EXISTING STRUCTURE

- 'signaling pathway' & 'signaling process' are siblings
- 'signaling pathway' and 'signal transduction' aren't connected
No generic ‘pathway’ term, but all the instances of the pathways are under signal transduction.

(all pathway terms will be given the synonym ‘x signal transduction pathway’)

Ligands are part of a signaling pathway, and can be annotated to ‘signal transduction’.

The first step in a pathway would be ligand-receptor binding (or in case of light receptors, light being received by the receptor).

A pathway would end with regulation of a process.
SIGNALING

1. Ligand synthesis

2. Ligand secretion

3. Ligand processing/maturation

4. Ligand transport between cells

5. L-R binding (start of signal transduction/signaling pathway)

6. Signal transduction (starts with L-R binding. Ends with regulation of a downstream process). Signaling pathways are instances of signal transduction, where one or more component is known.

Gene expression

protein synthesis

protein synthesis

glycogen synthesis

MAPK cascade

Negative regulation of signal transduction

PTP1B

IRS1

GRB

SHC

mTOR

GSK3 inactive

AKT

PDK1

PI3K

PIP2

PIP3

Insulin Receptor

Regulation of signal transduction

Cellular process
SUMMARY OF CHANGES

NEW TERMS:

multi-organism signaling ; GO:NEW
The transfer of information between living organisms.
synonym: signaling with other organism
synonym: signaling between organisms
synonym: multi-organism signalling
GOC:go_curators
is_a: multi-organism process ; GO:0051704
is_a: signaling ; GO:0023052
NB: This term is intended to replace the obsoleted term ‘signal transmission via air ; GO:0023070’.

multicellular organismal signaling ; GO:NEW
The transfer of information occurring at the level of a multicellular organism.
GOC:go_curators
is_a: multicellular organismal process ; GO:0032501
is_a: signaling ; GO:0023052
part_of child: endocrine signaling ; GO:NEW
is_a child: transmission of nerve impulse ; GO:0019226

endocrine signaling ; GO:NEW
Signaling between cells where the a cell producing an endocrine hormone acts on a distant receiving cell. The endocrine hormone is transported via the circulatory system (via blood, lymph or intercellular fluid) so that remote regions of an organism can be reached.
is_a: cell-cell signaling ; GO:0007267
part_of: endocrine process ; GO:50886
part_of: multicellular organismal signaling ; GO:NEW
part_of child: endocrine hormone secretion ; GO:0060986
ISBN:3527303782
ISBN:0199264678
NB: This term is intended to replace the obsoleted ‘signal transmission via vascular system ; GO:0023066’ terms, and its children.

Q: Can this be used for plants? (ISBN:0199264678 suggests it can)
Q: Do we want a split between endocrine/paracrine/autocrine signaling in GO?
paracrine signaling; GO:NEW
The transfer of information between cells where the signal producing cell is in the vicinity of the receiving cell, and the signal reaches the receiving cell by passive diffusion.
ISBN:3527303782
is_a: cell-cell signaling; GO:0007267
NB: This term is intended to replace the obsoleted term ‘signal transmission via diffusible molecule ; GO:0023017’.
NB: Will remove 'paracrine signaling' as synonym of 'cell-cell signaling ; GO:0007267.'

signal maturation; GO:NEW
Any process leading to the attainment of the full functional capacity of a signal. A signal is a physical entity or change in state that is used to transfer information to trigger a response.
Related synonym: ligand maturation
part_of: generation of a signal involved in cell-cell signaling ; GO:0003001
Is_a: cellular process ; GO:0009987
is_a child: epidermal growth factor ligand processing ; GO:0007174
is_a child: patched ligand maturation ; GO:0007225
OBSELOTIONS:

signal transmission ; GO:0023060 (0 direct annotations)
Comment: This term was made obsolete because it was an unnecessary grouping term.
consider: signaling ; GO:0023052

signal transmission via air ; GO:0023070 (0 annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: multi-organism signaling ; GO:NEW

signal transmission via diffusible molecule ; GO:0023017 (0 direct annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: paracrine signaling ; GO:NEW

signaling via chemical mediator ; GO:0023044 (0 direct annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: signaling ; GO:0023052
consider: signal transduction ; GO:0007165
(NB: although ‘chemical’ isn’t well defined in GO at the moment- GOCHE will fix this).

signaling via ionic flux ; GO:0023040 (0 direct annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: signaling ; GO:0023052
consider: signal transduction ; GO:0007165

signaling via lipid mediator ; GO:0023043 (0 direct annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: signaling ; GO:0023052
consider: phosphoinositide 3-kinase cascade ; GO:0014065

signaling via protein/peptide mediator ; GO:0023042 (0 annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: signaling ; GO:0023052
consider: signal transduction ; GO:0007165
NB: Obsoleted because most signaling molecules are proteins or peptides.

T cell activation of signal transmission via diffusible molecule ; GO:0023018 (0 annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: signaling ; GO:0023052
consider: signal transduction ; GO:0007165
consider: paracrine signaling ; GO:NEW

The signal transmission terms are up for obsoletion because they are ambiguous. They cover everything from signal release through to the end of signal transduction in the receiving cell.

From the existing terms, it’s unclear whether the ligand can be annotated, and whether the ‘mediators’ are ligands or downstream signaling molecules.

If you know what step a gene product is involved in, you can use a more specific term. If not, you can use the top level ‘signaling’ term.

The new ‘endocrine signaling’ and ‘paracrine signaling’ terms were created to replace some of the transmission terms.
OBSOLETIONS (CONT):

signal transmission via transcytosis ; GO:0023062
trancytosis involved in signal transduction ; GO:0023062
The directed movement of endocytosed material through the cell and its exocytosis from the plasma membrane at the opposite side, that contributes to signal transduction.
consider: transcytosis ; GO:0045056
NB: The current term isn’t connected to ‘transcytosis ; GO:0045056’.

signal transmission via vascular system ; GO:0023066 (0 annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: endocrine signaling ; GO:NEW
consider: vascular transport ; GO:0010232

signal transmission via blood ; GO:0023065 (0 annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: endocrine signaling ; GO:NEW
consider: vascular transport ; GO:0010232

signal transmission via lymphatic system ; GO:0023067 (0 annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: endocrine signaling ; GO:NEW
consider: vascular transport ; GO:0010232

signal transmission via phloem ; GO:0023068 (0 annotations)
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: endocrine signaling ; GO:NEW
consider: phloem transport ; GO:0010233

signal transmission via xylem ; GO:0023069
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: endocrine signaling ; GO:NEW
consider: vascular transport ; GO:0010232

consequence of signal transmission ; GO:0023050
Comment: This term was made obsolete because the term is no longer needed.
NB: With the x signaling pathway terms involved in x, and regulation of y by ‘x signaling pathway’ terms, the consequence terms are not required (and don’t make ontological sense).

signal initiation by chemical mediator ; GO:0023047
Comment: This term was made obsolete because the meaning of the term is ambiguous.
consider: initiation of signal transduction ; GO:0023036
MERGES:
MERGED behavioral signaling ; GO:0023032
into:
behavioral interaction between organisms ; GO:0051705
[and removed the signaling parent]
MERGED signaling pathway ; GO:0023033
into:
signal transduction ; GO:0007165
MERGED regulation of signaling pathway ; GO:0035466
into:
regulation of signal transduction ; GO:0009966
MERGED negative regulation of signaling pathway ; GO:0035467
into:
negative regulation of signal transduction ; GO:0009968
MERGED positive regulation of signaling pathway ; GO:0035468
into:
positive regulation of signal transduction ; GO:0009967
MERGED signaling process ; GO:0023046
into:
signaling ; GO:0023052
MERGED intracellular signaling pathway ; GO:0023034
Into:
intracellular signal transduction ; GO:0035556
New synonym: secondary signal transduction
Moved the following children of GO:0023034 to be direct children of ‘signal transduction ; GO:0007165’
GO:0010019 : chloroplast-nucleus signaling pathway
GO:0006984 : ER-nucleus signaling pathway
GO:0030522 : intracellular receptor mediated signaling pathway
GO:0031930 : mitochondria-nucleus signaling pathway
MOVED:

MOVED: transmission of nerve impulse ; GO:0019226
WAS: child of signal transmission ; GO:0023060
NOW: child of multicellular organismal signaling ; GO:NEW

MOVED: two-component signal transduction system (phosphorelay) ; GO:0000160
WAS: is_a child of signal transmission ; GO:0000160
NOW: is_a child of signal transduction ; GO:0000160

MOVED: patched ligand maturation ; GO:0007225
WAS: part_of smoothened signaling pathway ; GO:0007224
NOW: part_of regulation of smoothened signaling pathway ; GO:0045880
NOW: is_a child of ‘signal maturation ; GO:NEW’
NB: moved under ‘regulation of signaling pathway’ because the signaling pathway begins with receptor-ligand binding, and this step is upstream.

MOVED: termination of signal transduction ; GO:0023021 (0 annotations)
WAS: is_a signaling process
NOW: is_a negative regulation of signal transduction ; GO:0009968

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RENAMED:  
(keeping old names as synonyms)

RENAMED: regulation of signaling process ; GO:0023051  
TO: regulation of signaling ; GO:0023051

RENAMED: negative regulation of signaling process ; GO:0023057  
TO: negative regulation of signaling ; GO:0023057

RENAMED: positive regulation of signaling process ; GO:0023056  
TO: positive regulation of signaling ; GO:0023056

RENAMED: signal transmission via phosphorylation event ; GO:0023014  
TO: signal transduction via phosphorylation event ; GO:0023014  
[and rehoused under signal transduction]

RENAMED: regulation of gene expression as a consequence of signal transmission ; GO:0023019  
TO: signal transduction involved in regulation of gene expression ; GO:0023019  
WAS: is_a regulation of gene expression ; GO:0010468  
NOW: part_of regulation of gene expression ; GO:0010468  
[and rehoused under signal transduction]

RENAMED: signal transmission via conformational change ; GO:0023045  
TO: signal transduction via conformational transition ; GO:0023045  
REDEFINED FROM: The process whereby a signal is conveyed via a conformational transition  
TO: The process whereby a signal is passed on within a cell by triggering a conformational change in the molecule that is receiving the signal.  
[and rehoused under signal transduction]
**signal transduction ; GO:0007165**

**FROM:**
The process whereby a signal is converted into a form where it can ultimately trigger a change in the state or activity of a cell. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response.

**TO:**
The process whereby a signal is passed across a cell to trigger a change in the activity or state of a cell. Signal transduction begins with reception of a signal and ends with regulation of a downstream process. Signal transduction covers signaling from receptors located on the surface of the cell, and signaling via molecules located within the cell. For signaling between cells, signal transduction is restricted to events at and within the receiving cell.

Comment: signal transduction is defined broadly to include all events from a ligand interacting with a receptor, to a response being triggered. A change in form of the signal in every step is not necessary.

**signal transducer activity ; GO:0004871**

**FROM:**
Converts a signal into a form where it can be further conveyed, or can trigger a change in the state or activity of a cell. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response.

Comments: Ligands do NOT have the molecular function 'signal transducer activity'.

**TO:**
Conveys a signal across a cell to trigger a change in cell function or state. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response.

Comments: Ligands do not have the molecular function 'signal transducer activity'.
PROPOSAL FOR ‘INVOLVED IN’ SIGNALING TERMS

• signaling pathways end with regulation of a downstream process (but do not include the downstream process itself).

To make this clearer in the ontology, we propose changing:

• X signaling pathway involved in y process
  TO:
• X signaling pathway involved in REGULATION OF y process

• Where ‘regulation of y process’ terms already exist, I will move the signaling term.
• Where ‘regulation of y process’ term does NOT exist, I will create one, then move the signaling term.

E.g.
• BMP signaling pathway involved in forebrain neuron fate commitment
• Wnt receptor signaling pathway involved in somitogenesis
• transforming growth factor beta receptor signaling pathway involved in determination of left/right asymmetry

TO:
• BMP signaling pathway involved in regulation of forebrain neuron fate commitment
• Wnt receptor signaling pathway involved in regulation of somitogenesis
• transforming growth factor beta receptor signaling pathway involved in regulation of determination of left/right asymmetry
Q: Any terms that shouldn’t get a ‘regulation’ child?

TIMING:

I’d like to do the commits this week (w/c January 10th) and next week (w/c January 17th) so they’re in place for the signaling workshop mid-February.
regulation of regulation....

It would mean ‘regulation of x signaling pathway involved in regulation of y process for some terms......
OUTSTANDING QUESTIONS AT THIS STAGE

1. Does it make sense to have the endocrine/paracrine/autocrine split?
   • The autocrine term already exists: autocrine signaling; GO:0035425
   • The endocrine and paracrine terms were created to replace the ‘signal transmission’ terms that are up for obsoletion.

2. Can endocrine signaling be used in plants?
   • ISBN:0199264678 suggests it can, but we’re keen to hear from curators.