ever, they suggest that even if chaos does not appear in natural populations, human actions may push a population into chaos.

"Although the evidence does not seem to support the notion that natural ecosystems exhibit chaotic dynamics," they write, "we should emphasize that all self-replicating systems possess the seeds of chaos. . . . As all biological systems contain positive feedback processes, it is always possible to force them into the chaotic regime by increasing the value of the positive feedback parameter(s); for example, increasing growth rates through biotechnology, stimulating economic growth, etc." Scientists could look for chaos in insect populations that are being treated with pesticides, for example.

May argues that the study of chaos in population biology indicates ecologists may have been seeing mostly what they expected to see. The assumptions they make about what the systems were doing have influenced the way they collect data: "You can create yourself an imaginary world—get pseudo-data and then apply conventional techniques—but the conventional techniques cannot determine the important factors."

May suggests that ecologists "may have to go back to the drawing board" in order to get reliable data.

The study of nonlinear dynamics in population biology has implications for other fields too, May notes. "Populations aren't just creatures with four or six legs, or viruses and bacteria," he says. Population biology models can be used to study individual cells in an organism, for example, or the components of the immune system. He and Imperial College mathematician Roy Anderson have done just this with a model of how the AIDS virus behaves when it infects the human immune system.

In this model, T4 lymphocytes and AIDS viruses have both a host-pathogen relationship, where the virus infects the immune cells, and a predator-prey relationship, where the T4 cells prey on the virus via the production of B cells and antibodies specific to the AIDS virus. This arrangement, as Anderson points out, implies the system is nonlinear and thus has the capacity for oscillatory and even chaotic behavior.

"The real question, of course, is how relevant it is to practicality," Anderson says, but he adds, "There is some empirical evidence of this type of nonlinear behavior in the immune system." He and May say they plan to publish evidence for chaos in AIDS-infected immune systems in a coming report. It might be that the easiest place to find chaotic populations is not the forest or the plains or the ocean, but in the jungle of the human body. ■ ROBERT POOL

Troubles Encountered in Gene Linkage Land

Why are published data from gene linkage studies of four different mental disorders so difficult to replicate?

A DISCOURAGING REALITY is emerging from the quest to identify chromosome locations for genes that cause various human diseases. It is that the ideal scenario for doing gene linkage studies rarely exists—particularly for mental illnesses. The result is that when one group of researchers reports that a disease-associated gene is located on a specific region of a chromosome, other investigators frequently cannot substantiate the finding. No one is claiming to have found the disease genes themselves; at this point only their chromosome locations are in question.

"The only way to prove heterogeneity is to localize or isolate all the different genes. And that would be tremendously difficult. . . ."

Within the past few years, for example, researchers have reported that a gene locus associated with major depressive disorders is on the X chromosome, a gene for familial Alzheimer's is on chromosome 21, a gene that predisposes Old Order Amish to manic depression is on chromosome 11, and, most recently, that a "susceptibility locus" for schizophrenia is on chromosome 5. But other research groups are unable to confirm these gene locations in their studies of other families with the same disorders.

"The major problem [in this research area] is all the non-replications," says Elliot Gershon of the National Institute of Mental Health (NIMH) in Bethesda, Maryland. "The question is why." Researchers suggest several complicating factors: multiple causes of what appears to be the same mental disorder; the lack of large family pedigrees and large numbers of pedigrees; misdiagnosis of affected relatives; inappropriate statistical methodology; and the sheer complexity of mental illnesses.

One disorder that affects brain function and behavior and appears to have an undisputed chromosome location is Huntington's chorea. Huntington's is a rare neurodegenerative disorder caused by a dominant gene located on the short arm of chromosome 4, and it has become the gold standard for gene linkage analysis.

"Huntington's is very clear cut," says James Gusella of Massachusetts General Hospital in Boston. "You find an individual with the classical symptoms and you know that these symptoms are caused by the gene." In addition, researchers can trace the pattern of the gene's inheritance because affected family members usually show signs of the disease before the age of forty. "That's the opposite of other neuropsychiatric disorders," says Gusella.

For most mental illnesses it is still not well established that a genetic cause even exists. Diseases such as schizophrenia and major affective (mood) disorders often tend to run in families, but that does not necessarily mean they are genetically caused. So, in some cases the current search is for genes that may predispose an individual to a particular mental disorder rather than cause it directly, thus adding another level of obscurity to the process.

Major affective disorders such as depression are prime examples. "There are now a number of studies in the literature [including his] that have reported linkage on the X chromosome in major depressive illness and a number of other studies that have reported something different," says Miron Baron of Columbia University College of Physicians and Surgeons and the New York State Psychiatric Institute. The discrepancies could result from any of several factors, he suggests. One, for instance, is genetic heterogeneity, meaning that the same group of disorders has different genetic causes. Another is misdiagnosis of certain people in the families under study. The diagnostic criteria for mood disorders keep changing and each group of researchers tends to use slightly different criteria when they define the affected people in their study.

Given these vagaries, it may not be surprising that the data from different research groups suggest different chromosome locations for a gene associated with major de-

pression. Baron, for example, places the disease gene close to the gene for color blindness, on the long arm of the X chromosome. Other researchers have reported that the gene is at the opposite end of the X chromosome. Gershon and his colleagues do not find evidence for X-linkage in their families at either end of the chromosome.

Despite the discrepancies, most researchers still contend that depression, particularly manic depression, has a genetic basis. The notion was fueled by a 1987 report by Janice Egeland of the University of Miami School of Medicine in Florida, David Housman of Yale University School of Medicine in New Haven, Connecticut, and their colleagues. They reported that a dominant gene at the tip of the short arm of chromosome 11 conferred "a strong predisposition to manic depressive disease" (*Nature*, 26 February, 1987, page 783). In the same issue, however, two other reports failed to find the same linkage (pages 805 and 806).

Also, recent studies of families with Alzheimer's do not confirm that the disease gene is on the region of chromosome 21 reported by Gusella and his colleagues (*Science*, 20 February 1987, page 885). And new studies, some still unpublished, fail to find that a gene predisposing people to schizophrenia is on chromosome 5 (*Science*, 18 November 1988, page 1009). Do the discrepancies in data mean that researchers are wrong, or do they point to evidence of genetic heterogeneity?

"You shouldn't come to the conclusion that it's heterogeneity if you haven't replicated someone else's data," says Gershon. The first step is to confirm the linkage in one study. Then researchers have to do specific statistical tests to show that a particular disease has multiple genetic causes.

The ultimate test, however, is isolating the actual disease-causing genes. "The only way to prove heterogeneity is to localize or isolate all the different genes," says Gusella. "And this would be tremendously difficult with current approaches."

Some investigators are now suggesting a revision in the statistical criteria used to establish linkage of a disease gene to a particular chromosome. Linkage analysis depends on the use of chromosome markers that are thought to be close to the disease gene. The markers are either RFLPs (restriction fragment length polymorphisms), which are short, detectable stretches of DNA that have no known function, or other genes of known function. Researchers "score" how often the symptoms of disease occur together with its markers. Currently, a logarithmic ratio (called a lod score) of 3 is taken as evidence for linkage. It means that the likelihood is 1000 to 1 that the pattern of the disorder and the markers in a family pedigree result from gene linkage rather than from random distribution. It is a measure that the disease gene is linked to, and therefore physically close to, the marker under study. Gershon thinks that a higher lod score should be required to establish linkage in most psychiatric disorders because of genetic heterogeneity or variation in the degree to which someone is affected.

Kenneth Kidd of Yale University School of Medicine raises another fundamental issue about methodology. "A linkage analysis cannot be done without specifying a mode of inheritance, without specifying that a single gene causes the disease, without specifying how penetrant the gene is," he says. And for neuropsychiatric disorders this information is simply not known. Instead, researchers make assumptions about these parameters before they begin to do the statistical analysis of family pedigree data. "We are trying to associate a known gene marker with an unknown, hypothesized gene," Kidd says. "And the results we get are correct or incorrect to the degree that our assumptions are correct."

Everyone agrees that more data are required to resolve present inconsistencies. Ideally, researchers will be able to find several, large, multigenerational families that share a common genetic defect and exhibit similar behavioral symptoms. Failing that, they will collect data from many smaller families. The task has recently been undertaken at NIMH in its Genebank initiative.

Researchers who seek the chromosome location of a disease-causing gene ultimately want to find the gene itself and somehow correct the defect. Whether they ultimately accomplish this by gene therapy or by improved treatment remains to be seen. In either case, the overall goal now seems to be feasible. ■ **DEBORAH M. BARNES**

More Math Means More Money

If earning potential is your criterion in picking a spouse, a good place to start is by counting your lover's college math credits.

There is a positive correlation between the number of mathematics courses a person takes and earnings in the first decade of employment, according to two researchers at the U.S. Department of Education. Clifford Adelman and Nabeel Alsalam have analyzed the mathematics component of a data set known as the National Longitudinal Study, which tracked a sample of young people from high school graduation in 1972 to their early thirties in 1986.

Adelman and Alsalam presented their findings at a symposium on mathematics education and U.S. industrial competitiveness, sponsored by the Mathematical Sciences Education Board of the National Research Council. Employers recognize the importance of algorithmic and algebraic thinking on the job, Adelman says. "Our study shows how many people are prepared to do that."

Not surprisingly, students who took more mathematics in high school or college earned substantially more than others in their first decade of employment, Adelman and Alsalam find. The relationship is particularly strong for men. It is strong for women as well, but women studied substantially less mathematics after high school, and at more basic levels. The best predictor of high income is earned credits in calculus and advanced mathematics. "Baldly stated, more math means more money," the study says.

It is somewhat surprising, though, how little mathematics the sample of students took in college. Among those earning bachelor's degrees, 62% earned six or fewer math credits (three credits roughly equal a one-semester course)—and 21% studied no math at all, even when computer science and statistics courses taught in other departments are included.

On the other hand, there seems to be little relationship between the amount of mathematics studied in high school and the number of math credits earned in college. Some of this is due to colleges filling a void: 30% of all earned college math credits were in precollegiate-level courses. (The figure is 50% for 2-year colleges and 22% for 4-year colleges.) A higher percentage of business and education majors studied precollegiate mathematics than did students majoring in other fields.

The National Longitudinal Study consists of data on a sample of 22,500 students who were high school seniors in 1972, with follow-up survey data from 1973, 1974, 1976, 1979, and 1986, and a postsecondary transcript sample for 12,600 members of the original sample who attended college or other institutions at any time up to February 1984. The 1986 survey contained career data for 12,800 members of the original survey, with 7,500 of these overlapping with the transcript sample. Mathematics is the first course area to be analyzed from the study. ■ **BARRY A. CIPRA**

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