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Drosophila as a Powerful Modern Tool for Teaching Concepts in Biology and Biomedical Research

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Abstract: *Drosophila* is a potential teaching tool to help students in understanding core concepts in biology. Flies have gained significant importance as one of the forefront model organism for research in different areas of Biology and Biomedical sciences. It is easier to convey the outcome of contemporary research in Biology to the student community even among educational institutions with very modest laboratory infrastructure. The fruit fly *Drosophila melanogaster* has been used in biological research during the last century to study a broad range of biological processes i.e. genetics and inheritance, embryonic development, behavior and aging. Humans and flies look quite different, but fundamental biological mechanisms and pathways have been conserved during the evolutionary history. Flies and humans display similarities at the level of genes, cells, tissues and biological processes controlling health and disease. It is also one of the ideal model organisms for the study of neurodegenerative diseases. Our understanding and knowledge of regenerative biology and drug testing has been enhanced with the use of *Drosophila* mutants. These organisms offer excellent opportunities to design experiments and to seek reliable results in a short duration. As a model system, *Drosophila* is useful in understanding fundamentals of biology across various strata of educational institutions including schools, colleges and universities. Over the past several decades, developed nations in the west have adopted the fruit fly as a model teaching tool at the undergraduate Biology courses. However, many developing nations including India have yet to incorporate this model organism into their arsenal of teaching tools because work on fruit flies is affordable and cost effective. Through this article, we aim to inspire teachers and educators, the advantages of using this unassuming yet enigmatic study tool to improve scientific temper among the student community. Simple experiments on *Drosophila* flies can inspire students for inculcating scientific temper

Key words: *Drosophila* flies, model organism for Biology/Biomedical research, Cost effective and fast breeder

Introduction

During the last hundred years, seven scientists working on *Drosophila* have been awarded Nobel prize. The Nobel prizes given to scientists working with *Drosophila* include Thomas Hunt Morgan (1933; for the chromosomal theory of

inheritance). Hermann J Muller (1946; for X-ray induction of mutations); Ed Lewis, Christiane Nusslein-volhard and Eric Wieschaus (1995; for discovering genes that control body plan of *Drosophila*); Linda B Buck (2004, for explaining the

genetic basis of odorant receptors); and Jules Hoffmann (2011, for finding genetic basis of innate immunity). *Drosophila* has remained as the foremost model organism in several seminal studies and has enormously contributed to the advancement of research in Biology. As 75% of the human disease genes have homologues in the fly genome, *Drosophila* has emerged as a very useful model for biomedical research associated with human health and disease. Despite being a cost effective and affordable eukaryotic model system (with a life cycle of two weeks and life span of two months), its applications as a powerful modern tool in teaching fundamental concepts in biology at undergraduate level has not gained momentum in several third world countries. Our continued practice of teaching biology through preserved biological specimens and slides does not inspire the current generation of undergraduate students. It is increasingly evident that use of simple, living models (organisms) to demonstrate concepts of biology alone are able to inspire students towards understanding fundamental concepts. Such efforts can direct students towards learning the scientific method of research and thereby to develop scientific temper. We attempt to explain how use of *Drosophila* as a teaching/learning tool at undergraduate level can help in creating the curiosity for better understanding of biological concepts and mechanisms. Several institutions in India offer a large manpower of undergraduate and post-graduate students in Biosciences, but are often reluctant to adopt *Drosophila* as a model organism for

conduct of practicals in many areas of Biology as well as its application in frontier areas of research.

What *Drosophila* flies have taught us

The first use of *Drosophila melanogaster* by Thomas Hunt Morgan in the early decades of the twentieth century laid foundations for understanding chromosomal theory of inheritance, sex linkage, gene mapping and sex determination. Therefore, Mendelian inheritance was experimentally supported and advanced through the use of *Drosophila melanogaster*. During the last more than hundred years, advances in several disciplines of biology (cytogenetics, cell biology, developmental biology, neurobiology, molecular genetics and biomedical sciences) took place with the use of mutant strains of *Drosophila melanogaster*.

Drosophila is a model organism for teaching students the way to carryout hypothesis driven science and to understand its logical interpretation. *Drosophila* flies are fast breeding and can be a genetic workhorse to test ideas in a cost effective manner. Flies have taught us laws of inheritance and how genes are organized on chromosomes. *Drosophila* flies have helped us in finding genes responsible for information processing in nerve cells, in learning and knowing the genetic basis of biological 24h clock-circadian rhythm. In areas of health sciences, *Drosophila* flies have revealed the fundamental biology of stem cells and cancer; and genetic defects leading to brain disorders (Parkinson's and Alzheimer's diseases). These flies have shown the rules for gene pool dynamics in large

populations (population genetics) and how evolution works. They have also helped in understanding several key mechanisms of the immune system.

Drosophila as an ethically unproblematic tool

In some countries, both undergraduate and post-graduate students of zoology are no longer allowed to study anatomical details of diverse invertebrates (marine arthropods, mollusks, echinoderms, etc.) and vertebrate taxa (fishes, frogs, reptiles) due to legal constraints. Therefore, study of several animal species are ethically problematic now. *Drosophila* flies, apart from being cost effective and easy to handle, are ethically unproblematic. We all are aware of the fact that due to strict compliance of ethical guidelines, clinical trials for new drugs in India have reduced from 10,000 to just about one hundred during the last few years. *Drosophila* is emerging as a valuable model organism for clinical drug testing. Preliminary testing of the new drugs may be carried out faster in *Drosophila* than in mammalian models. *Drosophila* flies provide a whole organism testing facility and offer selection of drugs that are safer for subsequent testing in expensive mammalian models.

Cost effective model organism

It is important to respect all fields of research in biological sciences, but *Drosophila* as a eukaryotic model system has been successfully proved to be a low cost model system in advanced nations. For undergraduate students in biology, colleges at the United States of America lay greater emphasis on *Drosophila* laboratory

experiments and research endeavors to train students in a successful way. During the last several years, need for introducing *Drosophila* as a teaching and research model in India has been emphasized by our peers and national scientific academies, but still the ground reality is less than satisfactory. Here, we suggest ways to implement *Drosophila* as a practical teaching aid – a cost effective system for the benefit of student community.

Let us submit a possible way to do the same. There is general reluctance in the mind of teachers that breeding *Drosophila* flies in colleges is time consuming, cumbersome and not feasible. This leads to an opinion that this system cannot be implemented at colleges. Contrary to the general belief, culture medium of *Drosophila* is very economical and flies can be collected locally by simple methods. During favorable months when the ambient temperature ranges from 20 C to 25 C, flies can be easily cultured at room temperature. Excellent manuals which provide step- wise directions are available on internet, thus enabling interested individuals to improve their skills in handling *Drosophila* flies. The use of *Drosophila* system may aid in scientific conduct of research i.e. observations, hypothesis framing and testing. It also aids in mastering interpretation of the data obtained from experiments designed to address a biological query. Eventually, this would augment the existing protocol based practical learning to a broader understanding/gaining inquisitiveness in science through rigorous scientific analysis; thus improving the scientific

temper among the budding science students.

Learning Science using *Drosophila* in the classroom

Drosophila species are prevalent in all parts of the country and are easy to culture. Mutant strains of *Drosophila melanogaster* are well known and can stimulate interest among the young students to address questions related to almost all the branches of biology such as animal ecology, population studies, cytogenetics, cell culture, genetics to learn inheritance, gene mapping, life history, developmental biology, etc. Several of our national research institutes and central universities have well developed laboratories for conducting *Drosophila* research. However, there is an urgent need to adopt this model organism which is easy to culture across a large number of colleges and universities funded by both the government and private organizations.

In practical classes for undergraduate students, we often use metamorphosis of tadpoles to frogs and caterpillar to butterflies in order to illustrate life cycle of an organism. Such experiments involve many weeks to demonstrate this basic concept. However, with *Drosophila* flies, this can be done in a single day because all developmental stages (eggs, larvae, pupae and adults) are generally readily available. This also helps to distinguish the importance of short life cycle of *Drosophila* flies as compared with a vertebrate model like the frogs in a pond. Further, pupae can be isolated from vial and can be examined under stereo zoom

microscope to sex the pupae and to collect virgin flies required for genetic crosses.

Teaching biology in an inspiring way involves simple experiments with living organisms that are likely to reflect modern research in biomedical sciences. For example, simple observations to measure motor (neural) performance of young (one week) and old *Drosophila* flies (one month old) by a climbing test in independent scaled vials can reflect contemporary research in aging. This experiment is equivalent to comparing motor performance among human teenagers and elders. These simple experiments may explain the reasons for young people being capable of rigorous physical activity while elders/seniors prefer walking. This can be simulated among fruit flies by designing simple experiments, flies are tapped down and are given one minute to climb up any plastic or glass tube with a pasted paper slip with a scale in centimeters or inches. The data obtained from this can be used by the mentor to guide students in collecting and pooling of data, preparation of spread sheets and plotting of graphs using simple data analysis tools like 'Microsoft excel'. This would help the students to master the skills necessary for statistical training compared to the current practice of students plotting graphs from imaginary experiments and data points provided from experiments not conducted by them. Students can also apply standard statistical tests (means, SE, SD, etc.) manually or by using computers. Such simple experiments on *Drosophila* flies can inspire students to learn experimental design, reproducibility of data and sound interpretation.

Benefits of Drosophila flies for training students in hypothesis based research

Drosophila genome sequencing showed a remarkable gene similarity (more than two third) with humans. This is the main reason why fruit flies serve as a good model for human health and disease. In the modern society, people are becoming more health conscious due to stresses imposed by modern life style. We are confronted with numerous situations involving the use of health promoting food choices. In this respect, Drosophila flies provide a quick testing system to test effects of different types of foods and beverages on the longevity of Drosophila flies. We can also use these flies for testing the effects of genetically modified food products versus organically grown foods; effects of various types of herbal teas; and for judging the food preferences of flies, etc. These simple ideas can be tested by students to learn the scientific method of hypothesis based research. Such a training platform can arouse curiosity among students to do science with a cost effective living organism. The following list of simple experiments on fruit flies can help undergraduate students enjoy and arouse excitement in doing experiments relating to our health.

Simple experiments for classroom teaching--

- Effect of temperature on the life cycle of Drosophila.
- Food preferences in Drosophila.
- Variables contributing to create an effective fly bait.

- Effect of herbal extract on the longevity of Drosophila.
- Drosophila addiction to sugars and possible obesity effects.
- Effects of organic diet over GMO diet on Drosophila.
- Behavioral responses of Drosophila flies with respect to light, humidity and thermal gradients.
- Drosophila phenotypic adaptation to low and high temperatures.

Ecologically relevant field based studies using Drosophila as a model

Environmental conditions vary locally in different parts of the country. The local biotic factors such as temperature and relative humidity impose selective pressures on the fly populations and are reflected in changes on their behaviors such as stress adaptation and life history traits (fecundity, age of reproduction and life-span or longevity). Students can be encouraged to design simple experiments to study these aspects in field captured flies, if breeding facilities do not exist in their laboratories. Let us discuss a simple experiment on eco-behavioral variants (movers and sitters) on *Drosophila melanogaster*. The larvae (wandering stage before pupae formation) fall into two categories i.e. movers which tend to move away from their feeding site and pupate off the decaying fruit source (*in situ* on bait in the wild) while sitters remain confined to the fruit. This is a simple field ecology observation. Students can study differences between these variants in response to changes in abiotic conditions and/or food shortage verses abundance. Such experiments are likely to demonstrate genetic basis of food related behavior in *D.*

melanogaster. Another field based study can involve effects of diurnal changes in relative humidity on the mating behavior and fecundity of various *Drosophila* species due to co-occurring changes in the temperature. Such simple field based experiments can help students understand queries regarding oviposit site preference among different *Drosophila* species.

Drosophila as a potential model in field Biology

The Indian subcontinent (8°-33°N) has large geographical range with diverse climatic conditions and seasonality that favors adaptations of specific phenotypic variations related to different eco-physiological and eco-behavioral traits. For research related to climate change, *Drosophila* species offer suitable study material in temperate as well as tropical regions of the world, but such research efforts remain biased in favor of few insect taxa such as butterflies in temperate regions. In the circum-tropical regions of the world *Drosophila* species richness is the highest. India offers excellent opportunities to those who intend to explore field biology of diverse life forms. Despite the occurrence of numerous (thousands) generalist, cold and warm adapted species of *Drosophila*, there had been lesser emphasis on the field based ecological studies involving *Drosophila*. This can also be due to reluctance on the part of ecologists to adapt *Drosophila* as a model system for studying field based ecological genetics. Currently, it is a major challenge and a cause for concern to integrate laboratory experiments with field

Biology. In contrast, we are inclined to devote more time and energy on costly kit based molecular biology experiments.

Importance of Drosophila in Biomedical research

Let us discuss why *Drosophila* flies are being used for biomedical research. A smaller genome of *Drosophila* ($2n=8$; 14000 genes) is well known, but limited (or very less) genetic redundancy of genes in *Drosophila* is the real catch as compared to the mouse model. Genetic manipulations involving mutations in mice are sometimes less informative because many genes of interest (for human diseases) are redundant. In contrast, *Drosophila* possesses single copy genes which after mutation tend to exhibit mutant phenotypes. Furthermore, a large number of known mutant phenotypes in *Drosophila* backed by their genotypes are available. It is also easy to induce desired mutations in genes through modern molecular techniques.

Drosophila flies can help in understanding how nerve cells, action potentials and synapses constitute the nervous system function. Simple experiments with temperature sensitive mutant strains of *Drosophila melanogaster* when warmed to 37 C for few minutes (~40 minutes) show signs of paralysis reflecting the role of synapses in body coordination. Experiments on *Drosophila* mutant flies (for epilepsy) can be induced into seizures just by shaking flies in a vial. Many mutant flies can illustrate genetic basis of sexual and non-sexual behavioral patterns.

Drosophila flies help in understanding human nervous system

In humans, cable like extensions of neurons called axons grow up to a meter and transmit nerve impulses to other neurons via synapses. During development, axons grow along particular pathways and form circuits that control our body and coordinate our behavior. During normal ageing, we lose about fifty per cent of our axons i.e. become faulty, but in neurodegenerative diseases this rate is greatly accelerated and we are likely to develop neurodegenerative diseases such as Alzheimer's or Parkinson's diseases. In western nations with more ageing populations this is greater cause of concern. The key components of axons are microtubules and their binding proteins. Mutations in genes encoding microtubule binding proteins often cause neurodegenerative diseases in older populations. The neurons from embryos of Drosophila flies are grown in culture to study axon development in normal as well as mutant flies. Drosophila provides faster results along with ease for looking at the effects of many mutant genes affecting neuron system organization. Therefore, Drosophila flies are being increasingly used to understand structural and functional aspects of nervous system.

Role of Drosophila in studying neurodegenerative diseases

Since 1998, Drosophila flies have been used to study a wide range of human neurodegenerative diseases such as Alzheimers and Parkinsons diseases, etc. Between flies and humans, many key features of the development and functions

of nervous system remain similar. Sleep patterns of Drosophila flies are similar to humans. Flies deprived of sleep for one day, try to make up during the next day. Flies and humans take in information throughout the day which affects the neural synapses leading to saturation and induces craving for sleep. Nerve cells (neurons) are made up of a body and a tail like structure called axon. These axons are the cables that wire the brain. These are actively maintained by several physiological mechanisms to prevent nerve degeneration. The mechanisms maintaining the axons in a physiological state are being investigated among fruit flies. Axon swelling are frequently found in ageing brains. This finding correlates to the loss of 50% of axons in ageing population. Harmful axon swellings are likely to lead to nerve degeneration that causes paralysis. Experiments using Drosophila flies are being performed to mimic several human neurodegenerative diseases and gain understanding of their mechanisms. Thus, biomedical research is greatly dependent on Drosophila flies to find answers to questions which pose difficulties in pursuing on mammalian systems.

Drosophila provides a model for Regenerative Biology

Regenerative capacity of Drosophila imaginal discs is well known. It has been deduced that future identity of imaginal discs are not fixed until the initiation of cellular differentiation. Thus, the cellular pathways which are activated during early development of Drosophila seem similar during tissue regeneration. Studies on Drosophila embryos have contributed a

great deal in understanding molecular pathways that regulate stem cell activity. It was first demonstrated in *Drosophila* that cells undergoing programmed cell death (apoptosis) in response to damage or stress produce molecular signals which activate stem cell proliferation to initiate tissue regeneration. Therefore, use of *Drosophila* flies holds great promise for regenerative biology and medicine.

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References:

- Brookes M. (2001) Fly: the unsung hero of twentieth century sciences, Ecco, USA (<https://www.worldcat.org/title/fly-the-unsung-hero-of-twentieth-century-science/oclc/46565106>).
- Demerec M and Kaufman B P. (1973) *Drosophila* – a guide. Carnegie Institute Washington publication, Washington, DC, USA.
- Drosophila* information service (link: <http://www.ou.edu/journals/dis/>)
- Flybase (link: <http://flybase.org/>)
- Kohler R E. (1994) *Lords of the fly: Drosophila genetics and the experimental life*, University of Chicago Press, Chicago.
- Markow T A and O'Grady P M. (2006) *Drosophila* – a guide to species identification and use. Elsevier. (Available as e-book)
- Muller H J. (1928) The production of mutations by X-Rays. *Proc Natl Acad Sci USA* 14: 714-726.
- Ranganath HA. (1999) Teaching and learning genetics with *Drosophila*. Part 1, *Drosophila* as a model system. *Resonance* 4(2): 48-52. (link: <http://repository.ias.ac.in/41679/>)
- Ranganath HA and Tanuja M T. (1999) Teaching and learning genetics with *Drosophila*. Part 2, Mutant phenotypes of *Drosophila melanogaster*. *Resonance* 4 (9): 95-104. (link: <http://repository.ias.ac.in/41704/>)
- Ranganath HA and Tanuja M T. (1999) Teaching and learning genetics in *Drosophila*. Part 3; Pattern of inheritance of autosomal and sex linked genes/characters. *Resonance* 4(10): 78-87. (link :<http://repository.ias.ac.in/41694/>)
- Ranganath HA and Tanuja M T. (2000) Teaching and learning genetics in *Drosophila*. Part 4, Patterns of inheritance of characters when there is interaction of genes or linkage of genes. *Resonance* 5(7): 59-70. (link: <http://repository.ias.ac.in/41705/>)
- Strickerger M W. (1962) *Experiments in genetics with Drosophila*, Wiley and sons, NY. (Available as e-book)
- The Nobel Prize in Physiology or Medicine (1933) http://nobelprize.org/nobel_prizes/medicine/laureates/1933/
- The Nobel Prize in Physiology or Medicine (1946) http://nobelprize.org/nobel_prizes/medicine/laureates/1946/
- The Nobel Prize in Physiology or Medicine (1995) http://nobelprize.org/nobel_prizes/medicine/laureates/1995