The growth-dependent sex determination hypothesis, unifying ESD and GSD and suggesting a scenario for the evolution of male and female heterogamety

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Vertebrates have various sex-determining mechanisms. These have been broadly classified as either genotypic sex determination (GSD), usually by sex chromosomes, or environmental sex determination (ESD), where an environmental variable, often temperature, determines the sex of the developing embryo. Their distribution among extant vertebrate taxa reveals that in some cases both ESD and GSD are present at phylogenetically shallow levels. For example, within the amphibian family Ranidae ESD occurs as well as male and female heterogamety (XX/XY and ZZ/ZW respectively). However, the apparent existence of mixtures of ESD and GSD in some fish and turtles challenges this traditional classification. I will present a model that attempts to unify vertebrate sex determination, proposing that sex determination in all vertebrates is mediated by differential growth of the embryo. According to this model, testis or ovary differentiation depends on whether the undifferentiated gonad has reached a threshold size at a critical moment in development. Growth rate, in turn, is a quantitative phenotypic trait caused by environmental influences (*e.g.* temperature) and genetic factors, with ESD at one end of the continuum and GSD at the other. When genes dominate, sex would be genetically determined, and when environmental influences dominate, sex determination would be environmental. Supporting this view are the finding that in mammals males-to-be show faster embryonal growth than females-to-be, and some evidence that the mammalian Y-chromosome carries growth enhancing allele(s). In birds, with female heterogamety, it is thought that female embryos grow faster and the W-chromosome may carry growth promoters. In species with ESD it is usually the case that growth rates differ according to the variable that also determines sex. This model can easily account for the mixtures of ESD and GSD. It explains so-called 'sex reversals', where the phenotypic sex of an individual does not correspond to its genotypic sex. This has been observed in some fish and turtles in the wild, and tentatively in a bird in a laboratory experiment. It seems that in these cases the influence of temperature may overrule the genetic sex status of the individual. The model also explains the finding that autosomal deletions resulting in slow growth can give rise to XY females in mice, hypothesising that these slow growing embryos did not reach the threshold in time. The model may even explain some as yet unexplained 'sex-reversed' cases in our own species, for example XY females with an intact SRY-gene but a deletion at the short arm of chromosome 9. Furthermore, the model serves as the framework for a hypothesis on the evolution of male and female heterogamety in different vertebrate taxa. Here a transition is proposed from adaptive ESD to GSD with sex chromosomes, in which genes take over the role of the environment in bringing about differential growth. Heterogamety may be caused by the linkage of several growth-promoting alleles on one of the chromosomes in a pair. This evolutionary scenario predicts that the sex that grows fastest and has a size advantage under ESD is predisposed to become the heterogametic sex in that phylogenetic lineage. I will discuss a simulation model that analyses this evolutionary scenario, and suggest how to test its predictions by investigating phylogenetic trees combined with information on sex determining mechanism and size dimorphism.