CHILDREN'S MEDICAL RESEARCH INSTITUTE

Human chromosomes and chromosomal abnormalities

Want to be a cytogeneticist for the day...

The study of chromosomes by microscopy is called **cytogenetics**. By staining chromosomes with Giemsa dye and looking at them with a light microscope, we can see the unique banding patterns of each chromosome (see page two). The dye stains chromosomes according to the predominant DNA bases in different regions. The dark bands, called G bands, are rich in adenine (A) and thymine (T); the light bands, R bands, contain less A and T.

An organised profile of a person's matching chromosomes is called a **karyotype**. Chromosomes are arranged and numbered by size, from largest to smallest based on banding patterns and the position of the centromere.
Karyotyping is one of many techniques that can detect chromosomal abnormalities, by looking at the number and structure of chromosomes.

The following pages can be used as a classroom cytogenetic activity by cutting out and sorting the chromosomes.

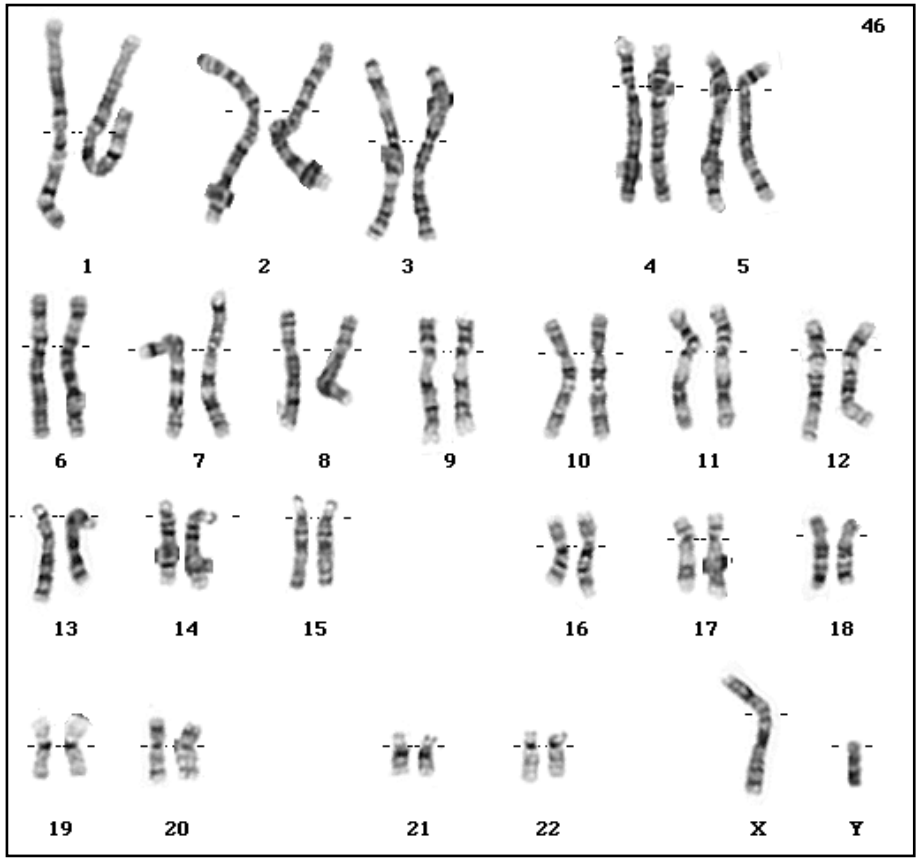
Using a pair of scissors, cut out the chromosomes, referring to the master karyotypes sort and match the chromosomes to produce karyotypes for each different page- male, female, male with Edward syndrome, female with Down syndrome, male with Klinefelter syndrome.

Other examples of chromosomal abnormalities and karyotypes can be found at http://www.pathology.washington.edu/Cytogallery/

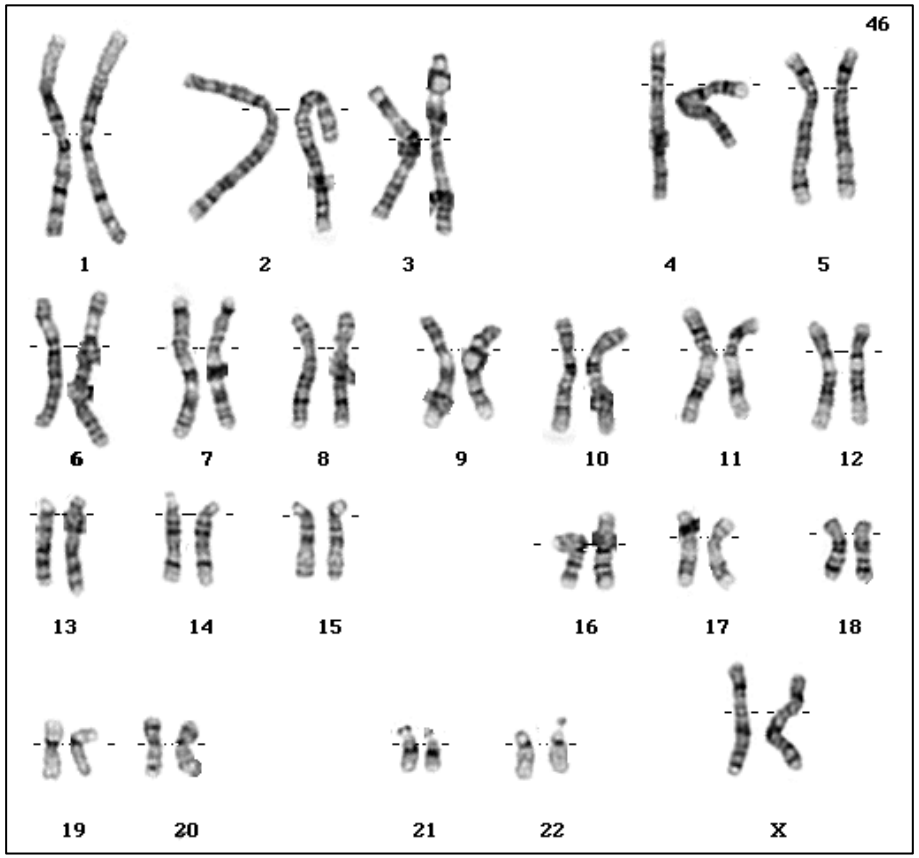
Human Karyotpyes

The images below are photographs of human karyotypes as seen down a microscope.

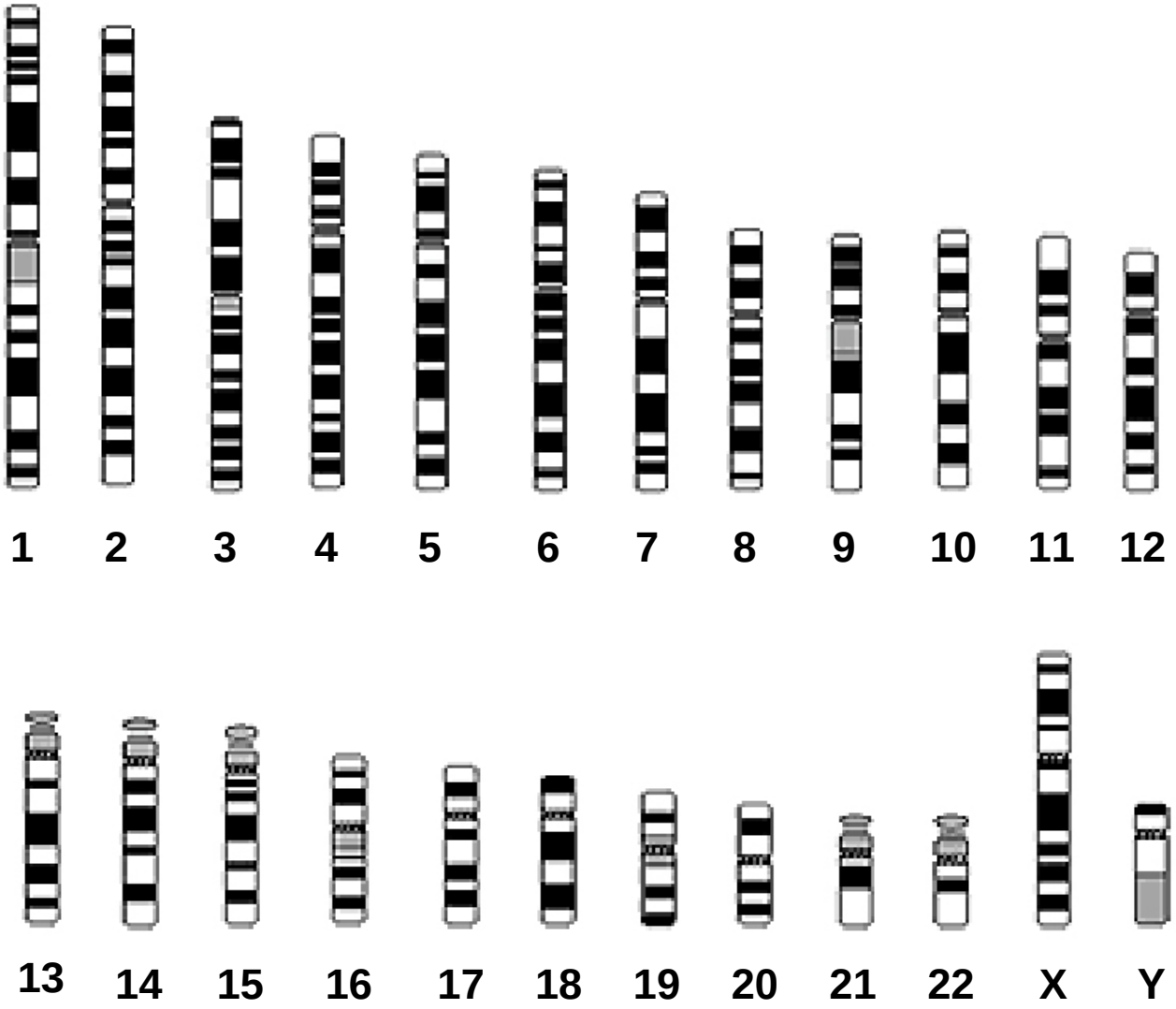
Male

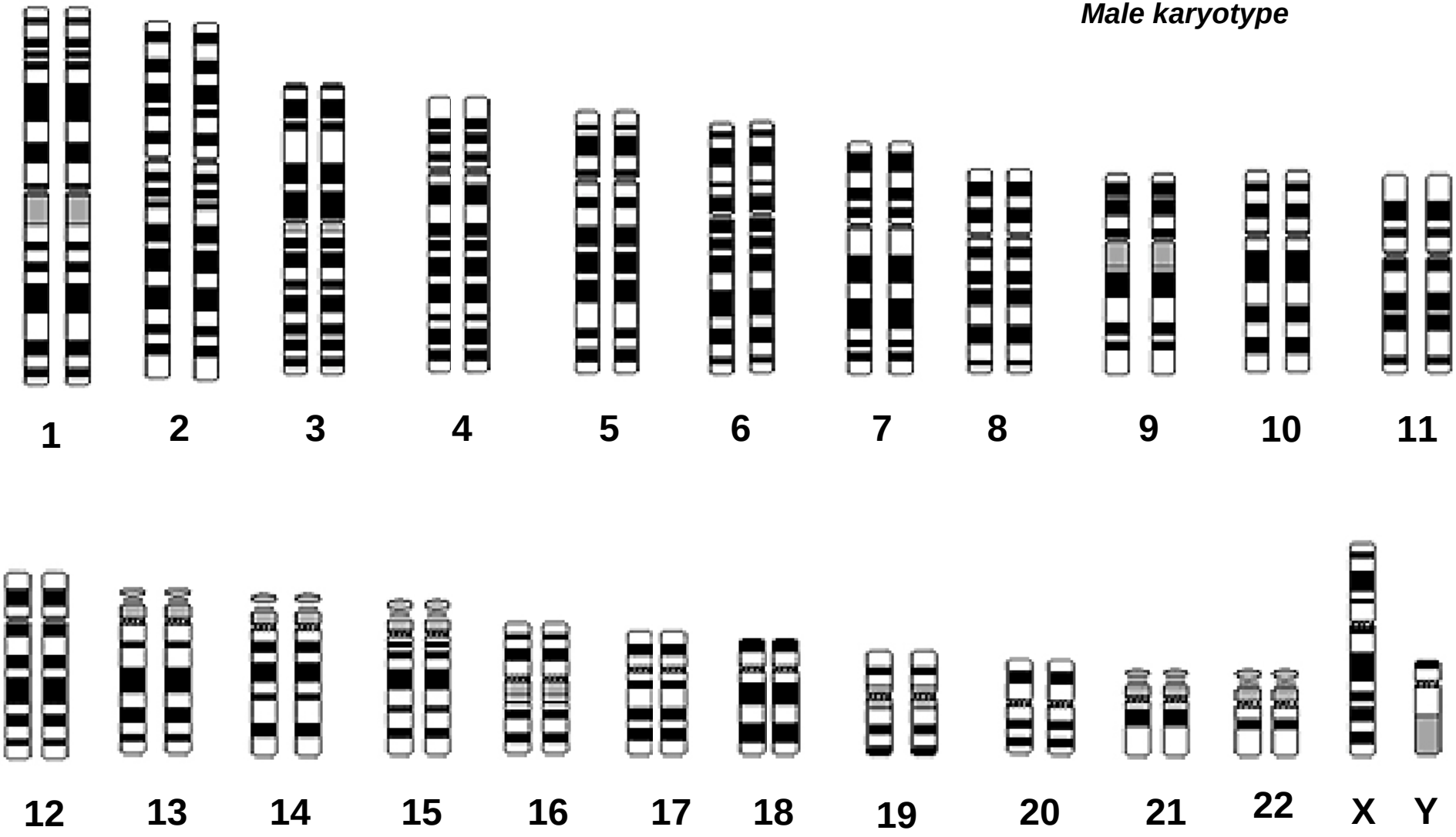


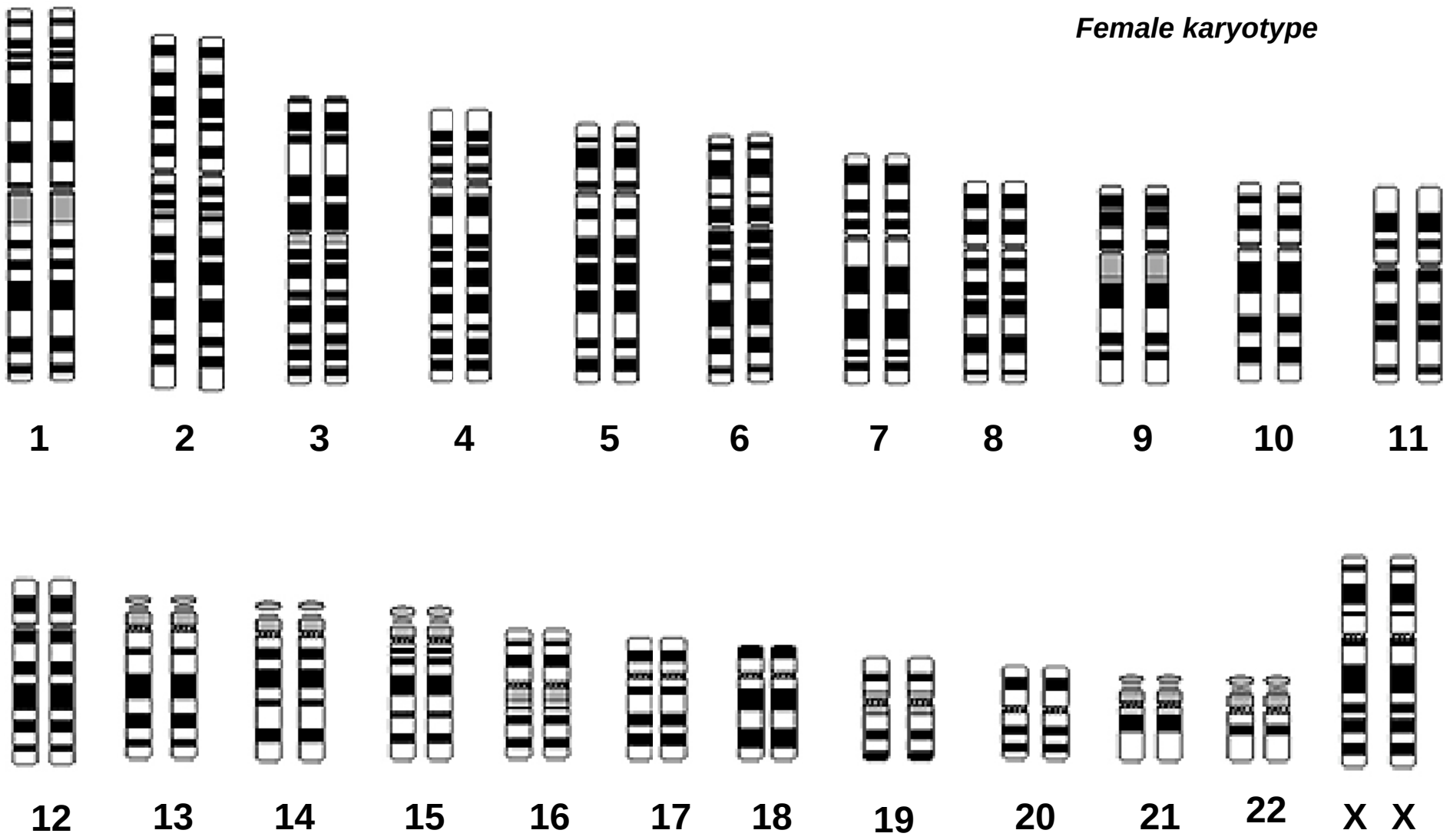
Female



Complete Human Chromosomes – Master copy




Male karyotype
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Y


Female karyotype
1
2
3
4
5
6
7
8
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10
11
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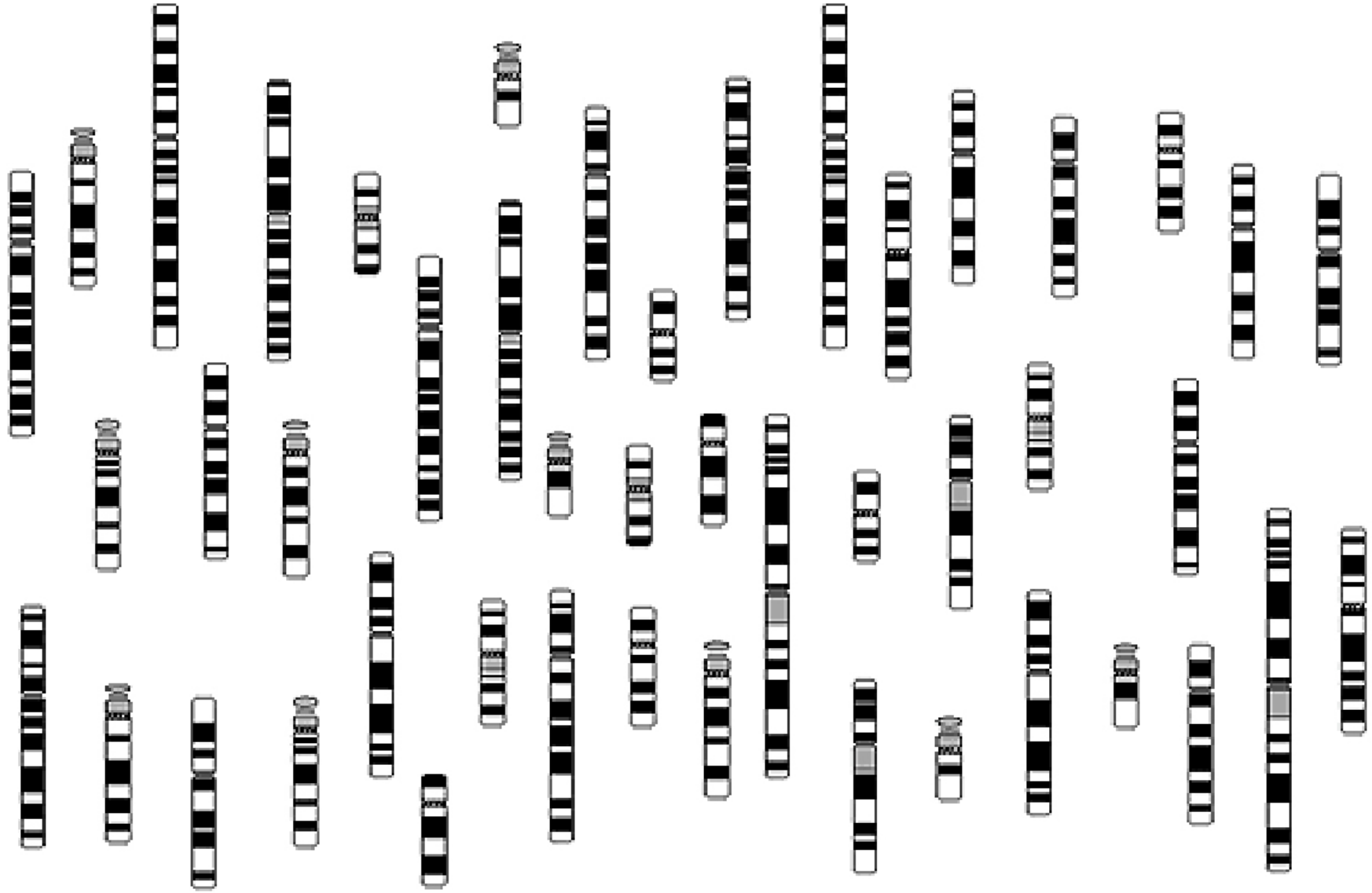
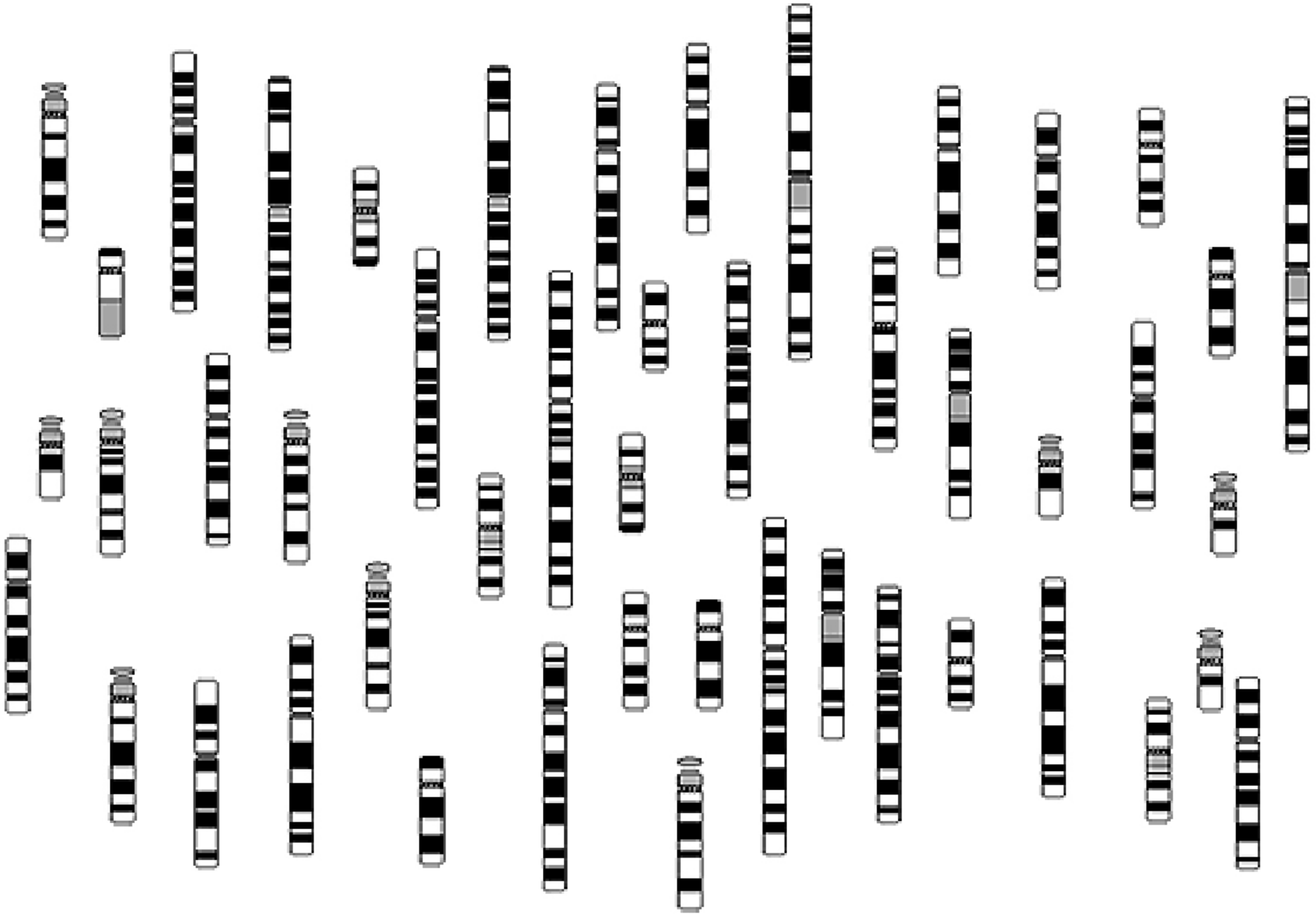
18
19
20
21
22
X
X

Female karyotype

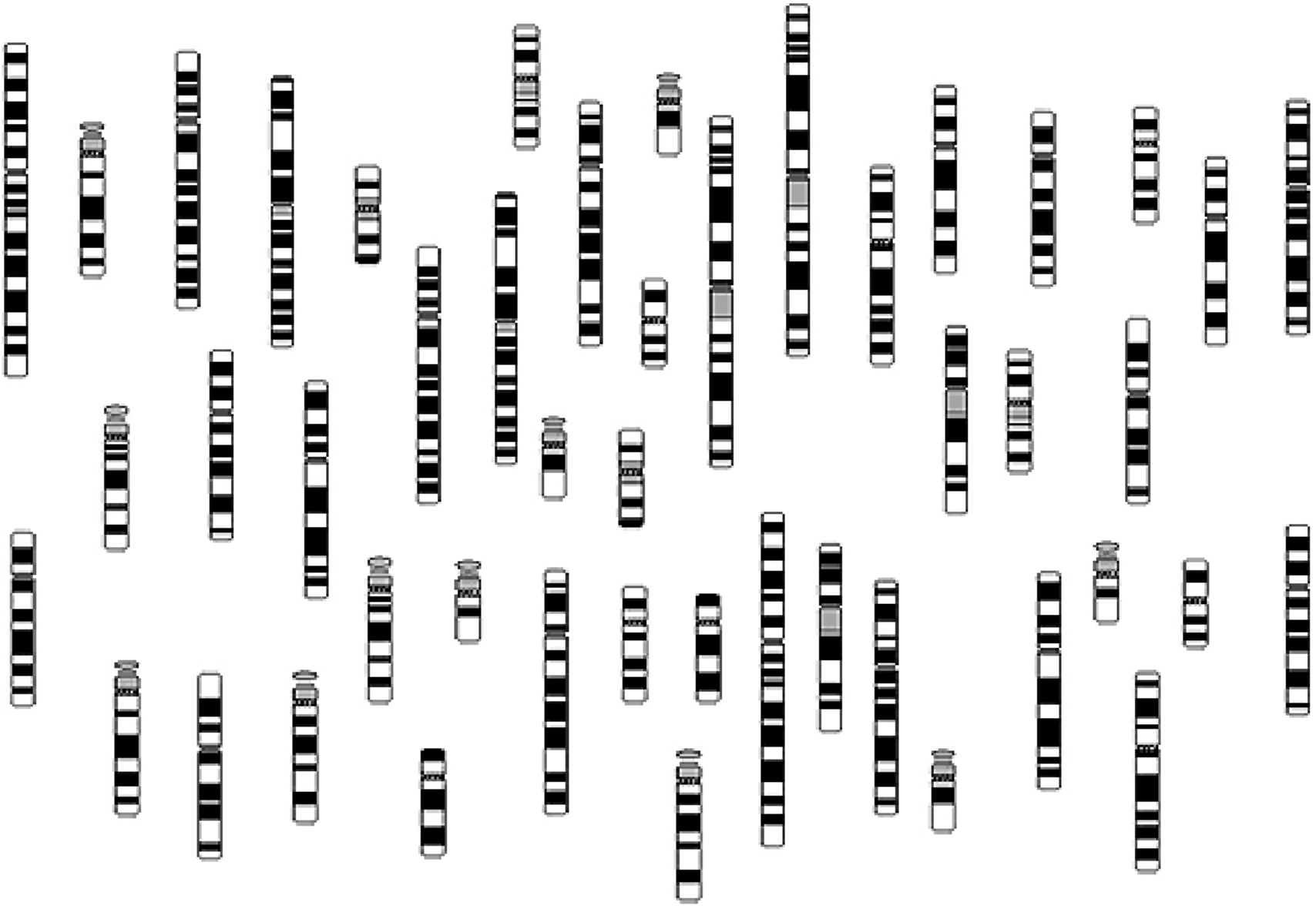


Male karyotype

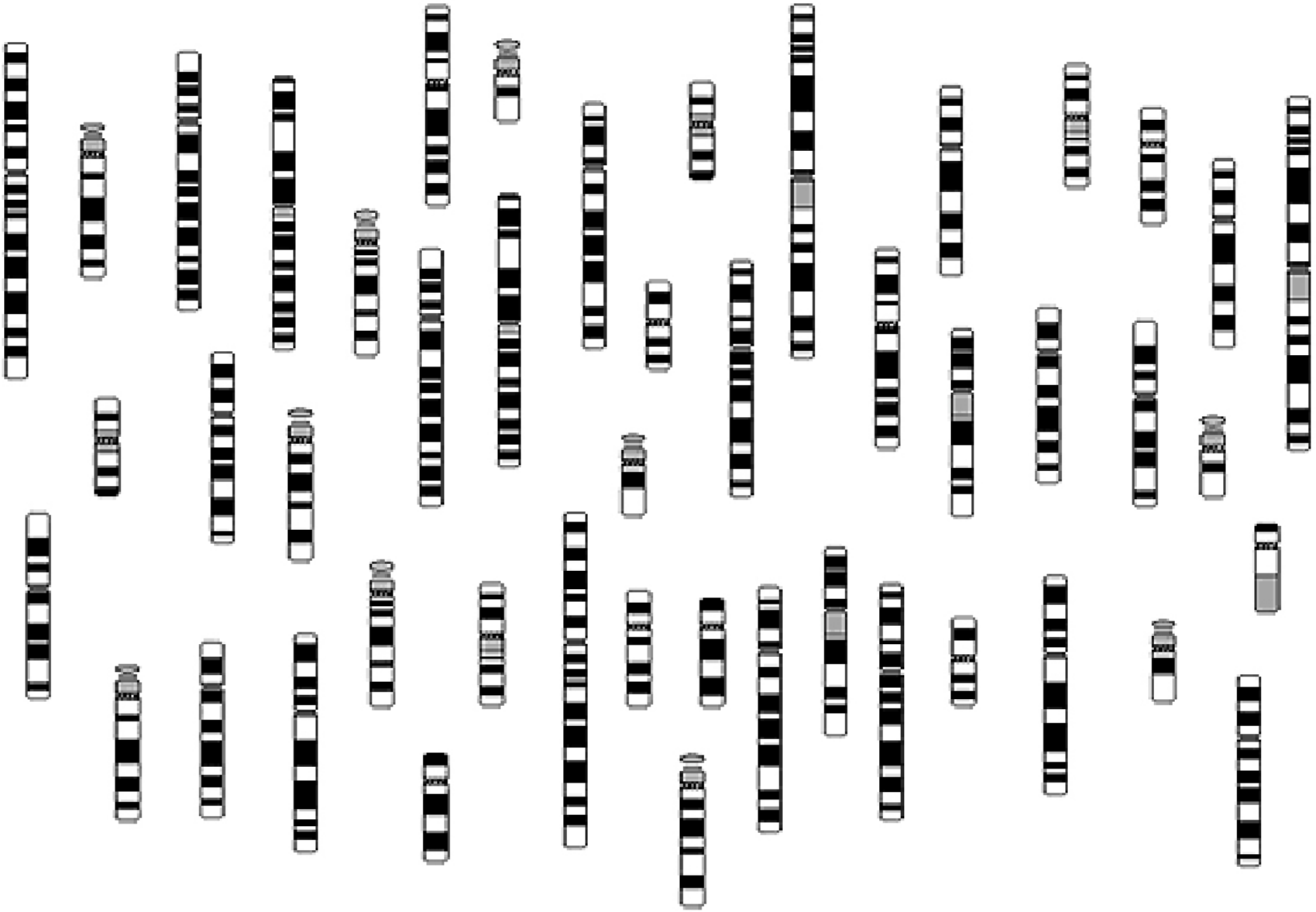
Karyotype – Male with Edward syndrome (Trisomy 18)



Karyotype – Female with Down syndrome (Trisomy 21)



Karyotype – Male with Klinefelter syndrome (XXY)



Edward syndrome

Incidence: 1:5000 live births, 1:50,000 stillbirths

A congenital disorder caused by an extra copy of chromosome 18 (trisomy - three copies instead of the normal two). Characteristics of the disorder include a number of malformed organs, including heart defects, and malformed features of the face and skeleton. In most cases, the child dies before it is born. 90% of babies born alive die within a year of birth.
Symptoms may be less severe when the trisomy occurs after fertilisation, i.e. non-disjunction occurs during mitosis in the zygote (10% of cases), resulting in **mosaicism** (some cells have a normal karyotype and others have the abnormality), rather than during meiosis to produce the egg or sperm (90% of cases).

Down Syndrome

Incidence: 1 in 660 births.

A congenital disorder in which a person is born with three copies of chromosome 21 (trisomy 21).
Clinical features include moderate to severe mental retardation, slanting eyes, a broad short skull, broad hands and short fingers. Other abnormalities include heart defects, oesophageal atresia (oesophagus not connected with the stomach) and an increased incidence of acute lymphocytic leukaemia.

Klinefelter syndrome

Incidence: 1 in 500 to 1 in 1000 newborn males.

Klinefelter only affects males and is caused by the presence of an extra X chromosome. Males normally have one X chromosome and one Y, but in Klinefelter the karyotype is XXY (or more rarely XXXY, XXXXY or sometimes XY/XXY **mosaic** (see section on Edward's syndrome)). The child appears normal at birth, but the syndrome usually becomes apparent during puberty when secondary sex characteristics fail to develop properly. They typically have high-pitched voices, asexual to feminine body contours as well as breast enlargement and relatively little facial and body hair. They are sterile or nearly so and their testes and prostate gland are small. As a result, they produce relatively small amounts of testosterone and high amounts of oestrogen. The feminising effects of this imbalance can be significantly reduced if Klinefelter syndrome boys are regularly given testosterone from the age of puberty on. They can have learning difficulties as children, especially with language and short-term memory. However, it is not unusual for Klinefelter syndrome adults with slight symptoms to be unaware that they have it until they are tested for infertility. Klinefelter syndrome males with more than two X chromosomes usually have more extreme symptoms and are often mentally retarded. Men who are mosaic (XY/XXY) generally have the least problems. They have a higher than average risk of developing osteoporosis, diabetes and other autoimmune disorders. This may be connected to low testosterone production.

The chromosomal abnormality can be detected in 0.003% of spontaneous miscarriages. It is associated with non-disjunction (failure of chromosomes to

separate) in paternal meiosis (53%), maternal meiosis I (34%) and maternal meiosis II (9%).

Detecting chromosomal abnormalities

Trisomies and other chromosomal abnormalities can be detected in the first few months of pregnancy by amniocentesis or chorionic villus sampling (CVS). These tests are carried out between the 12th – 18th weeks of pregnancy and involve collecting either placental tissue or cells from the amniotic fluid around the baby in order to karyotype the foetal cells. Karyotyping the foetal cells often makes it possible to determine the sex of the foetus and whether it is suffering from certain genetic diseases such as Down Syndrome. The presence of certain proteins can also be measured to reveal conditions such as spina bifida.