Jmol SMILES Aromaticity Algorithm -- Bob Hanson, hansonr@stolaf.edu 3/21/16

Four aromaticity models are distinguished here. The context can be 3D (involving one or more loaded molecular models) or only in terms of connectivity (when comparing one SMILES string to another). The default model for Jmol is **Jmol3D**, but additional /strict/, /open/, or /openStrict/ directives can be given to change that.

1. **Jmol3D** A ring is aromatic if it has 5-7 atoms, is planar, and has no more than one substituent, which must also be in the plane (if associated with a 3D representation).
2. **OpenSmiles** Satisfying a finite set of element/bonding/valence/charge options for the contribution of 0, 1, or 2 electrons to the ring and resulting in satisfaction of the Hueckel 4n+2 rule, regardless of bridging and allowing for exocyclic a=X bonds.
3. **Strict** A ring having a chemist's standard interpretation of the Hueckel 4n+2 rule (cyclic pi system without pi bonds to non-cycle atoms; fused but not bridged). (This excludes cyclic lactones, for instance.) Both Jmol3D and OpenSmiles can be made STRICT.
4. **MMFF94** A strictly aromatic Jmol3D ring which, in addition, is also either (a) a 5-membered ring or (b) a 6-membered that has only 1-electron atom contributions. (This excludes lone-pair-contributing hetero atoms and most charged atoms.)

An outline of Jmol's aromaticity algorithm follows. They are found in *org.jmol.smiles.SmilesSearch.java* and *org.jmol.smiles.SmilesAromatic.java*.

1. Identify rings of interest involving 5-7 atoms. *SmilesSearch.getRingData, SmilesSearch.subsearch*
2. Iterating over all such rings, identify potentially aromatic rings. *SmilesSeach.getRingData, SmilesAromatic.setAromatic, SmilesAromatic.isSp2Ring, SmilesAromatic.checkHuekelAromatic, SmilesRing*
    a. All atoms must be connected to only 2 or 3 other atoms.
    b. Planar geometry if Jmol3D (within specifications given elsewhere)
    c. Appropriate atom set, including element/valence/bond/charge considerations. Jmol assigns each ring a characteristic value -1 (cannot be aromatic), 1 (4n+2), or 0 (not 4n+2). Jmol also assigns atomic electron contributions at this time, adds atoms to a bitset of potentially aromatic atoms, and associates a set of bonds with each ring.
3. Generate ring sets. A ring set is defined as a group of rings that (a) for STRICT guidelines are fused (one bond in common between two rings) but otherwise may be bridged (more than one bond in common between two rings; definitely not 3D) rings, and (b) that, overall, obeys the 4n+2 rule. *SmilesAromatic.finalizeAromatic, SmilesAromatic.removeBridgingRings, SmilesAromatic.checkFusedRings, SmilesRingSet*
    a. Remove all bridged rings if STRICT. (Bridged rings cannot be planar and so cannot satisfy Hueckel 4n+2 rule.)
    b. Fuse rings into sets.
        i. Iterate over all edges in all potentially aromatic rings.
        ii. If no ring set is associated with any edge of a ring, start a new ring set.
        iii. If a ring set is associated with a ring's edge, either:
            1. Add this ring to that set if it is not already in a ring set.
            2. Add all rings in a ring's set to the matching set if the ring is already in a set.
        iv. If the ring set satisfies 4n+2, mark all its component rings and atoms as definitely aromatic (1).
4. Exclude rings by excluding any one of their component atoms. *SmilesAromatic.finalizeAromatic*
    a. Iterate over all aromatic atoms
        i. Check that the atom is not connected by a double bond to another aromatic ring but it itself is not in an aromatic ring.
        ii. If STRICT, check that no atom is doubly bonded to any nonaromatic atom.
        iii. Ensure that at least two atoms connected to this atom are aromatic.
        iv. If any one of these three conditions fails, mark the atom as not aromatic and restart iteration.