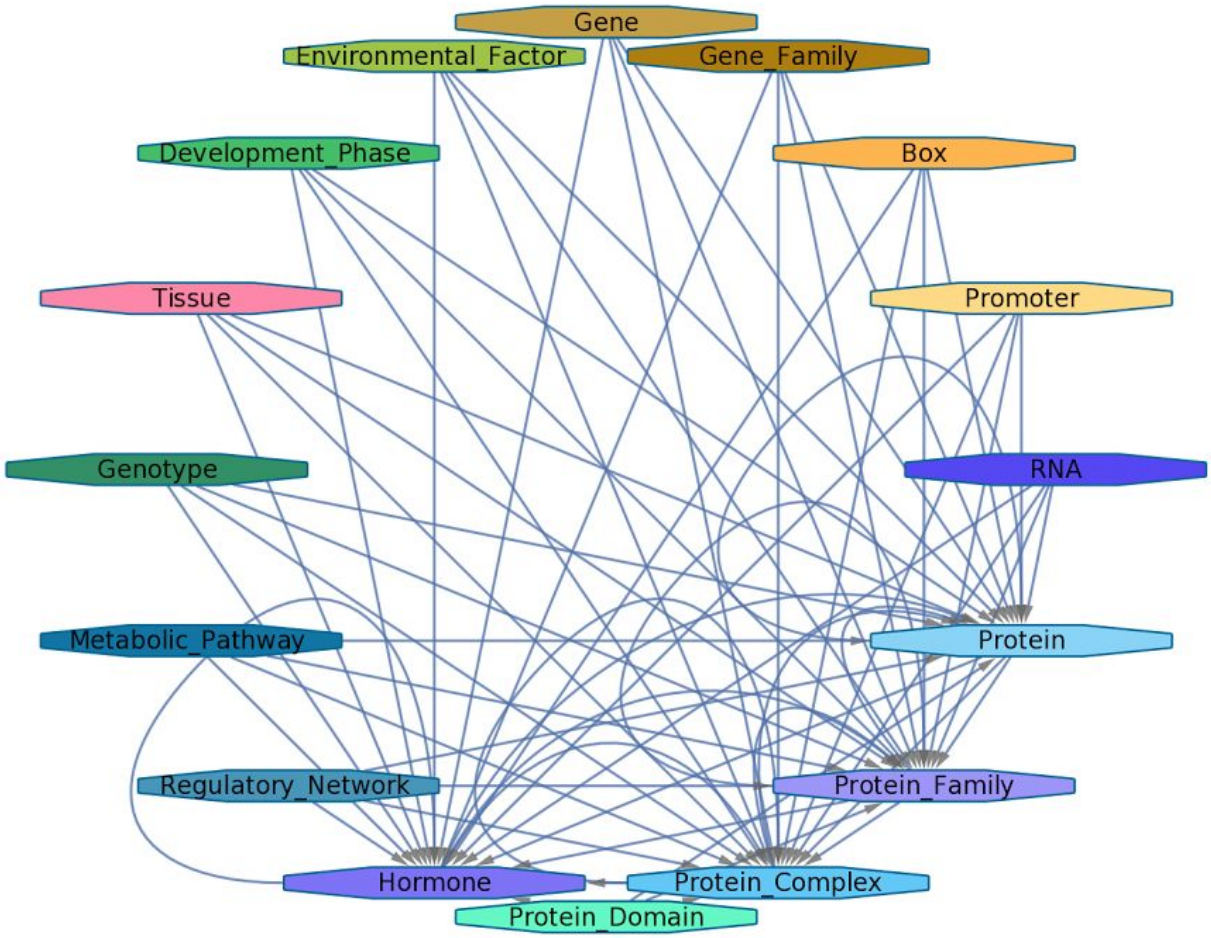
B.3.10Regulation_Of_Development_Phase



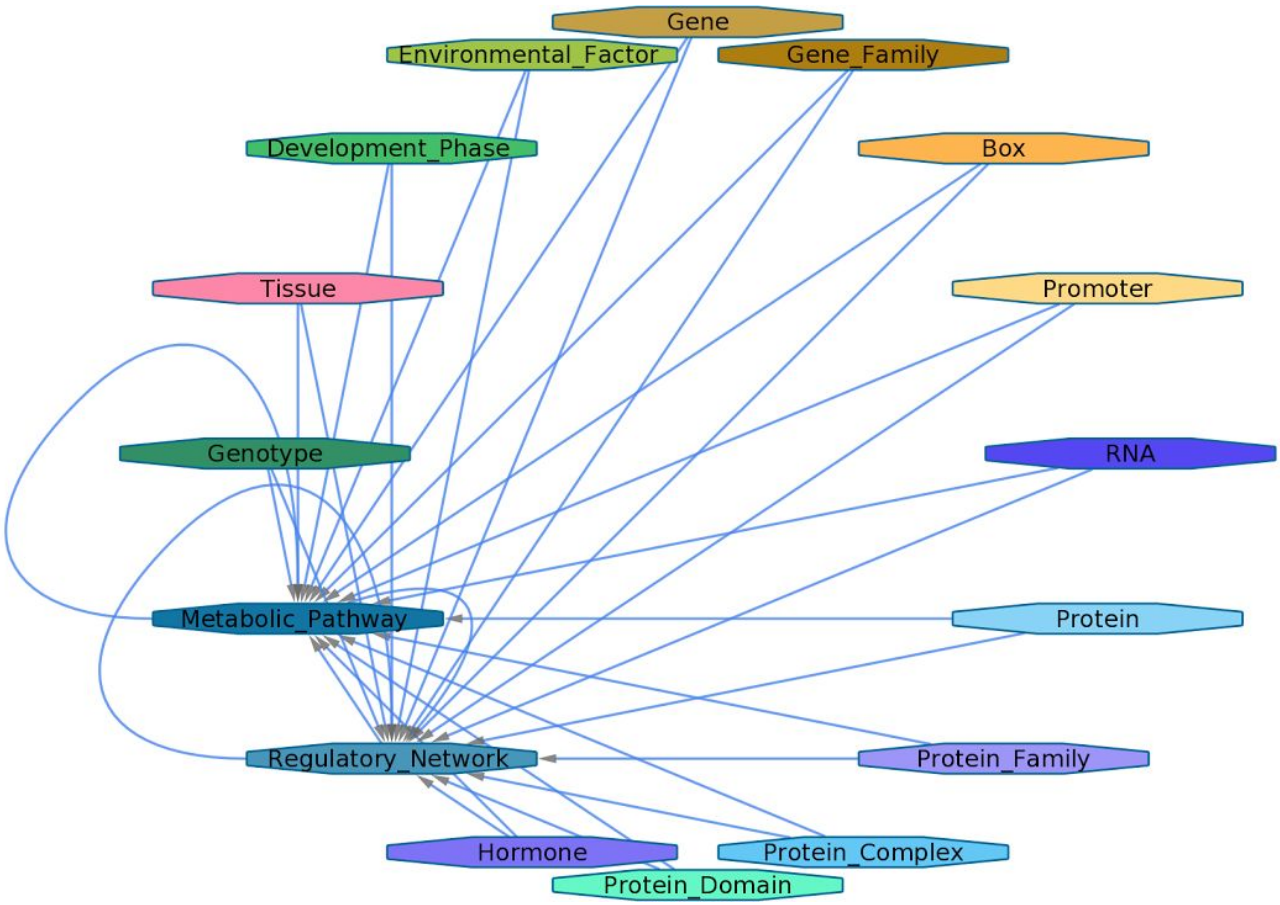
B.3.11 Regulation_Of_Expression



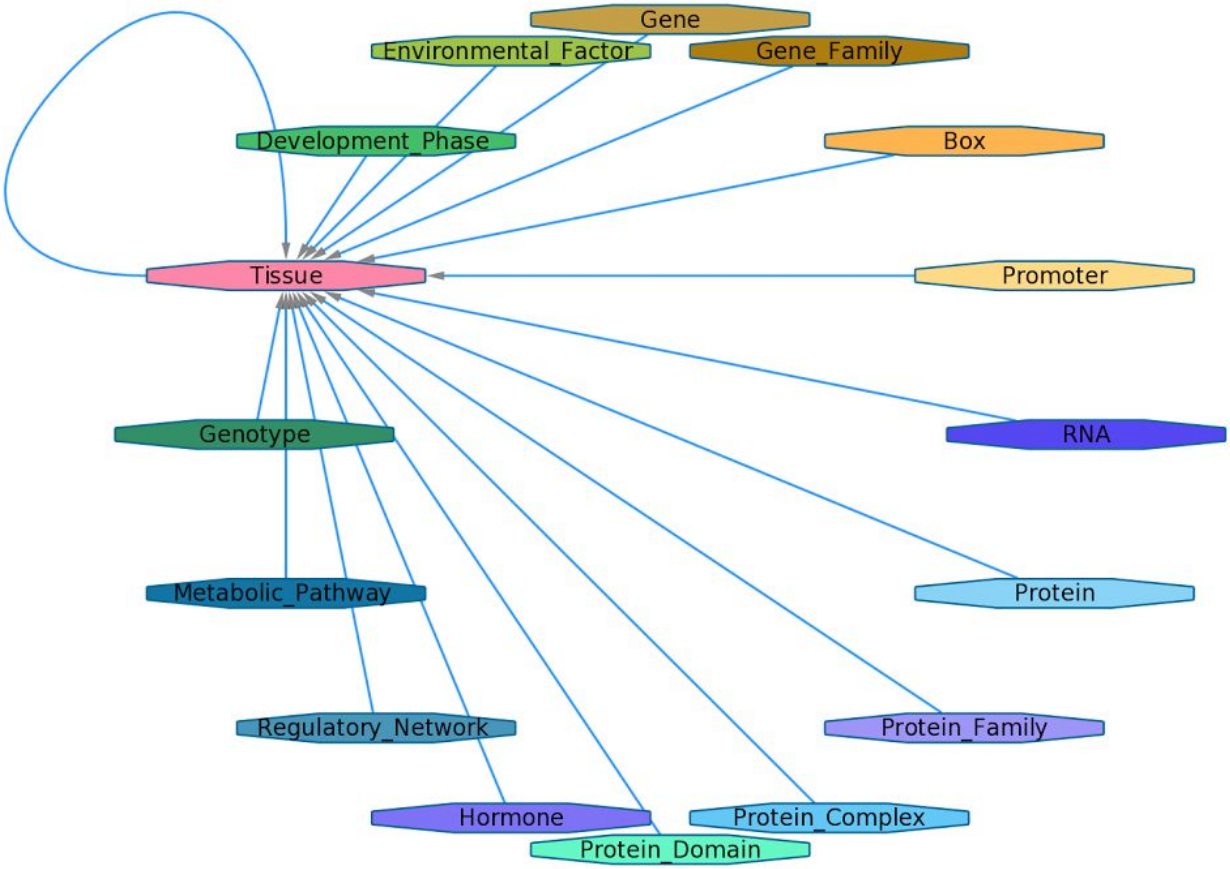
B.3.12Regulation_Of_Molecule_Activity



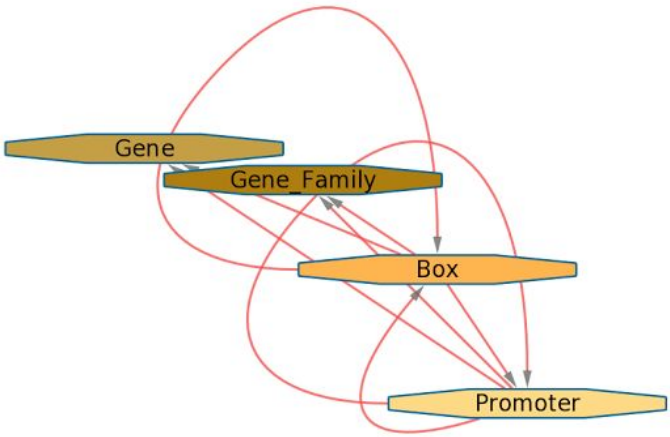
B.3.13Regulation_Of_Process



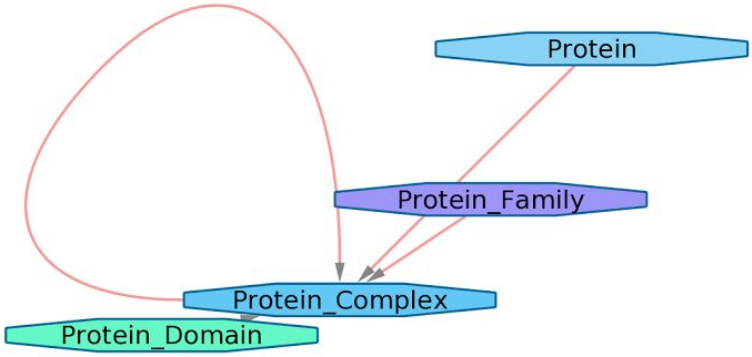
B.3.14Regulation_Of_Tissue_Development



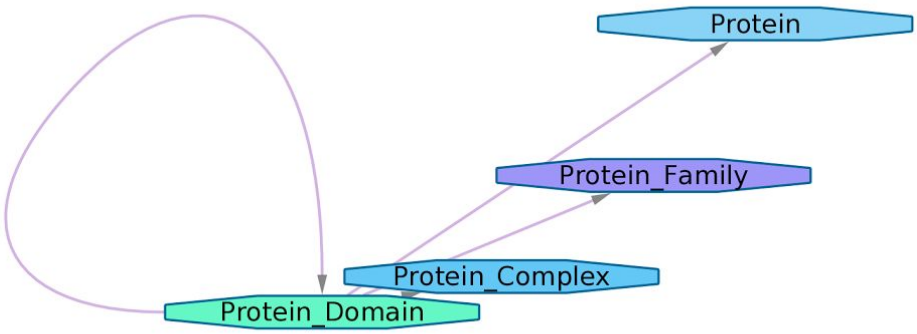
B.3.15Primary_Structure_Composition



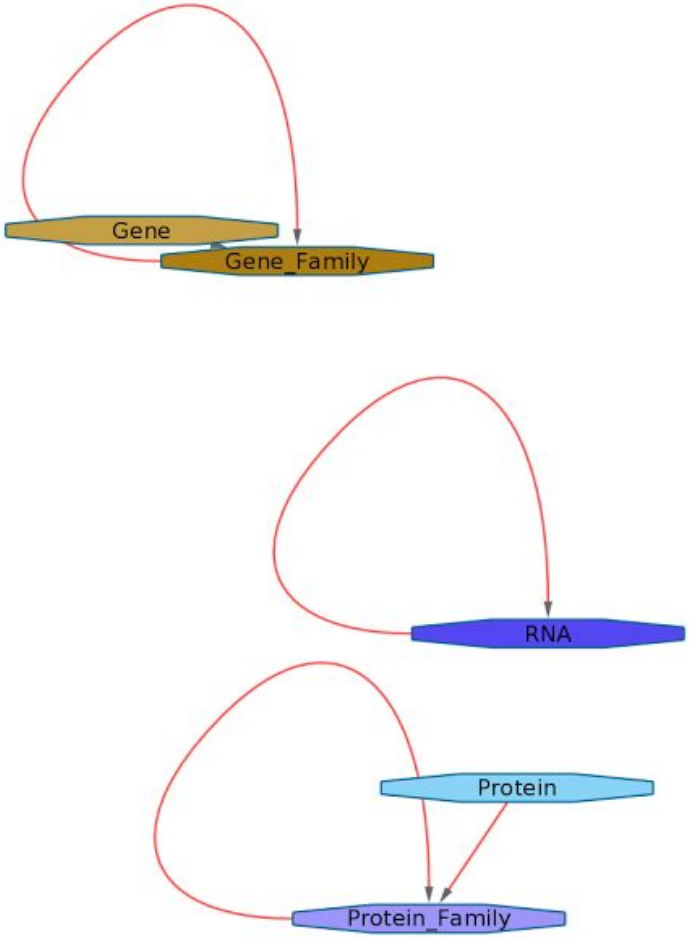
B.3.16Protein_Complex_Composition



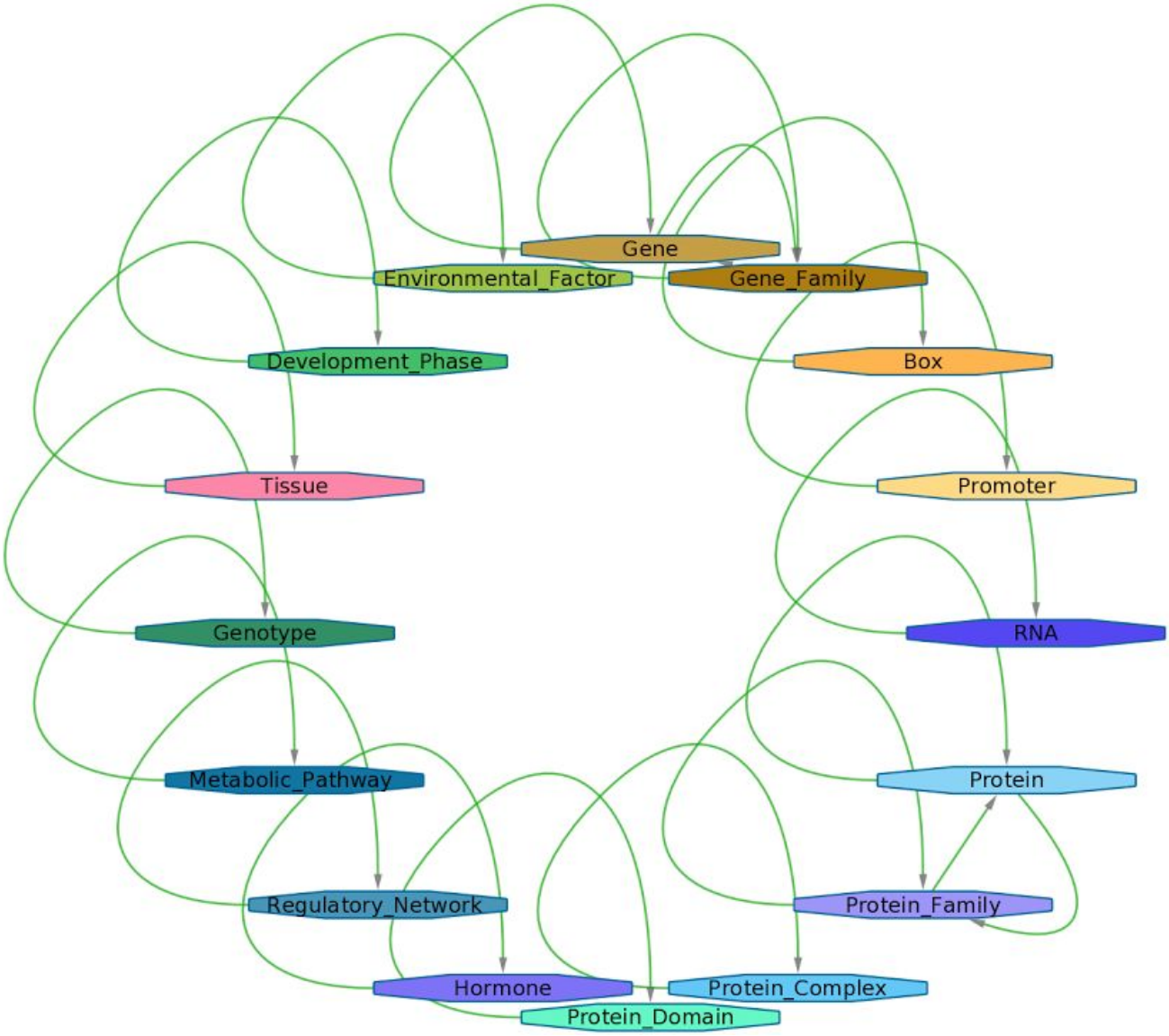
B.3.17Protein_Domain_Composition



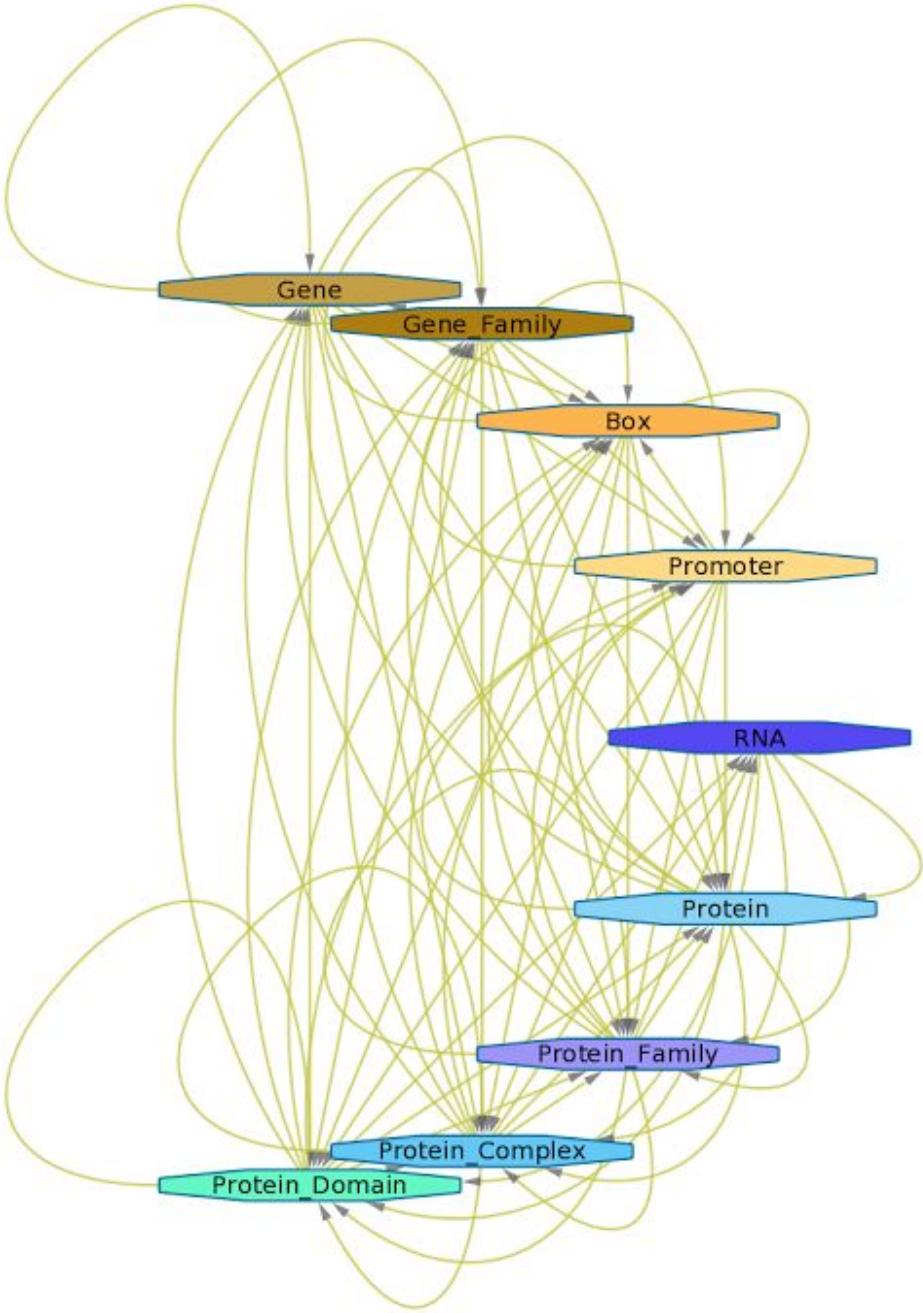
B.3.18Family_Membership



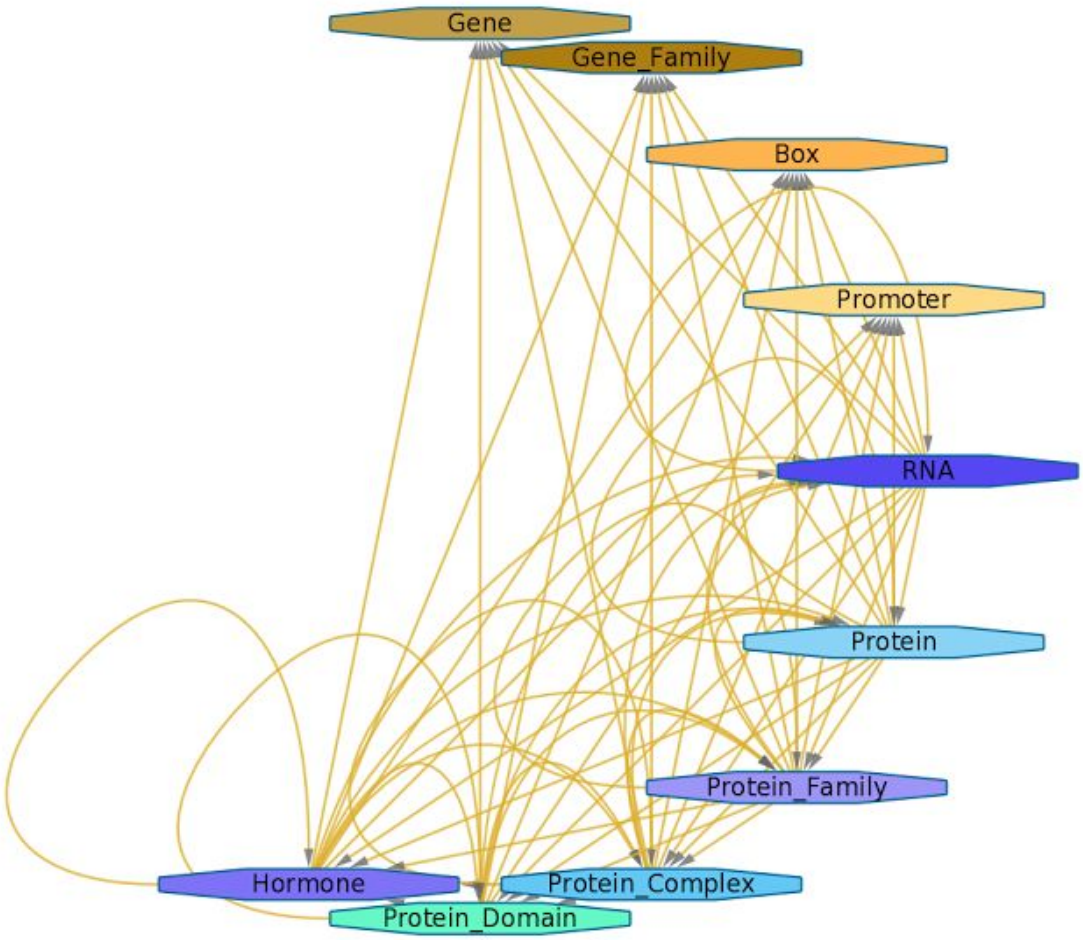
B.3.19Sequence_Identity



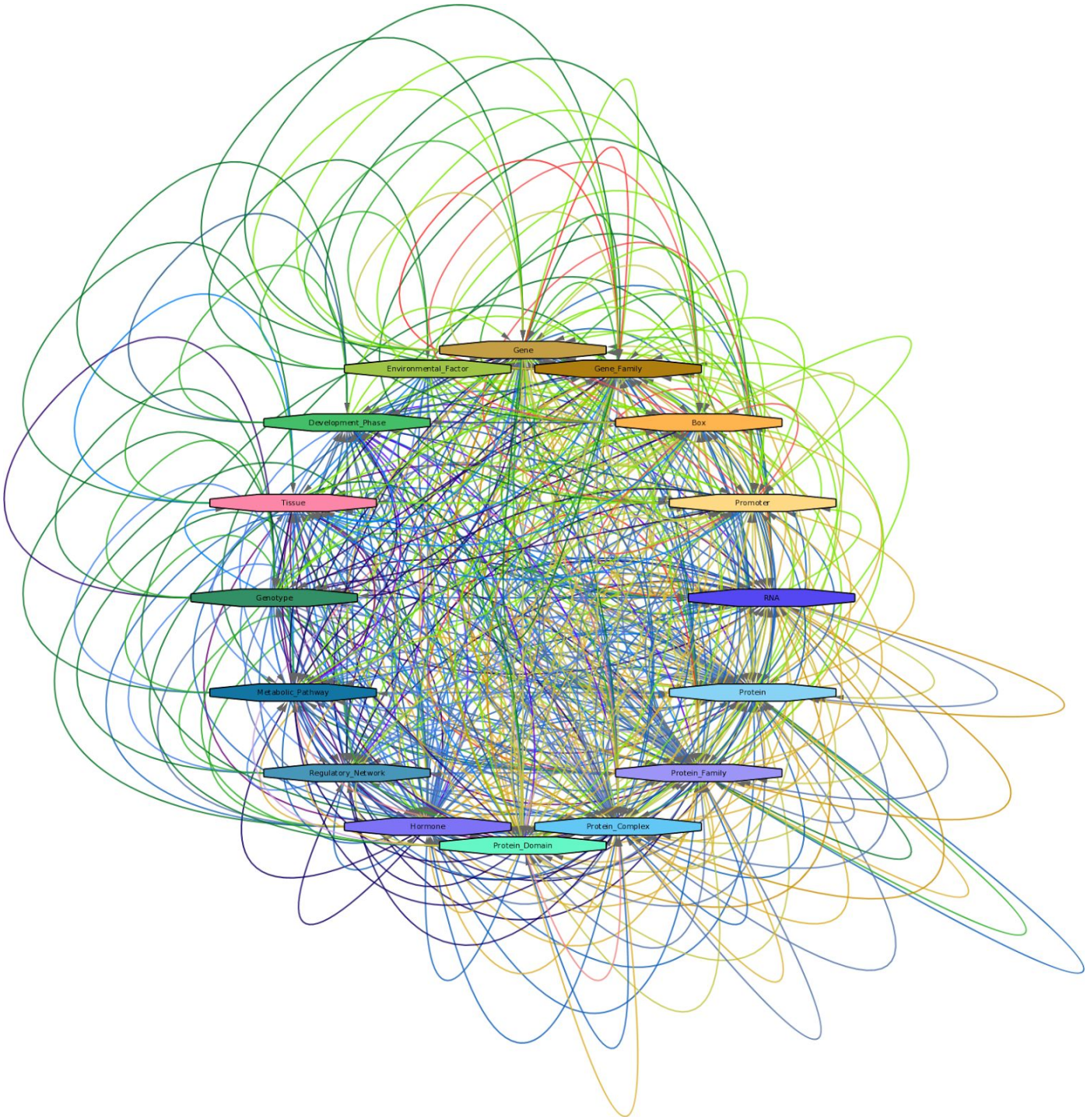
B.3.20Interaction



B.3.21 Binding



B.3.22 Visualization of all relations



Acknowledgement

This work is supported by the French National Institute for Agricultural Research (Inra), the Center for Data Science (CDS) and the Institute for Living Systems (IMSV), funded by the IDEX Paris-Saclay, ANR-11-IDEX-0003-02.