Key difference between type I and type II cryptochromes and implication for their role in magnetoreception

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All cryptochromes are currently classified as flavoproteins. In animals their best-described role is as components of the circadian clock. This circadian function is variable, and can be either light-dependent or -independent; the molecular origin of this difference is unknown. Type I (invertebrate) animal cryptochromes are photoreceptors that entrain an organism's clock to its environment, whereas Type II (mainly vertebrate, including mammals) regulate circadian timing in a light-independent manner. Here, we reveal that, in contrast to Type I, Type II animal cryptochromes lack the structural features to securely bind the photoactive flavin cofactor. We provide a molecular basis for the distinct circadian roles of different animal cryptochromes, which also has significant implications for the putative role of Type II cryptochromes in animal photomagnetoreception.