Mount Holyoke offers the following departmental and interdisciplinary majors:

- Africana Studies
- Ancient Studies
- Anthropology
- Architectural Studies
- Art History
- Art Studio
- Asian Studies
- Astronomy
- Biochemistry
- Biological Sciences
- Chemistry
- Classics
- Computer Science
- Critical Social Thought
- Dance
- East Asian Studies
- Economics
- English
- Environmental Studies
- Film Studies
- French
- Gender Studies
- Geography
- Geology
- German Studies
- Greek
- History
- International Relations
- Italian
- Latin
- Latin American Studies
- Mathematics
- Medieval Studies
- Middle Eastern Studies
- Music
- Neuroscience and Behavior
- Philosophy
- Physics
- Politics
- Psychology
- Psychology and Education
- Religion
- Romance Languages and Cultures
- Russian and Eurasian Studies
- Russian Literature and Culture
- Self-designed Studies
- Sociology
- South Asian Studies
- Spanish (Hispanophone Studies)
- Statistics
- Theatre Arts